~~Confidential~~

Helsinki, 20 February 2024

Addressee
Registrant of DPTU_Joint_Submission as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
18/12/2020

Registered substance subject to this decision ("the Substance")
Substance name: 1,3-diphenyl-2-thiourea
EC/List number: 203-004-2

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 the deadline of ***1 March 2027***.

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

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

1. 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:
   - Ten 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 and 1B (Reproductive toxicity);
   - Cohorts 2A and 2B (Developmental neurotoxicity); and
   - Cohort 3 (Developmental immunotoxicity).

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

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

3. Simulation testing on ultimate degradation in surface water (Annex IX, Section 9.2.1.2.; test method: EU C.25./OECD TG 309) at a temperature of 12°C.

4. Identification of degradation products (Annex IX, 9.2.3.; test method: EU C.25/OECD TG 309)

The reasons for the decision(s) are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The addressees of the decision and their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

You are only required to share the costs of information that you must submit to fulfil your information requirements.

How to comply with your information requirements

To comply with your information requirements, you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also **update the chemical safety report, where** relevant, including any changes to classification and labelling, based on the newly generated information.

You must follow the general requirements for testing and reporting new tests under REACH, see Appendix 4.

Appeal

This decision, when adopted under Article 51 of REACH, may be appealed to the Board of Appeal of ECHA within three months of its notification to you. Please refer to http://echa.europa.eu/regulations/appeals for further information.

Failure to comply

If you do not comply with the information required by this decision by the deadline indicated above, ECHA will notify the enforcement authorities of your Member State.

Authorised[1] under the authority of Mike Rasenberg, Director of Hazard Assessment

Appendix 1: Reasons for the decision
Appendix 2: Procedure
Appendix 3: Addressees of the decision and their individual information requirements
Appendix 4: Conducting and reporting new tests under REACH

[1] As this is an electronic document, it is not physically signed. This communication has been approved according to ECHA's internal decision-approval process.

Appendix 1: Reasons for the decision

Contents

Reasons related to the information under Annex IX 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 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.

1.1. Triggering of the information requirement

2 In your registration dossier, you consider that this information requirement is not triggered 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*".

3 However, ECHA notes that your dossier contains a repeated dose toxicity study based on OECD 407 (2012) which indicates concerns in relation with reproductive toxicity. Specifically, a dose-related decreased mean T4 level (-24 to -56%) and increased mean TSH level (+3-fold to +15-fold) were noted from 50 mg/kg/day in both sexes when compared to control values, reaching statistically significance at 1000 mg/kg/day for T4 level and from 250 mg/kg/day for TSH level. These findings were correlated with hypertrophy as observed through microscopic examination. Biologically relevant changes in hormone levels (related to reproductive toxicity) are considered triggers to conduct an extended one-generation reproductive toxicity study already at Annex IX to REACH (ECHA Guidance on IRs and CSA, section R.7.6.2.3.2, Stage 4.4. (iii.) and Appendix R.7.6-5).

4 Therefore, the concern for reproductive toxicity must be further investigated by conducting an extended one-generation reproductive toxicity (EOGRT) study.

1.2. Information provided in your dossier

5 Your registration dossier does not include an extended one-generation reproductive toxicity (EOGRT) study.

6 Therefore, the information requirement is not fulfilled.

7 In your comments to the draft decision, you express an intention to conduct a preliminary test according to OECD TG 421 before the main OECD TG 443 study.

1.3. Specification of the study design

1.3.1. Species and route selection

8 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.).

1.3.2. Pre-mating exposure duration

9 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.

10 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 premating exposure duration (Guidance on IRs and CSA, Section R.7.6.).

11 Therefore, the requested pre-mating exposure duration for the P0 animals is ten weeks.

1.3.3. Dose-level setting

12 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.

13 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.

14 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.

15 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.

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

17 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

18 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

19 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

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

1.3.4.3. Investigations of sexual maturation

21 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. Cohorts 2A and 2B

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

23 Existing information (OECD 407, 2012) on the Substance itself shows that it induces thyroid toxicity: changes in thyroid hormone (T4) and TSH levels and changes in thyroid histopathology, and so perturbs thyroid hormone signalling. Thyroid toxicity is considered a specific mode of action with an association to developmental neurotoxicity.

24 In your comments to the draft decision, you disagree with the inclusion of investigations on neurodevelopmental toxicity. You refer to the draft interim report of ECHA´s EOGRTS review project. You explain that the report states that "*this interim report, 11 DNT EOGRT study reports have been assessed. All the evaluated reports had deficiencies*". You consider that a "*clear improvement of the implementation and validation of the DNT arms of the EOGRTS, as well as guidance on neurobehavioral specific investigations and interference with the thyroid system" is needed before before launching new OECD TG 443 studies.*

25 ECHA notes that the EOGRTS review project you are referring to aims to assess how a sample of studies were conducted taking into account the requirements of the OECD TG 443, additional advice provided by relevant guidance documents, as well as the content of the draft decision requesting these studies. Therefore, this draft report does not draw conclusions on the adequacy or technical feasibility of the specific investigations included in the DNT cohort. In particular, the report indicates that the identified deficiencies "*seems to be a principal issue with proficiency of the testing laboratory and to be considered when selecting suitable test laboratory*".

26 Therefore, ECHA concludes that performing new OECD TG 443 studies, including the DNT cohorts, is not hampered by the issues identified in the EOGRTS review project´s draft interim report and advises to have the studies performed by test laboratories able to demonstrate proficiency in the conduct of such studies.

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

1.3.6. Cohort 3

28 The developmental immunotoxicity Cohort 3 needs to be conducted in case of a particular concern on (developmental) immunotoxicity.

29 Existing information (OECD TG 407, 2012) on the Substance shows evidence of immunotoxicity. Specifically, the following effects are reported in the animals exposed to the Substance:

- Reduced white blood cell counts (total and specific cell types):
  - Males: dose-dependently decreased, at high dose -26% compared to controls
  - Females: dose-dependently decreased, at high dose -42% compared to controls (statistically significant)
- Significantly decreased immunology organ weights:
  - Males: absolute spleen weight -20% (high dose) compared to controls; absolute thymus weight -61% (mid dose) and -73% (high dose) compared to controls
  - Females: absolute spleen weight -22% (mid dose) and -34% (high dose) compared to controls; absolute thymus weight -58% (mid dose) and -74% (high dose) compared to controls
- Histopathological findings:
  - Males: lymphoid atrophy in spleen (4/5 animals at high dose); lymphoid atrophy in thymus (1/5 in low dose, 3/5 in mid dose and 5/5 in high dose); none observed in control animals.
  - Females: lymphoid atrophy in spleen (1/5 animals at high dose); lymphoid atrophy in thymus (3/5 in mid dose, 4/5 in high dose); none observed in control animals.

30 The above changes in haematological and histopathological parameters, together with alterations in immune system organ weights, indicate that the Substance causes toxicity to the immune system. Furthermore, the Substance is classified as skin sensitiser (Skin Sens. 1). Therefore, there is a particular concern on developmental immunotoxicity.

31 For the reasons stated above, the developmental immunotoxicity Cohort 3 must be conducted.

1.4. Further expansion of the study design

32 The conditions to include the extension of Cohort 1B are currently not met. However, you may expand the study by including the extension of Cohort 1B 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.

2. Long-term toxicity testing on fish

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

2.1. Information provided

34 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.1. To support the adaptation, you have provided following justification: "*In accordance with column 2 of REACH Annex IX, long-term toxicity testing on fish does not need to be proposed by the registrant as the chemical safety assessment according to Annex I indicates no need to investigate further the effects on aquatic organisms (RCRs < 1 in all scenarios for freshwater and marine water). This waiver is also in accordance with the integrated testing strategy of ECHA's Guidance on information requirements and chemical safety assessment, chapter R7b (v4.0; June 2017; p. 59), which mentions that long-term toxicity testing should be conducted in daphnia first and then in fish, only when RCR is still superior to 1 on fresh and/or marine water after completion of the long-term study on daphnia*".

2.2. Assessment of the information provided

35 We have assessed this information and identified the following issue:

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

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

37 Your adaptation is therefore rejected.

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

39 In your comments to the draft decision, you agree with ECHA's assessment. However, you do not agree to perform the requested study. You provide the following justification to omit the study:

- you refer to a group of four thioureas (i.e., ETU, DETU, DBTU and DPTU) and indicate that they have similar physico-chemical and environmental fate properties;
- based on available information you consider they have similar acute toxicity profiles and that "*fish are less sensitive than aquatic invertebrates and algae*";
- you specify that all four thioureas have the thiourea moiety as common characteristic and that this moiety "*seems to be in the most part responsible of the trend of toxicity*";
- you refer to the QSAR toolbox and indicate that "*the QSAR models are not always applicable to Thioureas*". However, you consider this information sufficient to support a similar trend in physico-chemical and environmental fate properties. You indicate that "*the level of* [acute] *toxicity varies significantly across the Thioureas group*". You also note that "*the concentration ranges* [of experimental chronic toxicity fish data included in the QSAR Toolbox dataset] *are rather large it is difficult to complex to compare to QSAR data*". Nevertheless, you consider that "[t]*he most important information is that QSAR confirmed the lowest sensitivity to fish*".
- You state that "*under REACH regulation, testing on vertebrate animals can only be used as a last resort to fulfil information requirements for registration" and that "the adaptation seems appropriate* […] *to avoid unnecessary animal testing and to reduce the number of animal tests*". However, you do not specify the legal basis for the adaptation you intend to rely on to omit the study.

40 ECHA acknowledge your comments to the draft decision and emphasizes that you may only adapt this information requirement using the general rules for adaptation from Annex XI to REACH. However, your comments fail to provide an unambiguous legal basis for your justification to omit the study. In particular, ECHA notes the following:

- you refer to information from similar substances. However, it is unclear whether

your intention is to adapt this information requirement under Annex XI, Section 1.5. Furthermore, a read-across hypothesis and on supporting information needs to be fully described and justified and this information has not been provided in your comments. Therefore, no assessment or conclusions on the compliance of such adaptation can currently be made;

- you seem to infer that testing is not necessary because you consider fish to be less sensitive than algae and aquatic invertebrates. However, this justification to omit this information does not refer to any legal ground for adaptation under Annex XI to REACH;
- minimisation of vertebrate animal testing is not on its own a legal ground for adaptation under the general rules of Annex XI.

41 On this basis, the information provided in your comments does not change the assessment outcome. You remain responsible for complying with this decision by the set deadline.

2.3. Study design and test specifications

42 To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (Guidance on IRs and CSA, Section R.7.8.2.).

3. Simulation testing on ultimate degradation in surface water

43 Simulation testing on ultimate degradation in surface water is an information requirement under Annex IX to REACH (Section 9.2.1.2.).

3.1. Information provided

44 You have adapted this information requirement by using Column 2 of Annex IX, Section 9.2.1.2. To support the adaptation, you have provided following justification: "*In accordance with column 2 of REACH Annex IX, the biodegradation in water and/or sediments studies (required under sections 9.2.1.2 and 9.2.1.4) do not need to be conducted. First, the substance has a low potential for bioaccumulation. Therefore, no further degradation study is required in the framework of the PBT/vPvB assessment, as indicated in ECHA's guidance on information requirements and chemical safety assessment, chapter R.11 (v3.0, June 2017, p.20): "non indication of P or B properties" => "the assessment stops". The substance is not PBT nor vPvB. Second, the Chemical Safety Assessment does not indicate any risk for any environmental compartment in any scenario (RCRs < 1). Therefore, in accordance with column 2 of Annex IX of REACH regulation EC 1907/2006, no degradation simulation study is needed*".

3.2. Assessment of information provided

3.2.1. Your justification does not relate to any of the specific rules for adaptation from Annex IX, Section 9.2.1.2, column 2

45 Under Annex IX, Section 9.2.1.2, column 2, the study may be omitted if the Substance is highly insoluble in water or if the Substance is readily biodegradable.

46 However, your justification does not relate to any of the specific rules for adaptation from column 1 specified under Annex IX, Section 9.2.1.2, column 2. Therefore, ECHA assumes that you intend to adapt this information requirement under Annex IX, Section 9.2., Column 2 and has assessed your justification on that basis further below (Section 3.2.2.).

3.2.2. Annex IX, Section 9.2., Column 2 is not a valid basis to omit the study

47 Annex IX, Section 9.2., Column 2 provides that "further" biodegradation testing must be proposed if the chemical safety assessment according to Annex I indicates the need to investigate further the degradation of the substance and its degradation products. That provision allows a registrant to propose, or ECHA to require, biotic degradation testing not covered by the information on degradation listed under Annex IX, section 9.2., Column 1. Therefore, this provision cannot be used as a justification for omitting the submission of information on simulation testing on ultimate degradation in surface water required under Annex IX, Section 9.2.1.2, Column 1.

48 Therefore, your adaption is rejected.

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

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

3.3. Study design and test specifications

51 Simulation degradation studies must include two types of investigations (Guidance on IRs and CSA, Section R.7.9.4.1.):

1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and
2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

52 You must perform the test, by following the pelagic test option with natural surface water containing approximately 15 mg dw/L of suspended solids (acceptable concentration between 10 and 20 mg dw/L) (Guidance on IRs and CSA, Section R.11.4.1.1.3.).

53 The required test temperature is 12°C, which corresponds to the average environmental temperature for the EU (Guidance on IRs and CSA, Table R.16-8) and is in line with the applicable test conditions of the OECD TG 309.

54 As specified in Guidance on IRs and CSA, Section R.7.9.4.1., the organic carbon (OC) concentration in surface water simulation tests is typically 2 to 3 orders of magnitude higher than the test material concentration and the formation of non-extractable residues (NERs) may be significant in surface water tests. Paragraph 52 of the OECD TG 309 provides that the "*total recovery (mass balance) at the end of the experiment should be between 90% and 110% for radiolabelled substances, whereas the initial recovery at the beginning of the experiment should be between 70% and 110% for non-labelled substances*". NERs contribute towards the total recovery. Therefore, the quantity of the (total) NERs must be accounted for the total recovery (mass balance), when relevant, to achieve the objectives of the OECD TG 309 to derive degradation rate and half-life. The reporting of results must include a scientific justification of the used extraction procedures and solvents.

55 For the persistence assessment by default, total NERs is regarded as non-degraded Substance. However, if reasonably justified and analytically demonstrated a certain part of NERs may be differentiated and quantified as irreversibly bound or as degraded to biogenic NERs, such fractions could be regarded as removed when calculating the degradation half-life(s) (Guidance on IRs and CSA, Section R.11.4.1.1.3.). Further recommendations may be found in the background note on options to address non-extractable residues in regulatory persistence assessment available on the ECHA website (NER - summary 2019 (europa.eu)).

56 Relevant transformation/degradation products are at least those detected at ≥ 10% of the applied dose at any sampling time or those that are continuously increasing during the

study even if their concentrations do not exceed 10% of the applied dose, as this may indicate persistence (OECD TG 309; Guidance on IRs and CSA, Section R.11.4.1.).

4. Identification of degradation products

57 Identification of degradation products is an information requirement under Annex IX to REACH (Section 9.2.3.).

4.1. Information provided

58 You have provided no information for this information requirement.

4.2. Assessment of information provided

59 We have assessed this information and identified the following issue:

4.2.1. You have provided no information

60 You have provided no information on the identity of transformation/degradation products for the Substance.

61 Therefore, the information requirement is not fulfilled.

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

4.3. Study design and test specifications

63 Simulation degradation studies must include two types of investigations (Guidance on IRs and CSA, Section R.7.9.4.1.):

(1) a degradation pathway study where transformation/degradation products are quantified and, if relevant, are identified, and
(2) a kinetic study where the degradation rate constants (and degradation half-lives) of the parent substance and of relevant transformation/degradation products are experimentally determined.

64 Identity, stability, behaviour, and molar quantity of the degradation/transformation products relative to the Substance must be evaluated and reported. In addition, identified transformation/degradation products must be considered in the CSA including PBT assessment.

65 You must obtain this information from the degradation study requested in request 3.

66 To determine the degradation rate of the Substance, the requested study according to OECD TG 309 (request 3) must be conducted at 12°C and at a test concentration < 100 µg/L. However, to overcome potential analytical limitations with the identification and quantification of major transformation/degradation products, you may consider running a parallel test at higher temperature (but within the frame provided by the test guideline, *e.g.* 20°C) and at higher application rate (*i.e.* > 100 µg/L).

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

This decision does not prevent ECHA from initiating further compliance checks at a later stage on the registrations present.

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

The compliance check was initiated on 07 December 2021.

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

ECHA took into account your comments and partially amended the requests.

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.

In your comments on the draft decision, you requested an extension of the deadline to provide information from 24 to 36 months from the date of adoption of the decision. You justify the request by the CRO's current workload and provided documentary evidence to support the request for an extension. 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.

On this basis, ECHA has granted the request and extended the deadline to 36 months.

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.

You did not provide any comments on the proposed amendment(s).

The Member State Committee unanimously agreed on the draft decision in its MSC-85 written procedure. ECHA adopted the decision under Article 51(6) of REACH.

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

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

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

Registrant Name	Registration number	Highest REACH Annex applicable to you
[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.

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

This information is needed to assess whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

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

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