~~Confidential~~

Helsinki, 16 March 2021

Addressees
Registrant(s) of JS_IPPD-ERCA as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
24/08/2018

Registered substance subject to this decision ("the Substance")
Substance name: N-isopropyl-N'-phenyl-p-phenylenediamine
EC number: 202-969-7
CAS number: 101-72-4

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 ***21 June 2023.***

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

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

1. Extended one-generation reproductive toxicity study (Annex IX, Section 8.7.3.; test method: OECD TG 443) in rats, oral route, specified as follows:
- Ten weeks premating exposure duration for the parental (P0) generation;
- Dose level setting shall aim to induce systemic toxicity at the highest dose level;
- Cohort 1A (Reproductive toxicity);
- 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.

2. 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

3. Identification of degradation products (Annex IX, 9.2.3.; test method: using the simulation test method OECD TG 309)

Reasons for the request(s) are explained in the following appendices:

- Appendix entitled "Reasons common to several requests";
- Appendix entitled "Reasons to request information required under Annex IX of REACH"

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH:

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

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 testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". For references used in this decision, please consult the Appendix entitled "List of references".

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 Christel Schilliger-Musset, Director of Hazard Assessment

[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 A: Reasons to request information required under Annex IX of REACH

1. Extended one-generation reproductive toxicity study (Annex IX, Section 8.7.3.)

The basic test design of an extended one-generation reproductive toxicity (EOGRT) study (OECD TG 443) is a standard information requirement under Annex IX to REACH, 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.

You have provided

i. A reproductive toxicity screening study OECD TG 421 with the Substance, rel 4, according to GLP, in rats, gavage, made in 2009. *The doses were 20, 50, 125 mg/kg of body weight.*

ii. Sub-chronic toxicity study OECD TG 408 with the Substance, rel 1, according to GLP, in rats, feeding study, made in 1990. *Doses / Concentrations: 0, 180, 360, 720 ppm (males: 0, 13.5, 26.5, 54.0; females: 0, 15.6, 30.0, 59.0 mg/kg/d).*

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

- Issue: triggers for the information requirement at Annex IX

As already mentioned above, an EOGRT study is required if the available repeated-dose studies indicate adverse effects or concerns related to reproductive toxicity.

Adverse effects on reproductive organs or tissues or other concerns in relation with reproductive toxicity are observed in available studies. More specifically, in the screening study OECD TG 421 (*i*) that you have provided, at the highest dose (125 mg/kg) postnatal viability index was significantly decreased.

In your comments to the draft decision, you query the relevance of the decreased postnatal viability in F1 pups as a trigger of EOGRTS study at Annex IX and indicate the possibility to maternal neglect of pups.

Parameters such as precoital interval, mating index, fertility index, preimplantation loss, post-implantation loss, number of corpora luteae, number of implantations, number of resorptions, dead foetuses, abortions, gestation length, litters size, and number of live pups are measuring effects on fertility (some of these parameters may also reflect developmental toxicity). As noted in the ECHA Guidance R.7a, Section R.7.6.2.3.2, reduced survival of offspring and reduced maternal care are examples of triggers from a screening study to conduct EOGRTS at Annex IX. Furthermore, triggers should be considered relevant even if observed at the same dose level than the (other)systemic toxicity findings if it cannot be justified why the triggers are secondary to (other)systemic toxicity.

The endpoint study record concludes: *"A significant decrease in viability index was observed in pups of the high dose group resulted from high post partum mortality in high dose pups."* Also, the decreased postnatal viability index (58.9%) was used as one of the basis of effect levels to detect LOAEL for F1, therefore considered as valid effect by the author of the study report.

It was not proven that the findings would be secondary to the systemic toxicity therefore, they are relevant.

In your comments to the draft decision, you also state:

"Moreover, no effects on number of live fetuses per litter, early or late resorptions, post-implantation loss, total litter weights, mean fetal weights, total number of fetuses delivered and no teratogenic effects were observed in a developmental toxicity study with Sprague-Dawley rats (OECD TG 414; [redacted] 1994). Thus, this observation should not be considered a trigger for an EOGRT study."

ECHA notes that the OECD TG 414 has different exposure duration and aim, also the sacrification of animals one day before expected delivery do not allow observations of postnatal period. Furthermore, the study is not designed to study effects related to fertility. In summary, based on the data provided it is not possible to conclude that the reduced viability index would be solely due to maternal toxicity. Therefore the concern remains.

With the reference to the reliability score 4 given by you without further explanation, this OECD TG 421 study is considered to have an acceptable relevance and quality, in particular in number of animals in the control, mid and high dose groups.

In your comments to the draft decision, you point to the limitations of the OECD TG 421 study and claim that *"GLP and guideline study (OECD TG 421), study design with limitations (e.g. low dose group with 7 pregnant females was below the minimum acceptable number of pregnant females (8 females per group) according to TG 421; because of the limited number of pregnant females used in this study (number of pregnant females: control: 8, low dose: 7, mid dose: 8, high dose group: 10) a meaningful evaluation of the potential of the substance to affect fertility, pregnancy, maternal and suckling behavior, and growth and development of F1 offspring from conception to day 4 post-partum is limited. The study should be used only for supporting reasons."*

However, we find that there are still sufficient animals in control, mid-dose and high-dose groups, so the study is not disregarded. We consider that the observations and results at these dose levels remain relevant, in terms of deciding on the EOGRTS study design, in spite of the inadequate low-dose group. While the study alone would not meet a specific information requirement, its results can still be used when the overall evidnce to reproductive triggers is assessed.

An EOGRT study according to OECD TG 443 as specified in this decision is an information requirement for your registration, because Column 1 criteria at Annex IX, section 8.7.3 are met.

Weight-of evidence

In your comments to the draft decision, you propose to use a Weight of Evidence (WoE) approach to meet this information reguirement. In the WoE you include:

i. reproductive toxicity screening study OECD TG 421 with the Substance, rel 4, according to GLP, in rats, gavage, made in 2009,
ii. sub-chronic toxicity study OECD TG 408 with the Substance, rel 1, according to GLP, in rats, feeding study, made in 1990, and
iii. pre-natal developmental toxicity study OECD TG 414 with the Substance, rel 1, according to GLP, in rats, gavage, made in 1994.

We have assessed this information and identified the following issues:

Annex XI, Section 1.2 states that there may be sufficient weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

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 that the Substance has or has not the (dangerous) property investigated by the required study.

Annex XI, section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence approach. In your dossier, you have not included a justification for your weight of evidence adaptation for the information requirement, which would include an adequate and reliable (concise) documentation as to why the sources of information provide sufficient weight to conclude that the Substance has or has not the dangerous property investigated by the required study.

To be considered compliant and enable concluding if the Substance is a reproductive toxicant, the information from these studies has to meet the requirements of OECD TG 443 as specified in REACH. These include the following requirements:

1) Investigation of all relevant life stages required in OECD TG 443, including the extensive postnatal investigations of the fully exposed F1 generation up to the adulthood;
2) Investigation of mating, fertility, pregnancy, lactation;
3) The statistical power of the information must fulfil the criterion of 20 pregnant females for each test group as required OECD TG 443;

OECD TG 421/422 (wrong study for this endpoint) provided;
The study (*i*) you provided does not meet requirements 1) and 3) above.

OECD TG 408 (wrong study for this endpoint) provided;
The study (*ii*) you provided does not meet the requirements 1), 2) and 3) above.

OECD TG 414 (wrong study for this endpoint) provided;
The study (*iii*) you provided does not meet the requirements 1) and 2) above.

Based on the above, the information you provided in your dossier and in your comments where you indicated a WoE adaptation, it does not fulfil the information requirement.

The specifications for the study design

Premating exposure duration and dose-level setting

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

Ten weeks premating 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.

Therefore, the requested premating exposure duration is ten weeks.

In order to be compliant and not to be rejected due to too low dose levels, the highest dose level shall aim to induce systemic toxicity, but not death or severe suffering of the animals, to allow comparison of reproductive toxicity and systemic toxicity. The dose level selection should be based upon the fertility effects. A descending sequence of dose levels should be selected in order to demonstrate any dose-related effect and to establish NOAELs.

If there is no relevant data to be used for dose level setting, it is recommended that range-finding results are reported with the main study.

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

Cohorts 1A and 1B

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

Species and route selection
The study must be performed in rats with oral[2] administration.

Further expansion of the study design

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/or 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 the conduct of this study. Inclusion is justified if the available information meets the criteria and conditions which are described in Column 2, Section 8.7.3. 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 ECHA Guidance R.7a, Section R.7.6.

2. Simulation testing on ultimate degradation in surface water

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

i. You have provided the following information: key study River-die-away screening (1981) on the Substance, showing that half-lives for the Substance range from 2-11 hours.

ECHA understands that the information provided was submitted in order to meet the required information by way of adaptation under Annex XI, Section 1.1.2.

We have assessed this information and identified the following issue[s]:

Annex IX, Section 1.1.2 of REACH enables registrants to claim that the data from experiments not carried out according to GLP or the test methods referred to in Article 13(3) can be

[2] ECHA Guidance R.7a, Section R.7.6.2.3.2.

considered equivalent to data generated by those test methods where a number of cumulative conditions are met, in particular:

1. Adequate and reliable coverage of the key parameters foreseen to be investigated in the corresponding test methods referred to in Article 13(3), in this case OECD TG 309 which covers following key parameters:
    1) the rate of aerobic transformation of the test material in natural surface water, and
    2) the identity and rates of formation and decline of transformation/degradation

2. Adequate and reliable documentation of the study is provided;

In order to have adequate and reliable coverage of the key parameters of the OECD TG 309, the following specifications/conditions of the OECD TG 309 must be met:

a) Validity criteria of the test:
    - the reference substance must be degraded within the expected time interval
    - The water examined must have a bacterial biomass corresponding to 10^3 to 10^4 colony forming unit (CFU) per ml.
b) the surface water used to conduct the test has not been contaminated with the test material or its structural analogues within the previous 4 years;
c) to determine the transformation rates, the test material concentrations must reflect environmentally realistic concentrations and be ≤ 100 µg/L.
d) at least two different concentrations of test material are used, which must differ from each other by a factor of 5 to 10;
e) the mass balances during and at the end of the study are provided;
f) the results of the quantification of released CO2 and other volatile compounds during and at the end of the study are provided;
g) an assessment of transformation kinetics (i.e. lag phase, degradation rate constant and degradation half-life) for the test material and, where appropriate, for major transformation/degradation products is provided;

Regarding the point 1. 1) above, in the key study, you reported the half-lives of the Substance to be 2.5 h, 5.4 h and 11.3 h in active Mississippi river, sterile Mississippi river and purified water respectively.

Regarding the point 1. 2) above, you did not specify transformation products nor report rate of formation and decline of any transformation/degradation.

Regarding the adequacy and reliability of the coverage of these key parameters, you did not specify whether the validity criteria outlined under a) above were fulfilled for the key study. In your study record, you did not mention use of reference substance, and CFU of the water used. Thus you did not demonstrate that the validity criteria were fulfilled.

In addition, you did not specify or provide information on the conditions outlined b), e), f) and g) above.

Regarding conditions c) and d) above, higher initial test substance concentration than 100 µg/L was used in the study (1000 µg/L) and the study was conducted only at this concentration.

One of the key parameters (i.e. the identity and rates of formation and decline of transformation/degradation) was not covered by the key study (1981).

In addition, the key study (1981) does not provide adequate and reliable coverage of the key parameters of OECD TG 309 considering the critical deficiencies indicated above (conditions b) and c)) and the absence of reporting for the conditions a), d), e) and f) does not allow an independent assessment of their reliability and adequacy for covering the key parameters.

In your comments to the draft decision, you indicate you may conduct the test.

On this basis, the information requirement is not fulfilled.

Study design

Simulation degradation studies must include two types of investigations (ECHA Guidance 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.

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) (ECHA Guidance R.11.4.1.1.3.).

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

As specified in ECHA Guidance 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 substance concentration and the formation of non-extractable residues (NERs) may be significant in surface water tests. Therefore, non-extractable residues (NER) must be quantified. The reporting of results must include a scientific justification of the used extraction procedures and solvents. By default, total NER is regarded as non-degraded Substance. However, if reasonably justified and analytically demonstrated a certain part of NER may be differentiated and quantified as irreversibly bound or as degraded to biogenic NER, such fractions could be regarded as removed when calculating the degradation half-life(s) (ECHA Guidance 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.

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; ECHA Guidance R.11.4.1).

3. Identification of degradation products

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

ECHA understands that you provided an adaptation according to Annex XI, Section 1.2. In support of your adaptation, You have provided the following sources of information:

i. Weight-of-evidence: OECD TG 111 ([redacted] 1986) on the Substance, identifiying 4-hydroxydiphenylamine as hydrolysis products and Benzo-quinoneimine-N-phenyl as oxidation product, and
ii. Weight-of-evidence: River-die-away screening (1981) on the Substance

We have assessed this information and identified the following issues:

Weight-of evidence

Annex XI, Section 1.2 states that there may be sufficient weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

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 that the Substance has or has not the (dangerous) property investigated by the required study.

Annex XI, section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence approach.

You have provided summaries in separate endpoint study records for hydrolysis and simulation test in water. In those summaries you briefly present each of the sources of information, describe the results for these endpoints. Whilst these reports can be regarded as integrated summaries of the data sets, you have not submitted any explanation why the sources of information provide sufficient weight of evidence leading to the conclusion/assumption on the identification of the degradation products of the Substance.

In spite of this critical deficiency, ECHA has nevertheless assessed the validity of your adaptation and identified the following issues.

Relevant information that can be used to support weight of evidence adaptation for information requirement of Section 9.2.3 at Annex IX includes similar information that is produced by the OECD TG 307/308/309. This includes information on relevant transformation/degradation products ("key elements"):
- those representing over 10% of the applied dose, and
- those accumulating over time during the test.

The source of information i), a hydrolysis study according to OECD TG 111 ([redacted] 1986), shows primary degradation of the Substance and identifications of two transformation/degradation products, namely, 2 (4-hydroxydiphenylamine and its oxidation form Benzo-quinoneimine-N-phenyl.

In the source of information ii), no information on transformation/degradation products are specified. The source of information ii) does not provide any relevant information on identification of transformation/degradation products. Therefore, the source of information ii) does not provide information that would contribute to the conclusion on these key elements.

The source of information i) provides relevant information of two hydrolysis products. Therefore the source of information i) partially provides information on the key elements. However, although hydrolysis may be one of the degradation pathways for the Substance in water, there may be other degradation pathways for which no relevant information has been provided.

In this respect, ECHA notes that information in the technical dossier points towards other possible degradation pathways and other degradation products.

For instance, you mentioned in the water solubility endpoint that the key study ([redacted] 1978) was conducted "in the dark to preclude photodegradation" and supporting study ([redacted] 1986) was conducted while being shielded from light with alumonuim foil. Therefore, it is possible that apart from hydrolysis (and oxidation), photolysis may also be a relevant degradation pathway for the Substance.

In addition, although you indicated that the study is not reliable (reliability score 4: not assignable) because the original reference is not available, the other study submitted under water solubility ([redacted] 2007) showed "that the peak of the test substance completely disappeared while other (unknown) peaks appeared". Therefore, based on the available information in the technical dossier, it cannot be excluded that there are other degradation pathways than hydrolysis alone and there are more transformation/degradation products than those which were identified by the hydrolysis study.

For the reasons above, the identification of the degradation products and PBT/vPvB assessment cannot be considered complete by the source of information i) and two transformation/degradation products identified therein. The PBT/vPvB properties of all relevant transformation/degradation products that are representing over 10% of the applied dose, and are accumulating over time during the test, need to be addressed.

As a conclusion, sources of information as indicated above, provide some relevant information on identification of degradation products but not all relevant degradation pathways were covered and not all the relevant transformation/degradation products were investigated. Accordingly, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated for this endpoint.

In your comments to the draft decision, you indicate you may conduct the test.

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

Information on identity of relevant transformation/degradation products is required for the purpose of the PBT/vPvB assessment (Annex I, Section 4) and the risk assessment (Annex I, Section 6) of the Substance.

Study design

To determine the degradation rate of the Substance, the requested study according to OECD TG 309 (Section A.2) 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).

Appendix B: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. 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[3].

B. 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.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[4].

[3] https://echa.europa.eu/practical-guides
[4] https://echa.europa.eu/manuals

Appendix C: 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 4 December 2019.

ECHA notified you of the draft decision and invited you to provide comments within 30 days of the notification.

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

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

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 D: List of references - ECHA Guidance[5] and other supporting documents

Evaluation of available information
Guidance on information requirements and chemical safety assessment, Chapter R.4 (version 1.1., December 2011), referred to as ECHA Guidance R.4 where relevant.

QSARs, read-across and grouping
Guidance on information requirements and chemical safety assessment, Chapter R.6 (version 1.0, May 2008), referred to as ECHA Guidance R.6 where relevant.

Read-across assessment framework (RAAF, March 2017)[6]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[6]

Physical-chemical properties
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Toxicology
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

Environmental toxicology and fate
Guidance on information requirements and chemical safety assessment, Chapter R.7a (version 6.0, July 2017), referred to as ECHA Guidance R.7a in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7b (version 4.0, June 2017), referred to as ECHA Guidance R.7b in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.7c (version 3.0, June 2017), referred to as ECHA Guidance R.7c in this decision.

PBT assessment
Guidance on information requirements and chemical safety assessment, Chapter R.11 (version 3.0, June 2017), referred to as ECHA Guidance R.11 in this decision.

Guidance on information requirements and chemical safety assessment, Chapter R.16 (version 3.0, February 2016), referred to as ECHA Guidance R.16 in this decision.

Data sharing
Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

OECD Guidance documents[7]

[5] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[6] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[7] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

Guidance document on transformation/dissolution of metals and metal compounds in aqueous media – No 29, referred to as OECD GD 29.

Guidance Document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption – No 150, referred to as OECD GD 150.

Guidance Document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD 151.

Appendix E: Addressees of this decision and the corresponding information requirements applicable to them

You must provide the information requested in this decision for all REACH Annexes applicable to you.

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