

Helsinki, 04 June 2024

Addressee(s)

Registrant(s) of tert-butyl perbenzoate as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision

26 April 2022

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

Substance name: tert-butyl perbenzoate

EC/List number: 210-382-2

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 **9 September 2027**.

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

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

1. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) in rats, oral route, specified as follows:

- Ten weeks pre-mating 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 in request 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); and
- Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation.

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

The reasons for the request(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.

Authorised¹ under the authority of Mike Rasenberg, Director of Hazard Assessment

Appendix 1: Reasons for the request(s)

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 request(s)

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Reasons related to the information under Annex X of REACH**1. Extended one-generation reproductive toxicity study**

- 1 An extended one-generation reproductive toxicity (EOGRT) study (OECD TG 443) is an information requirement under Annex X, Section 8.7.3. Furthermore Column 2 defines the conditions under which the study design needs to be expanded.

1.1. Information provided

- 2 ECHA understands that you have adapted this information requirement by using Annex XI, Section 1.2. (weight of evidence) based on the following:
- (i) Screening for reproductive/developmental toxicity study (2019) with the Substance
 - (ii) Screening for reproductive/developmental toxicity study (2004) with the analogue substance Tertiary butyl alcohol (TBA), EC: 200-889-7
 - (iii) Multi-generation reproductive toxicity study (1960) with the analogue substance benzoic acid, EC: 200-618-2
 - (iv) Two-generation reproductive toxicity study (1997) with the analogue substance methyl tertiary-butyl ether, EC: 216-653-1
 - (v) Sub-chronic (90-day) repeated dose toxicity study in rat (1992) with the Substance
 - (vi) Sub-chronic (90-day) repeated dose toxicity study in mice (1992) with the Substance
 - (vii) Sub-chronic (90-day) repeated dose toxicity study in rat (1988) with the analogue substance benzyl acetate, EC: 205-399-7
 - (viii) Sub-chronic (90-day) repeated dose toxicity study in mice (1988) with the analogue substance benzyl acetate, EC: 205-399-7
 - (ix) Prenatal developmental toxicity study in rat (2014) with the Substance
 - (x) Prenatal developmental toxicity study in rabbit (2019) with the Substance
 - (xi) Basic toxicokinetic study (1992) with the Substance
 - (xii) QSAR Toolbox DART Scheme v.1.2; Derek Nexus v.6.0.1; v.2.1.7; VEGA - developmental/Reproductive Toxicity library (PG), v.1.0.0) – no alerts for reproductive toxicity.

- 3 You state that *"Based on this information it can be concluded that the weight of the evidence shows that t-BP and its degradation products have no effect on fertility and no further testing with t-BP to investigate the effect of this substance on fertility is warranted"*.

1.2. Assessment of the information provided

- 4 Annex XI, Section 1.2. states that there may be sufficient weight of evidence from several independent sources of information enabling, through a reasoned justification, a conclusion on the information requirement, while the information from each single source alone is insufficient to fulfil the information requirement.
- 5 The justification must have regard to the information that would otherwise be obtained from the study that must normally be performed for this information requirement.
- 6 According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide sufficient weight to conclude on the corresponding information requirement.

1.2.1. Lack of robust study summaries for some sources of information

- 7 Annex XI, Section 1.2. requires that whenever weight of evidence is used adequate and reliable documentation of the applied method must be provided. Such documentation must include a robust study summary for each source of information used in the adaptations.
- 8 A robust study summary must provide a detailed summary of the objectives, methods, results, and conclusions of a full study report providing sufficient information to make an independent assessment of the study (Article 3(28)).
- 9 In addition, for weight of evidence adaptations, the robust study summary must clearly indicate which key parameters of the study normally required for the information requirement are investigated in the study.
- 10 In your justification document you refer to 90-day repeated dose toxicity feeding studies in rats and mice (sources of information (vii) and (viii)), performed with the analogue substance benzyl acetate (Morrissey et al., 1988), stating that *"the endpoints that are missing from the four-generation study with benzoic acid are available for benzyl acetate"*.
- 11 The above-described sources of information do not contain detailed summaries of the objectives, methods, results, and conclusions of the respective studies the information refers to. Therefore, it is not possible to make an independent assessment of the relevance of the studies including whether any of the key parameters of the studies normally required for the information requirement are investigated in the respective studies.
- 12 Consequently, you have failed to provide robust study summaries as required by Annex XI, Section 1.2 for these sources of information. The sources of information (vii) and (viii), cannot be considered in the assessment of your weight of evidence adaptation because it is not possible to independently confirm the relevance and reliability of the information provided.
- 13 Beside these critical deficiencies, ECHA has also assessed the other aspects of your adaptation.
- 14 Information that can be used to support weight of evidence adaptation for the information requirement of Annex X, Section 8.7.3 includes similar information that is produced by the OECD TG 443. The OECD TG 443 requires the study to investigate the following key parameters: 1) Sexual function and fertility; 2) Toxicity to the offspring and 3) Systemic toxicity.

1.2.2. Aspect 1) sexual function and fertility

- 15 Sexual function and fertility on both sexes must include information on mating, fertility, gestation (length), maintenance of pregnancy (abortions, total resorptions), parturition, lactation, organ weights and histopathology of reproductive organs and tissues, oestrous cyclicity, sperm count, sperm analysis, litter sizes, nursing performance and other potential aspects of sexual function and fertility.
- 16 The sources of information (ix) and (x) are reported as prenatal-developmental toxicity studies, therefore, they do not provide relevant information on this aspect.
- 17 The source of information (xii) is reported as QSARs which do not provide relevant information on any of the key elements of aspect 1).
- 18 Sources of information (vii) and (viii) that are lacking robust study summary cannot be considered as contributing for this aspect with any relevant and reliable information.
- 19 Sources of information (v) and (vi) are sub-chronic (90-day) repeated dose toxicity studies, that provide relevant information on organ weights and histopathology of reproductive organs and tissues of both male and female animals, however, they do not inform on

mating, fertility, gestation (length), maintenance of pregnancy (abortions, total resorptions), parturition, lactation, litter sizes, nursing performance and other potential aspects of sexual function and fertility. Therefore, these sources provide partially relevant information on this aspect.

- 20 Source of information (iii) is reported as multi-generation reproductive toxicity study, that provides relevant but very limited information for maintenance of pregnancy, organ weight and histopathology of testes, but do not provide information on the mating procedure, oestrous cyclicity, sperm parameters, reproductive function, and performance, organ weights and histopathology of the uterus, ovaries, epididymides, prostate, seminal vesicle.
- 21 The sources of information (i), (ii) and (iv) provide relevant information on all key elements of aspect 1).
- 22 However, the sources of information have deficiencies affecting the reliability of their contribution to the weight of evidence adaptation.

1.2.2.1 Reliability of the contribution of the information on analogue substances methyl tertiary-butyl ether and benzyl acetate (studies (iv), (vii) and (viii))

- 23 You intend to predict the relevant property of the Substance from the information obtained with analogue substances in a read-across approach as part of your weight of evidence adaptation. For this information to be considered reliable, it would have to meet the requirements for Grouping of substances and read-across approach.
- 24 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.
- 25 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).
- 26 With the sources of information (iv), (vii) and (viii) you predict the properties of the Substance from information obtained from the following analogue substances:
- source substance 1: methyl tertiary-butyl ether (MTBE, EC: 216-653-1)
 - source substance 2: benzyl acetate (EC: 205-399-7).
- 27 You provide the following reasoning for the prediction of toxicological properties: You state that the Substance *"is extremely rapidly degraded in rat and human blood" as well as "[...] in contact with liver enzymes"* to benzoic acid and t-butanol. You also provide toxicokinetic study (xi) to prove it.
- 28 Further, you reason the use of source substance 1 *"Based on metabolism studies which demonstrate that MTBE is metabolized to tertiary butyl alcohol in vivo, data from the two-generation study with MTBE is relevant for the evaluation of the reproductive and developmental toxicity of tert-butyl alcohol"* and for source substance 2 – *"benzyl acetate, a chemical that is metabolized completely to benzoic acid"*.
- 29 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 substances.
- 30 We have identified the following issue(s) with the prediction(s) of toxicological properties:

1.2.2.1.1 *Missing supporting information on the formation of common compounds and on the impact of non-common compounds for source substances 1 and 2*

- 31 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(s) (Guidance on IRs and CSA R.6, Section R.6.2.2.1.f.).
- 32 Supporting information must include toxicokinetic information on the formation of the common compounds and information on the impact of exposure to parent compounds on the prediction.
- 33 As indicated above, your read-across hypothesis is based on the (bio)transformation of the Substance and the source substances 1 and 2 to common compounds. In this context, information characterising the rate and extent of the (bio)transformation of the Substance and of the source substances is necessary to confirm the formation of the proposed common (bio)transformation product and to assess the impact of the exposure to the parent compounds.
- 34 In addition, exposure to the Substance and the source substances may also lead to exposure to other compounds than the common compound of interest. The impact of exposure to these non-common compounds on the prediction of properties of the target needs also to be assessed, to ensure that a reliable prediction can be made.
- 35 In your justification document you indicate that metabolism studies “*demonstrate that MTBE [source substance 1] is metabolised to tertiary butyl alcohol in vivo*” and that “*benzyl acetate [source substance 2] [...] is metabolized completely to benzoic acid*”.
- 36 However, you have not provided any experimental toxicokinetic information with the source substances to support your claims. Further, you have not provided any information to characterise the exposure to the non-common compounds (parent compounds). No experimental data or other adequate and reliable information addressing the impact of exposure to these non-common compounds on the prediction of the properties of the Substance is included in your documentation.
- 37 In the absence of such information, you have not established that a reliable prediction of the property under consideration of the Substance can be derived on the basis of your read-across hypothesis. Therefore, you have not provided sufficient supporting information to scientifically justify your read-across hypothesis

1.2.2.2 *Reliability of information provided via inhalation route for source of information (iv)*

- 38 To allow conclusive determination of a particular toxicological property for systemic toxicity, the choice of the route of administration must ensure that systemic availability (internal dose) of the substances is maximised.
- 39 Annex X, section 8.7.3. of REACH specifies that the reproductive toxicity studies should be conducted via the “most appropriate route of administration, having regard to the likely route of human exposure” and the ECHA guidance on IRs and CSA R 7.a. (R.7.6.2.3.2., Stage 4.1., point iv) stipulates: “According to the test methods for reproductive toxicity which focus on the detection of reproductive hazards, the oral route (gavage, in diet, or in drinking water) is the “default” route, except for gases”.
- 40 Study (iv) is conducted via inhalation route for the source substance 1 which is not a gas.

41 The information is not provided via the default oral route that is assumed to maximise the systemic availability of the substances. You have not provided any information such as toxicokinetic information to demonstrate that the source substance 1 administered via inhalation is absorbed, distributed in the body, and become systemically available in the same way as would be expected after administration via the default oral route, and will not underestimate the hazard.

42 Therefore, you have not demonstrated that the systemic availability of the source substance 1 would be maximised via the non-default inhalation route and the information from study (iv) via inhalation route does not reliably contribute to a weight of evidence intended to identify the reproductive toxicity properties of the Substance.

1.2.2.3 Reliability of the contribution of the studies (i) –(iii) with regard to aspect 1)

Investigations/specification in an extended one-generation reproductive toxicity study (OECD TG 443) include, among others:

- a) 20 pregnant females are included for each test and control group;
- b) at least three dose levels and a concurrent control are tested;

43 In sources of information (i) and (ii) that are reported as screening for developmental toxicity studies (OECD TG 421), 10 and 12 pregnant females, respectively (i.e., less than 20 pregnant females) are included in each group.

44 In the source of information (iii), reported as a multi-generation reproductive toxicity study:

- a) there were 20 animals in each dose group and control group, however it is unclear whether all 20 females were pregnant;
- b) only two dose levels were tested, and no concurrent controls were included

45 Based on the above, the information provided does not cover the specifications, required by the OECD TG 443; in particular, the statistical power is not equivalent to the OECD TG 443. Therefore, the reliability of the contribution of the results obtained from these studies to the weight of evidence is limited.

1.2.3. Aspect 2) toxicity to the offspring

46 Toxicity to offspring must cover information on deaths before, during or after birth, growth, external malformations, clinical signs, sexual maturity, oestrous cyclicity, organ weights and histopathology of reproductive organs in adulthood and other potential aspects of toxicity to offspring.

47 Sources of information (vii) and (viii) that are lacking robust study summaries cannot be considered as contributing for this aspect with any relevant and reliable information.

48 Sources of information (v), (vi), (ix), (x) and (xiii) do not provide relevant information for this aspect.

49 The sources of information (i), (ii) provide relevant information on some of the key elements (deaths before, during or after birth, growth, external malformations, clinical signs, sexual maturity, oestrous cyclicity), however, they do not report on organ weights and histopathology of reproductive organs in adulthood and other potential aspects of toxicity to offspring (e.g. anogenital distance in pups and presence and number of nipples/areolae in male pups).

50 The source of information (iii) provides very limited information on histopathology of testis, only examined in the third generation of animals on week 16. However, it does not provide information on organ weights and histopathology of reproductive organs in F1 and F2, as

well as no information on deaths before, during or after birth, growth, external malformations, clinical signs, sexual maturity, oestrous cyclicity in adulthood and other potential aspects of toxicity to offspring.

51 The source of information (iv) provides relevant information on aspect 2).

52 However, these sources of information have deficiencies affecting their reliability, as explained above in Sections 1.2.2.1, 1.2.2.2, 1.2.2.3 under aspect 1) - they equally apply here.

1.2.4. Aspect 3) systemic toxicity

53 Systemic toxicity must include information on clinical signs, survival, body weights, food consumption, haematology (full-scale), clinical chemistry (full-scale), organ weights and histopathology of non-reproductive organs (full-scale) and other potential aspects of systemic toxicity in the parental P and F1 generation up to adulthood.

54 Sources of information (vii) and (viii) that are lacking robust study summaries cannot be considered as contributing for this aspect with any relevant and reliable information.

55 The source of information (xii) does not provide relevant information on any of the key elements of aspect 3).

56 The sources of information (iii), (v) and (vi) provide relevant information on some of the key parameters, however, they do not cover the haematology (full-scale) and clinical chemistry (full-scale). In addition, source (iii) does not provide information on organ weights and histopathology of non-reproductive organs for P0 and F1.

57 The sources of information (ix) and (x) provide limited information on maternal toxicity (clinical signs, survival, body weights, food consumption) but they do not cover all the other key elements of aspect 3). Therefore, they provide partially relevant information on this aspect.

58 The sources of information (i), (ii) and (iv) provide relevant information on all key elements of aspect 3).

59 However, these sources of information have deficiencies affecting their reliability, as explained above in Sections 1.2.2.1, 1.2.2.2, 1.2.2.3 under aspect 1) - they equally apply here.

1.2.5. Conclusion on the weight of evidence

60 Taken together, the sources of information as indicated above, provide relevant information on the three aspects.

61 However, the reliability of the contribution of the information is hampered by:

- a) the use of information on analogue substances (studies (iv) and (vii) and (viii)).
- b) limitations of the study design and/or reporting listed above, directly affecting the reliability of the results of studies (i) - (iv) and their contribution to the weight of evidence adaptation.

62 Therefore, it is not possible to conclude, based on any source of information alone or considered together, on the information requirement for the extended one-generation reproductive toxicity.

63 Based on the above, your adaptation is rejected.

64 Therefore, the information requirement is not fulfilled.

1.3. Study design

1.3.1. Species and route selection

- 65 According to the test method OECD TG 443, the rat is the preferred species. Therefore, the study must be conducted in the rat.
- 66 As the Substance is a liquid, the study must be conducted with oral administration of the Substance (Annex X, Section 8.7.3., Column 1).

1.3.2. Pre-mating exposure duration

- 67 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.
- 68 Ten weeks pre-mating exposure duration is required to obtain results adequate for classification and labelling and/or risk assessment. There is no substance specific information in the dossier supporting shorter pre-mating exposure duration (Guidance on IRs and CSA, Section R.7.6.).
- 69 Therefore, the requested pre-mating exposure duration is ten weeks.

1.3.3. Dose-level setting

- 70 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; introductory part of Annex IX/X to REACH; Annex I, Section 1.0.1. to 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.
- 71 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; Annex I, Section 3.7.2.4.4. of the CLP Regulation) or severe suffering such as persistent pain and distress (OECD GD 19, paragraph 18) in the P0 animals.
- 72 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.
- 73 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.

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

75 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.

1.3.4. Cohorts 1A and 1B

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

1.3.4.1. Histopathological investigations in Cohorts 1A and 1B

77 In addition to histopathological investigations of cohorts 1A, 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) if

- the results from Cohort 1A are equivocal,
- the test substance is a suspected reproductive toxicant or
- the test substance is a suspected endocrine toxicant.

1.3.4.2. Splenic lymphocyte subpopulation analysis

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

1.3.5. Investigations of sexual maturation

79 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.

1.3.5.1. Further expansion of the study design

80 The conditions to include the extension of Cohort 1B are currently not met. Furthermore, no triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) and Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B, Cohorts 2A and 2B and/or 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 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.

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

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 (2023).

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

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 23 August 2022.

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

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

ECHA took into account your comments and did not amend the request(s) but amended the deadline.

In your comments on the draft decision, you requested an extension of the deadline to provide information from 30 to 36 months from the date of adoption of the decision as you consider that *"30 months could not be enough, as we do not know the demands at the CRO's in the coming years"*. ECHA notes that due to a clerical error, the deadline in the initial draft decision was 30 months whereas it should have been 36 months. Therefore, ECHA has modified the deadline to 36 months.

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;
- 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
████████████████████	████████████████████	██████
████████████████████	████████████████████	██████

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

(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

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>).