EUROPEAN CHEMICALS AGENCY

Helsinki, 18 May 2020

Addressees
Registrants of JS_2020956_BG listed in the last Appendix of this decision

Date of submission for the jointly submitted dossier subject of this decision
7 November 2017

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: 6-phenyl-1,3,5-triazine-2,4-diyldiamine
EC number: 202-095-6
CAS number: 91-76-9

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 ***23 February 2023***.

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

1. *In vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.; test method: Bacterial reverse mutation test, EU B.13/14. /OECD TG 471), with the Substance;

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

1. 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.; test method: OECD TG 476 or OECD TG 490), with the Substance;

C. Requirements applicable to all the Registrants subject to Annex IX of REACH

1. Extended one-generation reproductive toxicity study also requested, and specified, at D.2 below (triggered by Annex IX, Section 8.7.3.);

D. Requirements applicable to all the Registrants subject to Annex X of REACH

1. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.; test method OECD TG 414) in a second species (rabbit), oral route, with the Substance.

2. Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) in rats, oral route, with the Substance, 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.

Conditions to comply with the requests

Each addressee of this decision is bound by the requests for information corresponding to the REACH Annexes applicable to their own registered tonnage of the Substance at the time of evaluation of the jointly submitted dossier.
To identify your legal obligations, please refer to the following:

- you have to comply with the requirements of Annex VII of REACH, if you have registered a substance at 1-10 tonnes per annum (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- you have to comply with the requirements of Annexes VII, VIII and IX of REACH, if you have registered a substance at 100-1000 tpa;
- you have to comply with the requirements of Annexes VII to X of REACH, if you have registered a substance at above 1000 tpa.

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

The 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.

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 on reasons common to several requests

1. Deadline to comply with information requests

In your comments on the draft decision, you requested an extension of the timeline to comply with the information requests in this decision to 36 months. You justified your request by the suggestion of a sequential testing strategy for the requested extended one-generation reproductive toxicity study (EOGRTS, OECD 443) in rats, and pre-natal developmental toxicity study (PNDT, OECD 414) in rabbits, making the performance of the PNDT study dependent on the outcome of the EOGRTS.

As explained in Appendix D.1, ECHA does not agree with your reasoning and the suggested sequential testing strategy. Therefore, ECHA has not modified the deadline of the decision.

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

1. *In vitro* gene mutation study in bacteria (Annex VII, Section 8.4.1.)

An *in vitro* gene mutation study in bacteria is a standard information requirement in Annex VII to REACH.

You have provided a key study and supporting study in your dossier:

i. Bacterial reverse mutation assay ([redacted] 1999) according to OECD 471
ii. Bacterial reverse mutation assay ([redacted] 1988) according to OECD 471.

In your comments to the draft decision, you refer to information obtained through the full translation of [redacted] studies now available, and you indicate that these studies fulfil the information requirement for this endpoint. You state that these studies provide a negative result. You indicate your intention to provide this information.

We have assessed this information and identified the following issue:

To fulfil the information requirement, the study has to meet the requirements of OECD TG 471 (1997). Two of the key parameters of this test guideline include:

a) One positive control must be included in the study. The positive control substance must produce a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control.
b) The test must be performed with 5 strains: four strains of *S. typhimurium* (TA98; TA100; TA1535; TA1537 or TA97a or TA97) and one strain which is either *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).

In the study [redacted] 1999, "the positive controls did not induce the appropriate responses. There was no evidence of induced mutant colonies over background."
The study was conducted with the following strains, *S. typhimurium* TA 1535, TA 1537, TA 98 and TA 100, *E. coli* WP2 uvr.
The study [redacted] 1998 was conducted with the following strains, *S. typhimurium* TA 98, TA 100, TA 1535, TA 1537 and TA 1538.

The reported data for the study [redacted] 1999 did not include a positive control that produced a statistically significant increase in the number of revertant colonies per plate compared with the concurrent negative control.
The study [redacted] 1988 did not include results for the required fifth strain, *S. typhimurium* TA102 or *E. coli* WP2 uvrA or *E. coli* WP2 uvrA (pKM101).

None of the information currently provided in your dossier covers the key parameters required by OECD TG 471. You did not provide any further details on the nature of the newly identified information mentioned in your comments. In particular, you have not described how this new information relates to the missing elements identified in the above mentioned studies ([redacted] 1999, [redacted] 1988). Therefore, based on your comments we are not in a position to conclude on whether this new information addresses the issues identified and whether the information requirement could be fulfilled.

Therefore the information requirement is currently not fulfilled.

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

1. **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.; test method: OECD TG 476 or OECD TG 490), with the Substance;**

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 test in bacteria and the *in vitro* cytogenicity test.

You have provided a key study in your dossier: *in vitro* mammalian cell gene mutation test according to OECD TG 476 ([redacted] 1993).

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

Your dossier contains:

i. for Annex VIII, Section 8.4.2 - a negative result for an adequate *in vivo* cytogenicity study (*In Vivo* Mammalian Erythrocyte Micronucleus Test, OECD TG 474, [redacted] 2000), adapting the information requirement for an *in vitro* cytogenicity study, and
ii. for Annex VII, Section 8.4.1 - inadequate data for the *in vitro* gene mutation in bacteria.

The *in vitro* gene mutation study in bacteria provided in the dossier is rejected for the reasons provided in Appendix A, Section 1 above, and a new study is requested. The result of the request for information in Appendix A, Section 1 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 in Annex VIII, Section 8.4.3, the *in vitro* gene mutation study on mammalian cells has to meet the requirements of OECD TG 476 or OECD TG 490. The key parameters of these test guidelines include that data on the cytotoxicity and the mutation frequency for the treated and control cultures must be measured. The results should allow a clear assessment and unambiguous conclusion on the endpoint.

The reported study you have provided [redacted] 1993) does not include data on the cytotoxicity and the mutation frequency for the treated and control cultures. The test results were ambigious above the solubility level and with metabolic activation.

The information provided does not inform on key parameters required by the relevant OECD TG 476 and does not allow an independent assessment of the data and reaching an unambiguous conclusion.

Therefore, the information requirement is not fulfilled.

Consequently, you are required to provide information for this endpoint, if the *in vitro* gene mutation study in bacteria provides a negative result.

Information on the study design

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.

In your comments to the draft decision, you agreed with ECHA's assessment and agreed to perform a new *in vitro* gene mutation study in mammalian cells, in case of a negative result in the Ames test.

Appendix C: Reasons for the requests to comply with Annex IX of REACH

Under Articles 10(a) and 12(1) of REACH, a technical dossier registered at 100 to 1000 tonnes or more per year must contain, as a minimum, the information specified in Annexes VII to IX to REACH.

1. **Extended one-generation reproductive toxicity study also requested, and specified, at D.2 below (triggered by 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.

In your dossier you noted that: *"According to the [...] studies [Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test, [redacted] (1997) and Prenatal developmental toxicity study, [redacted] (2016)], the test item has no adverse effects on reproductive organs or tissues and does not reveal other concerns in relation with reproductive toxicity and developmental toxicity."*

However, concerns in relation with reproductive toxicity are observed in available studies. More specifically, the OECD TG 422 study [redacted] 1997) shows the following results:

- an increased number of stillborns at high dose (reduced birth index)
- reduced post-natal survival of offspring at mid and high dose (reduced viability index)
- reduced body weight of offspring independent of litter size (body weight of live newborns is statistically significantly lower at high dose)
- reduced maternal care.

Furthermore, reduced body weight of offspring was also noted in the high dose group of the OECD TG 414 study ([redacted] 2016). Reduced body weight of offspring just before birth (OECD TG 414) or after birth (OECD TG 422) reflects developmental toxicity which can be followed up only in an EOGRT study where post-natal body weight and further development of offspring until adulthood is investigated.

Accordingly, 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.

The examination of the adaptation that you provided for the information requirement, as well as the specifications of the study design are addressed in Appendix D for the Annex X request.

In your comments to the draft decision, you agreed with ECHA's assessment and agreed to provide the requested information.

Appendix D: Reasons for the requests to comply with Annex X of REACH

Under Articles 10(a) and 12(1) of REACH, a technical dossier at a tonnage abve 1000 tonnes per year must contain, as a minimum, the information specified in Annexes VII to X to REACH.

1. Pre-natal developmental toxicity study (Annex X, Section 8.7.2.) in a second species

Pre-natal developmental toxicity (PNDT) studies (OECD TG 414) in two species is a standard information requirement under Annex X to REACH.

You have provided a study conducted with the Substance according to the test guideline OECD TG 414 (Prenatal Developmental Toxicity Study) in the rat as a first species ([redacted] 2016).

In order to be compliant and enable concluding if the Substance is a developmental toxicant, information provided has to meet the requirements of OECD TG 414 in two species.

You have not provided any information on the pre-natal developmental toxicity of the Substance in a second species.

Based on the above, the information you provided does not fulfil the information requirement.

Information on study design

Species

The test in the first species was carried out by using a rodent species (rat). A PNDT study according to the test method OECD TG 414 must be performed in rabbit as preferred non-rodent species.

Route of administration

The study shall be performed with oral[2] administration of the Substance.

In your comments to the draft decision, you agreed with ECHA's assessment and agreed to provide the requested information.

However, you proposed sequential testing, where you would first perform the requested extended one-generation reproductive toxicity study (EOGRTS, OECD 443) in rats, and second, perform the requested PNDT study in rabbits (OECD 414), if needed, based on the outcome of the EOGRTS. You base this suggested testing strategy on the statement of Annex IX 8.7.2 Column 2 that "a decision on the need to perform a study at this tonnage level or the next on a second species should be based on the outcome of the first test and all other relevant available data".

The legal provision you refer to applies to the information requirement of Annex IX, 8.7.2. The present request addresses the standard information requirement of Annex X, 8.7.2., i.e. a PNDT study in a second species. This information requirement cannot be adapted on the basis of the results of the EOGRTS.

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

2. Extended one-generation reproductive toxicity study (Annex X, 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 X to REACH. Furthermore Column 2 of Section 8.7.3. defines when the study design needs to be expanded.

You have adapted the standard information requirement(s) mentioned above according to Annex XI, Section 1 of REACH without specifying further subsection. As you have provided two sources of information ECHA has interpreted your adaptation and evaluated it according to Annex XI, Section 1.2 of REACH (weight of evidence).

In support of your adaptation, you have provided the following sources of information obtained with the Substance:

i. Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test according to OECD TG 422 conducted in rats via the oral route [redacted] 1997);
ii. Prenatal developmental toxicity study according to the OECD TG 414 conducted in rats via the oral route ([redacted] 2016).

Based on the presented sources of information, you argue that the available data gives sufficient information to conclude on the reproductive toxicity of the Substance and that conducting *"the EOGRTS seems to be scientifically not necessary"* because *"most of the required endpoints referring to the reproductive systems for males and females are covered by the "Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (Rat) OECD 422". The following reproductive endpoints are examined: effects on reproductive organs for females, oestrous cycle, conception (achievement of pregnancy), sperm measures, mating behaviour, parturition, lactation. For the developmental toxicity, most of the requested endpoints are covered by the "Prenatal Development Toxicity Study (Rat) OECD 414": pre- and post-implantation loss Pregnancy (effects and duration) Resorption (early/late; total litter losses), offspring viability (body weight, sex ratio and reduction in number of live offspring), malformations (external, skeletal and visceral)."*

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.4.4, 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 of the information for the given regulatory endpoint. Subsequently, relevance, reliability, 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.

However, you have not submitted any explanation why the sources of information provide sufficient weight of evidence leading to the assumption that the substance has or has not a particular dangerous property investigated by the required study.

Irrespective of the above mentioned deficiencies on the documentation, which in itself could lead to the rejection of the adaptation, ECHA has assessed the provided sources of information.

Relevant information that can be used to support a weight of evidence adaptation for the information requirement of Section 8.7.3 at Annex IX/X includes similar information to that produced by the OECD TG 443 design as specified in this decision. At general level, it includes information on sexual function and fertility, toxicity to offspring, systemic toxicity - and if column 2 triggers are met, also information on sexual function and fertility of the offspring, developmental neurotoxicity and/or developmental immunotoxicity.

In more details, sexual function and fertility on both sexes includes information on mating, fertility, gestation, parturition, lactation, organ weights and histopathology of reproductive organs and tissues, oestrous cyclicity, sperm count, sperm analysis, hormone levels, litter sizes, nursing performance and other potential aspects of sexual function and fertility. Toxicity to offspring includes information on deaths before, during or after birth, growth, sexual maturity, oestrous cyclicity, histopathology of reproductive organs in adulthood and other potential aspects of toxicity to offspring. Systemic toxicity includes information on clinical signs, survival, body weights, food consumption, haematology, clinical chemistry, organ weights and histopathology of non-reproductive organs and other potential aspects of systemic toxicity in both the parental and F1 generations. Furthermore, if column 2 triggers are met, information on sexual function and fertility of the offspring, developmental toxicity in F2 generation, developmental neurotoxicity and/or developmental immunotoxicity is relevant. Developmental toxicity includes assessment of neurotoxicity (auditory startle test, functional observation battery, motor activity), information on neurohistopathology and other potential aspects of developmental neurotoxicity. Developmental immunotoxicity includes splenic lymphocyte subpopulation analysis, T-cell dependant antibody response assay, assessment of imune organs and other potential asepcts of developmental immunotoxicity.

Sexual function and fertility

Both sources of information (i. and ii.) provide relevant information on sexual function and fertility in parental animals, although the source (ii.) informs on sexual function and fertility only for one aspect, maintenance of pregnancy. However, these sources of information have the following deficiencies affecting their reliability.

Information on sexual function and fertility (functional fertility and histopathology of reproductive organs and tissues) must be investigated in parental P0 animals as indicated in OECD TG 443 after at least ten weeks premating exposure duration if extension of Cohort 1B is not included[3].

In the case of your Substance, the conditions to include the extension of Cohort 1B are currently not met. The source of information (i.) investigates sexual function and fertility with the premating exposure duration of two weeks for the parental P0 animals. The other source (ii.) does not have any premating exposure.

Neither of the sources of information investigate sexual function and fertility in the P0 generation with sufficient premating exposure duration to ensure the coverage of full spermatogenesis and folliculogenesis before mating.

[3] ECHA Guidance R.7a, Section R.7.6

In the absence of information on the sexual function and fertility after exposure to the Substance over a pre-mating period of 10 weeks, no reliable conclusion can be drawn on sexual function and fertility as required by the information requirement.

Toxicity to the offspring

Both sources of information (i. and ii.) provide partially relevant information on toxicity to the offspring.

The source of information (i.) provides some information on toxicity to the offspring up to post-natal day 4. The other source (ii.) informs on *in utero* development of offspring.

Information provided on toxicity to offspring is limited and does not cover all relevant and essential aspects as defined above. Neither the sources of information (i.) nor (ii.) inform on toxicity to the offspring up to adulthood. Therefore, no conclusion can be drawn on toxicity to the offspring as required by the information requirement.

Systemic toxicity

Both sources of information (i. and ii.) provide partially relevant information on systemic toxicity.

The source of information (i.) informs on systemic toxicity, especially haematology, clinical chemistry and organ weight and histopathology of non-reproductive organs from 5 parental animals/sex/group and the other source (ii.) includes only very limited investigations in dams.

Information provided on systemic toxicity is limited and does not cover all relevant and essential aspects as defined above. In particular, there is no information on systemic toxicity from the F1 generation, such as clinical signs, body weights, haematology, clinical chemistry, organs weights and histopathology of non-reproductive organs in adulthood. Without such information no conclusions on the parental toxicity and its relationship with reproductive toxicity can be made.

Taken together, the sources of information as indicated above provide relevant information on the sexual function and fertility on the parental P0 generation but its reliability is affected by insufficient premating exposure. There is only partially relevant information provided covering toxicity to offspring, lacking information on relevant life stages of the F1 generation (post-natal period up to adulthood). Furthermore, essential information on systemic toxicity is limited for the parental generation and lacking for the F1 generation from postnatal period up to adulthood. Therefore, a significant amount of essential investigations are limited or totally lacking that would inform on sexual function and fertility, toxicity to offspring and systemic toxicity in order to make a conclusion on these aspects.

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 in an OECD TG 443 study. Therefore, your adaptation is rejected and the information requirement is not fulfilled.

Based on the above, the information you provided 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 at least 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.

Species and route selection

The study must be performed in rats with oral[4] administration.

Cohorts 1A and 1B

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

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., Annex IX/X. 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[5].

In your comments to the draft decision, you agreed with ECHA's assessment and agreed to provide the requested study.

[4] ECHA Guidance R.7a, Section R.7.6.2.3.2.
[5] ECHA Guidance R.7a, Section R.7.6.

Appendix E: 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 REACH.

The compliance check was initiated on 9 April 2019.

The decision making followed the procedure of Articles 50 and 51 of REACH.

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 and 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 F: 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'[6].

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. 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"[7].

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

5. List of references of the ECHA Guidance and other guidance/ reference documents[8]

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)[9]

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[10]
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.

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

Appendix G: List of the registrants 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.