EUROPEAN CHEMICALS AGENCY

Helsinki, 13 February 2020

Addressees
Registrants of [redacted] listed in the last Appendix of this decision

Date of submission for the jointly submitted dossier subject of this decision
14/12/2018

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: 3,3'-[(2,5-dichloro-p-phenylene)bis[imino(1-acetyl-2-oxoethylene)azo]]bis[4-chloro-N-(5-chloro-o-tolyl)benzamide]
EC number: 226-971-2
CAS number: 5580-58-5

Decision number: [Please refer to the REACH-IT message which delivered this communication (in format CCH-D-XXXXXXXXXX-XX-XX/D)]

DECISION ON A COMPLIANCE CHECK

Based on Article 41 of Regulation (EC) No 1907/2006 (REACH), ECHA requests that you submit the information listed below by the deadline of ***22 August 2022.***

A. Requirements applicable to all the Registrants subject to Annex VIII of REACH

1. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) or in vitro micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) with the Substance;

2. Only if a negative result in Annex VIII, Section 8.4.2. is obtained, In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method OECD TG 476 or TG 490) with the Substance;

3. Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.; test method OECD 412), in rats, inhalation route with the Substance. The study must include measurements of lung burden and bronchoalveolar lavage fluid (BALF) analysis as described in the current version (25 June 2018) of the test guideline;

4. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.; test method OECD 421/422) in rats, oral route with the Substance;

Conditions to comply with the requests

You are bound by the requests for information corresponding to the REACH Annexe applicable to your own registered tonnage of the Substance at the time of evaluation.

Therefore you have to comply with the requirements of Annexes VII and VIII of REACH, if you have registered a substance at 10-100 tpa.

Registrants are only required to share the costs of information that they are must submit to fulfil the information requirements for their registration.

The Appendix on general considerations addresses common arguments that are applicable throughout the present decision while the other Appendices state the reasons for the requests for information to fulfil the requirements set out in the respective Annexes of REACH.

The Appendix entitled Observations and technical guidance addresses the generic approach for the selection and reporting of the test material used to perform the required studies and provides generic recommendations and references to ECHA guidance and other reference documents.

You must submit the information requested in this decision by the deadline indicated above in an updated registration dossier and also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information. The timeline has been set to allow for sequential testing where relevant.

Appeal

This decision can be appealed to the Board of Appeal of ECHA within three months of its notification. An appeal, together with the grounds thereof, has to be submitted to ECHA in writing. An appeal has suspensive effect and is subject to a fee. Further details are described under: http://echa.europa.eu/regulations/appeals.

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 on general considerations

Assessment of the Grouping of substances and read-across approach, in light of the requirements of Annex XI, Section 1.5.

You seek to adapt the information requirements for the following standard information requirements by grouping substances in the category and applying a read-across approach in accordance with Annex XI, Section 1.5:

- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.) if a negative result in Annex VIII, Section 8.4.2. is obtained.
- Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)
- Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

ECHA has considered the scientific and regulatory validity of your grouping and read-across approach in general before assessing the specific standard information requirements in the following appendices.

Grouping of substances and read-across approach

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 (addressed under 'Scope of the grouping'). 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 (addressed under 'Assessment of prediction(s)').

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance R.6 and related documents.

A. Scope of the grouping

i. Description of the grouping

In your registration dossier you have formed a group (category) of 'yellow disazo condensation pigments'. You have provided a *'justification for the analogue approach'* as a document in IUCLID Section 13.

For the purpose of this decision, the following abbreviations are used for the group members:

	Abbreviation/Name	CAS number	EC number
1)	**PY93**/Pigment Yellow 93 3,3'-[(2-chloro-5-methyl-p-phenylene)bis[imino(1-acetyl-2-oxoethylene)azo]]bis[4-chloro-N-(3-chloro-o-tolyl)benzamide]	5580-57-4	226-970-7
2)	**PY94**/Pigment Yellow 94 3,3'-[(2,5-dichloro-p-phenylene)bis[imino(1-acetyl-2-oxoethylene)azo]]bis[4-chloro-N-(5-chloro-o-tolyl)benzamide]	5580-58-5	226-971-2
3)	**PY95**/Pigment Yellow 95 3,3'-[(2,5-dimethyl-p-phenylene)bis[imino(1-acetyl-2-oxoethylene)azo]]bis[4-chloro-N-(5-chloro-o-tolyl)benzamide	5280-80-8	226-107-4

4) **PY128**/Pigment Yellow 128 79953-85-8 279-356-6
3,3'-[(2-chloro-5-methyl-p-phenylene)bis[imino(1-acetyl-2-oxoethylene)azo]]bis[4-chloro-N-[2-(4-chlorophenoxy)-5-(trifluoromethyl)phenyl]benzamide]
5) **PY155**/Pigment Yellow 155 68516-73-4 271-176-6
1,4-Benzenedicarboxylic acid, 2,2'-[1,4-phenylenebis[imino(1-acetyl-2-oxo-2,1-ethanediyl)azo]]bis-, tetramethyl ester

You provide the following reasoning for grouping the substances "*The category members [...] share the same core structure. The core structure includes all functional groups which might be relevant for metabolism (eg azo, carboxamide). Structural differences are the substituents on the phenylene or phenyl part.*" You also argue that they are not bioavailable and thus of no toxicological relevance due to their low solubility in different media and low toxicity determined by lower-tier tests.

You define the the structural basis for the grouping as "yellow disazo condensation pigments". ECHA understands that this is the applicability domain of the grouping and will assess your predictions on this basis.

ii. Assessment of the grouping

ECHA notes the following shortcomings with regards to your grouping approach.

1. Applicability domain of the category

According to the ECHA Guidance Chapter R.6.2, Section R.6.2.4.1, a category hypothesis should address "*the set of inclusion and/or exclusion rules that identify the ranges of values within which reliable estimations can be made for category members for the given endpoint. These rules, can be described as the applicability domain for an endpoint and provide a means of extending the category membership to chemicals not explicitly included in the current definition of a category.*"

You describe the applicability domain of the substances covered by the grouping as: "*yellow disazo condensation pigments.*" Based on your description of the structural basis of your grouping/category approach, ECHA understands that all category members are yellow disazo pigments, derived from condensation reactions, which share common 'core structures' with some variation in ring-substituents. They vary further in terms of their substitutions of the 'mid' and 'end' moieties.

You have not defined the allowed substitutions on the 'core', 'mid' or 'end' structures, resulting in many more potential unidentified category members than those listed in your hypothesis, which are unaccounted for in your prediction. This applicability domain does not introduce unambiguous inclusion/exclusion criteria which would identify the structural requirements and ranges of physico-chemical, environmental fate, toxicological or ecotoxicological properties within which reliable estimations can be made for the (sub)category members.

B. Predictions for properties

You have provided the following reasoning for the prediction of toxicological properties: The "*category hypothesis is fundamentally based on the low bioavailability. None of the pigments are sufficiently soluble either in water or in octanol for systemic uptake or metabolism.*" You also state that "*theoretical considerations, uptake and metabolism should result in the release of aromatic amines; such compounds have a characteristic toxicity profile. As this was not observed, the substances are not considered to have been taken up by the body.*"

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

You intend to predict the properties for the category members from information obtained from the following category members:

I. In vitro gene mutation study in bacteria (Annex VII, Section 8.4.1.) according to OECD TG 471
   a. Pigment Yellow 93 (CAS 5580-57-4, EC 226-970-7), 2008, 1997
   b. Pigment Yellow 94 (CAS 5580-58-5, EC 226-971-2), 2011
   c. Pigment Yellow 95 (CAS 5280-80-8, EC 226-107-4), 2011
   d. Pigment Yellow 128 (CAS 79953-85-8, EC 279-356-6), 2000, 2001
   e. Pigment Yellow 155 (CAS 68516-73-4, EC 271-176-6), 1997, 2000

II. In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.) according to OECD TG 473
   a. Pigment Yellow 95 (CAS 5280-80-8, EC 226-107-4), 2012

III. In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.) according to OECD TG 476
   a. Pigment Yellow 95 (CAS 5280-80-8, EC 226-107-4), 2012
   b. Pigment Yellow 155 (CAS 68516-73-4, EC 271-176-6), 2012

IV. Repeated dose toxicity (Annex VIII-IX, Section 8.6)
   a. Pigment Yellow 93 (CAS 5580-57-4, EC 226-970-7) according to OECD TG 407, 2009
   b. Pigment Yellow 155 (CAS 68516-73-4, EC 271-176-6), according to OECD TG 422, 2012

V. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1) and Pre-natal developmental toxicity (Annex IX, Section 8.7.2)
   a. Pigment Yellow 155 (CAS 68516-73-4, EC 271-176-6), according to OECD TG 422, 2012

ECHA notes the following shortcomings with regards to predictions of toxicological properties.

1. Missing supporting information

Annex XI, Section 1.5 of the REACH Regulation states that "*adequate and reliable documentation of the applied method shall be provided*". Within this documentation "*it is important to provide supporting information to strengthen the rationale for the read-across*"[2]. The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

"*Adequate and reliable documentation*" must include
   i. supporting information on the absence of bioavailability and
   ii. bridging studies to compare such properties of the category members.

[2] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.2.1.f

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar target and source substances cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the target and source substance is necessary to confirm that both substance cause the same type of effects. Such information can be obtained, for example, from bridging studies, and from studies demonstrating absence of bioavailability.

In your read-across hypothesis, you state that the category members have a molecular weight between [redacted] as well as low solubility in water and organic solvents, which results in a very low bioavailability and thus no or low toxicity. Furthermore, you have submitted short-term toxicity studies on two of five category members, PY93 and PY155, which demonstrate no effect levels at the limit dose of 1000 mg/kg bw/d. This data set reported in the technical dossier does not include relevant, reliable and adequate information for the target and the source substances to support your read-across hypothesis.

In your comments to the draft decision

- you indicate your intention to update your read-across justification according to the requirements of the read across assessment framework
- you consider formation of methyl-aniline or chloro-aniline by cleave unlikely because *"amide bonds are chemically stable and require extreme pH level and temperatures above 100°C to be hydrolysed."*
- you claim *"hazard for toxicity to reproduction is not possible, because disazocondensation yellow pigments are too large and insoluble for significant systemic uptake"*
- you state *"metabolism is not expected due to lack of absorption after oral administration"* because a *"characteristic toxicity profile"* of the potential metabolites was not observed in the available screening study with PY 155.

ECHA notes that enzymatic cleavage (i.e. hydrolysis) of amide bonds may occur in living organism which do not require extreme pH and temperatures. The existing information gives some indications about low bioavailability based on molecular size and solubility. However, in the absence of data demonstrating absence of bioavailability (e.g. toxicokinetic studies), it is not possible to conclude on bioavailability for any of the category members. Furthermore, your theoretical considerations on the absence of metabolism have not been substantiated by experimental data such as studies on toxicity after repeated exposure (e.g. OECD TG 407/421/422), and are thus rejected.

Bridging studies to compare such properties of the analogue substances

You did not provide appropriate bridging studies (such as a screening study OECD TG 421 or 422) to compare the properties of the category members with regard to repeated dose and reproductive/developmental toxicity. As also explained in the next section (data density), your hypothesis of low bioavailability is not supported by results from repeated dose toxicity studies with representative analogue substances across the category.

In the absence of such information, you have not established that the target and the source substances are likely to have similar properties. The allegation on potential metabolism is unsubstantiated, without further explanation on its impact on the prediction of hazardous effects by potentially bioavailable parent substance.

Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

2. *Data density to derive a regular pattern*

Annex XI, Section 1.5. provides that "*substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances.*

According to the ECHA Guidance, one of the factors in determining the robustness of a category is the density and distribution of the available data across the category.[3] To identify a regular pattern and/or to derive reliable prediction of the properties of the members of the category, adequate and reliable information covering the range of structural variations identified among the category members needs to be available.

You have provided the following studies:

1. For *in vitro* genotoxicity with bacteria (Annex VII, Section 8.4.1), two category members (pigment yellow 94 and pigment yellow 128) have been tested in valid tests according to OECD TG 471 with modified metabolic activation for azo-substances, such as the category members, whereas the other three substances were tested in invalid test systems, because they lacked this relevant modification.

2. For *in vitro* genotoxicity with mammalian cells (Annex VIII, Section 8.4.2 and 8.4.3), one category member (pigment yellow 95) has been tested in *in vitro* cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.) and *in vitro* mammalian chromosome aberration test (OECD TG 473, 2012) and two members (pigment yellow 95 and 155) were tested in *in vitro* gene mutation studies in mammalian cells (OECD TG 476; Annex VIII, Section 8.4.3.).

3. For repeated dose toxicity (Annex VIII, Section 8.6.1 and Annex IX, Section 8.6.2), one category member (pigment yellow 93) has been tested in an oral short-term (28-day) toxicity study (OECD TG 407, 2009) and one of the category members (pigment yellow 155) in a combined repeated dose toxicity and screening for reproductive/developmental toxicity (OECD TG 422, 2012). No repeated dose toxicity studies by the inhalation route have been provided. No sub-chronic toxicity studies (90-day) have been provided.

4. For screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1) and pre-natal developmental toxicity (Annex IX, Section 8.7.2), one of five category members (pigment yellow 155) has been tested in a combined repeated dose toxicity and screening for reproductive/developmental toxicity (OECD TG 422, 2012). No pre-natal developmental toxicity studies have been provided.

Based on these studies you claim that there are similar properties between the category members.

The category members have multiple structural differences, but no information has been provided to establish whether and to what extent any of the category members are representative of the whole category or a subset of it. In addition, the available studies cover only a small subset of these structural differences for each endpoint. Information for two (1.+3., above) or one (2.+4., above) category members is not sufficient to conclude which substances are representative of the category members for *in vitro* genotoxicity, repeated dose toxicity and toxicity to reproduction and pre-natal development in the absence of (lower

[3] Guidance on information requirements and chemical safety assessment Chapter R.6: QSARs and grouping of Chemicals, Section R.6.2.1.5.

tier) toxicity studies with all category members for the relevant endpoint. Considering the deficiencies regarding the applicability domain of the category and the distinct structural differences between the members of the category, there are too few data points (i.e. low data density) in the current data matrix for demonstrating consistency and predicting properties for the listed toxicological endpoints as proposed by you. Therefore, the information provided is not sufficient to conclude that toxicological properties are likely to follow a regular pattern.

C. Conclusions on the grouping of substances and read-across approach

As explained above, you have not established that relevant properties of the registered substance can be predicted from data on the analogue substance. Therefore, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.

Appendix A: Reasons for the requests to comply with Annex VIII of REACH

In accordance with Articles 10(a) and 12(1) of REACH, a technical dossier registered at 10 to 100 tonnes or more per year must contain, as a minimum, the information specified in Annexes VII and VIII to REACH.

1. **In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)**

An *In vitro* cytogenicity study in mammalian cells or an *In vitro* micronucleus study is a standard information requirement in Annex VIII to REACH.

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

In your comments on the initial draft decision you consider that "*Requested mutagenity studies is considered to be unjustified, because read-across data for each requested study is available, even some information gaps might be included. Therefore an updated read-across justification according to the requirements of the read across assessment framework will be submited*". However, as explained in the Appendix General consideration, your adaptation according to Annex XI, Section 1.5 is rejected.

To fulfil the information requirement for the Substance, both *In vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) and *in vitro* micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) are considered suitable.

2. **Only if a negative result in Annex VII, Section 8.4.1. and Annex VIII, Section 8.4.2. is obtained, in vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.);**

An *in vitro* gene mutation study in mammalian cells is a standard information requirement in Annex VIII to REACH in case of a negative result in the *in vitro* gene mutation in bacteria and the *in vitro* cytogenicity test.

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

In your comments on the initial draft decision you consider that "Requested mutagenity studies is considered to be unjustified, because read-across data for each requested study is available, even some information gaps might be included. Therefore an updated read-across justification according to the requirements of the read across assessment framework will be submited". However, as explained in the Appendix General consideration, your adaptation according to Annex XI, Section 1.5 is for the moment rejected. Your updated dossier will be evaluated after the deadline of this decision.

Your dossier contains negative results from an *in vitro* gene mutation study in bacteria, and an adaptation for an *in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study, which is rejected for the reasons provided in the Appendix on General considerations.

The result of the requests for information in section 1. of this Appendix will determine whether the present requirement for an *in vitro* mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

To fulfil the information requirement for the Substance, both the *in vitro* mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) and the thymidine kinase gene (OECD TG 490) are considered suitable.

3. Short-term repeated dose toxicity (28 day), (Annex VIII, Section 8.6.1.)

A Short-term repeated dose toxicity study (28 days) is a standard information requirement in Annex VIII to REACH.

You have adapted this information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5. You provided a repeated dose oral toxicity (OECD TG 407) study (2009) and a Combined repeated dose toxicity study with the reproduction/ developmental toxicity screening test (OECD TG 422) with analogue substances.

As explained in the Appendix on general considerations above, your adaptation is rejected. Therefore, the information requirement is not fulfilled

Following the criteria provided in Annex VIII, Section 8.6.1, Column 2, the inhalation route is the most appropriate route of administration to investigate repeated dose toxicity. The sub-chronic toxicity study must be performed according to the OECD TG 412, in rats and with administration of the Substance by inhalation. The information provided in the technical dossier and the chemical safety report on properties of the Substance and its uses (professional and consumer uses, including PROCs 7 and 11 industrial and non-industrial spraying, and PROC 24) indicate that human exposure to the Substance by the inhalation route is likely. More specifically, the Substance is reported to occur as a dust with a significant proportion [redacted] of particles of inhalable size ([redacted]). Furthermore, the Substance is respirable ([redacted]), of low water solubility and consequently there is a potential for accumulation of the Substance in the lungs.

In your comments on the initial draft decision you considered that testing by inhalation route is not relevant. You provided further details on the uses, and explained that spraying application is not included anymore. However, you did not provide any data (e.g. exposure scenarios) to demonstrate that for your identified uses, exposure of humans via inhalation is not likely despite the respirable size of the Substance.

There is evidence that the lower respiratory tract is the primary site of deposition and retention of the Substance, because it is poorly soluble in water and respirable. Therefore, you are requested to perform measurements of lung burden and bronchoalveolar lavage fluid (BALF) which are specifically designed to address such situation. The latest guidance on how to perform such measurements are described in the revised version of the OECD 412 test guideline adopted on 25 June 2018.

4. Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.)

A Screening for reproductive/developmental toxicity study (OECD TG 421 or 422) is a standard information requirement under Annex VIII to REACH, if there is no evidence from analogue substances, QSAR or in vitro methods that the Substance may be a developmental toxicant. There is no information available in your dossier indicating that your Substance may be a developmental toxicant.

You have adapted this information requirement by using a Grouping of substances and read-

across approach under Annex XI, Section 1.5.

In your comments on the draft decision you consider that "*since the information requirements defined by EC regulation 1907/2008, Annex VIII, 8.7.1 are fulfilled by adaption as described in Annex XI, 1.5 and another reproductive toxicity screening study (OECD 421 / 422) within this category is not expected to add any further relevant knowledge on this endpoint and due to animal welfare aspects and/or laws, an additional study is not warranted*". However, as explained in the Appendix General consideration, your adaptation according to Annex XI, Section 1.5 is rejected.

A study according to the test method OECD TG 421/422 should be performed in rats with oral[4] administration of the Substance.

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

Appendix B: Procedural history

For the purpose of the decision-making, this decision does not take into account any updates of registration dossiers after the date on which you were notified the draft decision according to Article 50(1) of the REACH Regulation.

The compliance check was initiated on 14 January 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 requests or the deadline.

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 C: Observations and technical guidance

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

2. Failure to comply with the requests in this decision, or to otherwise fulfil the information requirements with a valid and documented adaptation, will result in a notification to the enforcement authorities of the Member States.

3. Test guidelines, GLP requirements and reporting

   Under Article 13(3) of REACH, all new data generated as a result of this decision needs to be conducted according to the test methods laid down in a European Commission Regulation or according to international test methods recognised by the Commission or ECHA as being appropriate.

   Under Article 13(4) of REACH, ecotoxicological and toxicological tests and analyses shall be carried out according to the GLP principles (Directive 2004/10/EC) or other international standards recognised by the Commission or ECHA.

   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: 'How to report robust study summaries'[5].

4. Test material

   Selection of the test material(s)

   The registrants of the Substance are responsible for agreeing on the composition of the test material to be selected for carrying out the tests required by the present decision. The test material selected must be relevant for all the registrants of the Substance, i.e. it takes into account the variation in compositions reported by all members of the joint submission. The composition of the test material(s) must fall within the boundary composition(s) of the Substance.

   While selecting the test material you must take into account 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.

   Technical reporting of the test material

   The composition of the selected test material must be reported in the respective endpoint study record, under the Test material section. The composition must include all constituents of the test material and their concentration values and other parameters relevant for the property to be tested. Without such detailed reporting, ECHA may not be able to confirm that the test material is relevant for the Substance and to all the registrants of the Substance.

   Technical instructions are available in the manual "How to prepare registration and PPORD dossiers"[6].

[5] https://echa.europa.eu/practical-guides
[6] https://echa.europa.eu/manuals

5. List of references of the ECHA Guidance and other guidance/ reference documents[7]

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 in this decision.

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 in this decision.

ECHA Read-across assessment framework (RAAF, March 2017)[8]

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.

OECD Guidance documents[9]
Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD23.
Guidance Document on Mammalian Reproductive Toxicity Testing and Assessment – No 43, referred to as OECD GD43.

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

Appendix D: List of the registrant to which the decision is addressed and the corresponding information requirements applicable to them

Registrant Name	Registration number	(Highest) Data requirements to be fufilled
[redacted]	[redacted]	[redacted]

Note: where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas the decision is sent to the actual registrant.