~~Confidential~~

Helsinki, 14 January 2022

Addressees
Registrant(s) of JS_597-82-0 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
18/03/2020

Registered substance subject to this decision ("the Substance")
Substance name: O,O,O-triphenyl phosphorothioate
EC number: 209-909-9
CAS number: 597-82-0

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 ***22 April 2025***.

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 (triggered by Annex IX, Section 8.7.3., column 1; test method: OECD TG 443) by oral route, in rats, specified as follows:

   - Ten weeks premating exposure duration for the parental (P0) generation;
   - Dose level setting shall aim to induce systemic toxicity at the highest dose level;
   - Cohort 1A (Reproductive toxicity);
   - Cohort 1B (Reproductive toxicity) with extension to mate the Cohort 1B animals to produce the F2 generation which shall be followed to weaning;
   - Cohorts 2A and 2B (Developmental neurotoxicity);
   - investigations on learning and memory function as described in paragraph 37 of the OECD TG 426; and
   - Cohort 3 (Developmental immunotoxicity).

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

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

- Appendix entitled "Reasons to request information required under Annex IX of REACH", respectively.

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 Mike Rasenberg, 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

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 study 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 two screening for reproductive/developmental toxicity studies (2011, 2017) with the substance (OECD TG 421).

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

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

You consider that no adverse effects on reproductive organs or tissues have been observed in the available repeated dose toxicity study(ies), and/or that these studies did not reveal other concerns in relation with reproductive toxicity: *"there are no results from available repeated dose toxicity studies that indicate adverse effects on reproductive organs or tissues, or reveal other concerns in relation with reproductive toxicity."*

However, adverse effects on reproductive organs or tissues or other concerns in relation with reproductive toxicity are observed in available studies. More specifically, changes in thyroid hormone (T4) levels were observed in an OECD TG 421 study and changes in thyroid histopathology were observed in an OECD TG 408 and an OECD TG 421 study, indicating a hormonal effect which is relevant for reproduction. In addition, an increased percentage of male pups with nipples/areolae and increased mean number of nipples in males were observed in an OECD TG 421 study.

According to the ECHA/EFSA Guidance for the identification of endocrine disruptors[2], '*In the absence of substance-specific data which provide proof of the contrary, humans and rodents are considered to be equally sensitive to thyroid-disruption (including cases where liver enzyme induction is responsible for increased TH clearance).*' We emphasise that even though the ECHA/EFSA Guidance[4] was developed for hazard identitification for endocrine-disrupting properties for other regulatory purposes, the same scientific principles apply also under the REACH Regulation.

In your comments on the draft decision you argue that the observed changes in thyroid histopathology and hormones is due to a perturbance of the liver-thyroid axis. You support your argument with observations of liver weight increases, observations on the type of changes in the histopathology of both organs, and on changes in thyroid hormone levels.

Based on the clarification provided in the comments, we do not consider that the provided information demonstrates the causality between changes in liver and (subsequent) changes in thyroid. Instead, the provided data allows interprepration that these changes to the organs may be independent of each other.

Specifically, we want to emphasise that the hypothalamic–pituitary–thyroid (HPT) axis is highly conserved across evolution in vertebrates. The regulation of serum THs levels and of TH action in various tissues involves a complex interplay of physiological processes. The thyroid function depends on iodine uptake, TH synthesis and storage in the thyroid gland,

[2] https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2018.5311

stimulated release of hormone into and transport through the circulation, hypothalamic and pituitary control of TH synthesis, cellular TH transport, tissue-specific TH de-iodination and degradation of THs by catabolic hepatic enzymes. Interference in any of these processes can adversely affect the thyroid function, resulting in reducted TH levels and adverse outcomes. Which adverse outcome(s) are expected depends on the lifestage exposed.

You argue that the observed effects on the thyroid should be considered non-relevant to humans. However, such a conclusion is currently not supported by the data that you have provided. The assumption that thyroid effects observed in rat are not human relevant must be substantiated using, for instance, evidence of species specific differences in metabolic capacity, and based on weight of evidence[3]. To investigate whether liver enzyme induction is responsible for the effects seen on TH levels and thyroid histopathology, as well as whether the effect is or not likely to be human relevant, the following three pieces of information are needed (see Appendix A of the ECHA/EFSA Guidance[4] for details):

1. Results of analysis of serum/plasma samples for TSH, T3 and T4 in the existing repeated dose toxicity- and screening for reproductive/developmental toxicity studies.
2. Comparative studies of enzyme activity induced by the test substance in liver *in vitro* systems should be measured in both the relevant test species (i.e. rats) and humans.
3. The presence of other possible thyroid-disrupting modes of action such as interference with TSH synthesis should also be excluded, e.g. by evaluating *in vitro* the potential for inhibition of the sodium–iodide symporter and thyroid peroxidase.

Regarding point 1., existing studies have investigated TSH and T4 levels.

Regarding point 2., there is no information provided which investigates the differences in liver enzyme induction in rats. However, in order to assess relevance to humans, a qualitative and quantitative comparison of liver enzyme induction between rats and humans must be provided.

Regarding point 3., you have not ruled out any of the other possible MoA(s). To support non-relevance it must be demonstrated that the liver enzyme induction is the primary MoA causing the effects on the thyroid.

Based on the above, ECHA considers that your comments do not demonstrate that the thyroid effects would not be relevant to humans, and they do not dismiss the indications of one or more modes of action related to endocrine disruption, i.e. thyroid disruption. Furthermore, the EOGRTS is designed to investigate potential reproductive and developmental effects that may occur as a result of pre- and postnatal chemical exposure. ECHA considers it pre-mature to dismiss potential adverse effects as non-human relevant, before such effects have been identified. This is because any conclusion on non-human relevance must consider the nature and the severity of the effects as well as the life-stage of the organism exposed.

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

To be considered compliant and enable concluding if the Substance is a reproductive toxicant, the study has to meet the requirements of OECD TG 443 as specified in REACH.

The studies you provided do not cover all relevant life stages required in an OECD TG 443, as the extensive postnatal investigations of the fully exposed F1 generation up to the adulthood are not included. Furthermore, the statistical power of the information provided is not

[3] Boobis AR et al. (2008) IPCS framework for analyzing the relevance of a noncancer mode of action for humans. Crit Rev Toxicol 38(2):87-96.

sufficient because it does not fulfil the criterion of 20 pregnant females for each test group as required in an OECD TG 443. In addition, the criteria for extension of the Cohort 1B are met for the Substance and there is a particular concern for developmental neurotoxicity according to column 2 of Annex IX, Section 8.7.3. and information for those properties are missing.

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 if there is no substance specific information in the dossier supporting shorter premating exposure duration as advised in the ECHA Guidance[1]. In this specific case ten weeks exposure duration is supported by the lipophilicity of the Substance (logKow = 5 at 23°C) to ensure that a steady state in parental animals has been reached before mating.

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.

Extension of Cohort 1B

If the Column 2 conditions of 8.7.3., Annex IX are met, Cohort 1B must be extended.

The extension is inter alia required, if the use of the registered substance is leading to significant exposure of consumers and professionals (column 2, first paragraph, lit. (a) of Section 8.7.3., Annex IX) and

- if there are indications that the internal dose for the registered substance will reach a steady state in the test animals only after an extended exposure (column 2, first paragraph, lit. (b), second indent of Section 8.7.3., Annex IX), or
- there are indications of one or more relevant modes of action related to endocrine disruption from available *in vivo* studies or non-animal approaches (column 2, first paragraph, lit. (b), third indent of Section 8.7.3., Annex IX).

The use of the Substance is leading to significant exposure of consumers and professionals because the Substance is used by consumers and professionally as lubricants and greases

(PROCs 1, 2, 8a, 8b, 10, 11, 13, 17, 18, 20).

Furthermore, there are indications that the internal dose for the Substance and/or any of its metabolites will reach a steady state in the test animals only after an extended exposure. Specifically, the $\log K_{ow}$ for the substance is above 4.5 indicating potential accumulation. In addition, effects are observed at more than 3 times lower exposure levels in the 90-day study compared to effects in 28-day study.

In addition, there are indications of one or more modes of action related to endocrine disruption because changes in thyroid hormone (T4) levels and thyroid histopathology were observed in an OECD TG 408 and an OECD TG 421 study with the Substance. Furthermore, there were increases in ovary weights observed in the latter study.

Therefore, Cohort 1B must be extended.

The F2 generation shall be followed to weaning allowing assessment of nursing and lactation of the F1 parents and postnatal development of F2 offspring. Investigations for F2 pups must be similar to those requested for F1 pups in OECD TG 443 and described in OECD GD 151[4]. It is recommended to aim at 20 litters per dose group.

Cohorts 2A and 2B

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

Existing information on the Substance itself derived from available *in vivo* studies (OECD TG 408 and 421) show evidence of effects on thyroid histopathology in OECD TGs 408 and 421 and TSH/T4 levels in OECD TG 421. In the latter study, circulating thyroid hormone (T4) level in male animals was reduced to 80% with concomitant increase of TSH to 140% of the control group, as well as a weight increase of the thyroid glands in female rats, without signs of other general toxicity. Signs of thyroid toxicity rise a particular concern on developmental neurotoxicity (ECHA Guidance R.7a).

In your comments on the draft decision you argue that the observed changes in thyroid histopathology and hormones is due to a perturbance of the liver-thyroid axis. Please refer to our reply above on this topic.

Therefore, the developmental neurotoxicity Cohorts 2A and 2B need to be conducted.

Cognitive functions: learning and memory

Paragraph 41 of OECD 443 provides "If existing information indicates the need for other functional testing (e.g. sensory, social, cognitive), these should be integrated without compromising the integrity of the other evaluations conducted in the study." You have provided an *in vitro* steroidogenesis screening assay ("[redacted]") which showed that the Substance decreased testosterone levels and increased estradiol levels. In your OECD TG 421 study (2018), the percentage of male pups having nipple / areolae was statistically significantly increased in test group 3 (1000 mg/kg bw/d) when examined on PND 13 and the mean number of nipple / areolae in the respective male pups was also statistically significantly increased in test group 3; you state these changes are "assumed to be treatment-related". The *in vivo* findings are consistent with an anti-androgenic effect and the *in vitro* findings provide support for anti-

[4] http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV/JM/MONO(2013)10&doclanguage=en

androgenicity as a mechanism. ECHA considers that the substance exerts an anti-androgenic effect *in vivo*. Perinatal reduction of testosterone levels[5] and treatment with anti-androgens[6] affect spatial cognitive abilities. As the substance has anti-androgenic effects, there is a need for investigating the spatial cognitive abilities (learning and memory) of F1 animals.

Additionally, the substance caused changes in thyroid hormone (T4) levels in an OECD TG 421 study and changes in thyroid histopathology in an OECD TG 408 and an OECD TG 421 study, and so perturbs thyroid hormone signalling. It is known that perturbation of thyroid hormone signalling in offspring affects spatial cognitive abilities[7,8,9]. As the Substance perturbs thyroid hormone signalling, this is an independent and separate basis which shows that there is a need for investigating the spatial cognitive abilities (learning and memory) of F1 animals.

In your comments on the proposed amendments, you consider that the Substance does not have anti-androgenic activity, and therefore additional investigations for spatial learning and memory are not justified. Your conclusion is based on the following arguments:

1) The Substance does not show (anti)estrogenic or (anti)androgenic activity in yeast estrogen and androgen screening assays, respectively.
2) Decrease in testosterone production is only observed at one concentration in one steroidogenesis assay and therefore the results are equivocal.
3) Although the OECD TG 421 study showed statistically significant increases in male pups having nipple/areolae in test group 3 (90.0%* vs 44.7% in controls) and the mean number of nipple/areolae in the respective male pups (2.5* vs. 1.2 in controls), the values fall within extended historical control values (ranges 0-100% for male pups with nipples/areolae, and 0-4.7 for number of nipples/areolae). Therefore, you conclude that there is no direct evidence of an anti-androgenic activity.
4) In the OECD TG 408 study with the Substance no relevant findings indicative of an anti-androgenic activity were made.

ECHA acknowledges the negative results in the yeast estrogen and androgen screening assays. However, these negative results do not provide a basis for discounting the results of the steroidogenesis assay in H295R cells for which you confirm a clear result (decrease of testosterone production) at one concentration. This finding at the top dose is biologically plausible and there is no reason to consider the results to be equivocal. This *in vitro* finding provides support for anti-androgenicity as a mechanism.

Increased nipple retention in male offspring is a hallmark of anti-androgenicity (OECD GD 150). While "retained nipples/areolae" as a qualitative endpoint may have high biological variability, nipple retention is a sensitive endpoint if measured quantitatively, i.e. if the number of nipples is recorded (OECD, 2015[10]). ECHA notes that in the OECD TG 421 study, the mean number of nipple / areolae in the male pups was statistically significantly increased in test group 3 when compared to the concurrent controls; according to the IUCLID dossier these changes are "assumed to be treatment-related". ECHA considers that the primary statistical comparison is between the treated and the concurrent control groups, and that

[5] Williams, C.L. et al. (1990) Behavioural Neuroscience 104, 84-97
[6] Lund, T.D. and Lephart, E.D. (2001) BMC Neuroscience 2, 21; Isgor, C. and Sengelaub, D.R. (1998) Hormones and Behaviour 34, 183-198
[7] Axelstad, M. et al. (2008) Tox. App. Pharm. 232, 1-13
[8] van Wijk, N. et al. (2008) Exp. Physiol. 93, 1199-1209
[9] Amano, I. et al. (2018) Endocrinol. 159, 1910-1921
[10] OECD (2015), "Feasibility study for minor enhancements of TG 421/422 with ED relevant endpoints", OECD Series on Testing and Assessment, No. 217, OECD, Paris, www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2015)24&doclanguage=en.

historical control data may also be useful as an aid to the interpretation of the study. ECHA considers that simply using the data range from a larger historical control dataset is not a sound basis for statistical analysis. ECHA has considered the historical control data provided and considers that this is consistent with the primary statistical analysis showing that treatment group is different (statistically significant) from the controls. Therefore, ECHA considers that the effects on nipple retention are a biologically significant and relevant effect. Specifically, ECHA notes that retention of nipples in male rat pups is a sensitive indicator of impaired androgen action during the development. A study in adult animals, such as OECD TG 408, may thus fail to detect anti-androgenic signalling as the measured parameters are less sensitive to anti-androgenic signalling. Therefore, lack of anti-androgenic effects in the OECD TG 408 study does not provide a basis for discounting the anti-androgenic effect observed during development in the OECD TG 421 study.

In conclusion, due to effects on the thyroid and thyroid hormones, the developmental neurotoxicity Cohorts 2A and 2B need to be conducted. Further, ECHA considers that it is necessary to conduct spatial learning and memory tests since there are two independent and sufficient triggers; the substance exerts an anti-androgenic effect *in vivo* and effects on the thyroid and thyroid hormones. The spatial learning and memory tests shall be performed in accordance with OECD 426 paragraph 37, i.e. at adolescence (PND 25±2 days) and young adulthood (PND 60 and older). Investigations of learning and memory should not compromise the integrity of the study[11].

Observations for the spatial learning and memory testing

OECD TG 426, paragraph 37 presents options of suitable test methods. Based on OECD TG 426, paragraph 37 you may consider to conduct the Morris water maze test or Radial arm maze test at one time point, and the Cincinnati water maze test at the other time point.

Taking into account practical aspects of conducting the OECD TG 443 study, ECHA notes that as an alternative to Cohort 2A, the investigations on learning and memory may also be conducted in Cohort 1A animals which can be allocated to two sets of animals, 10 males and 10 females in both; the first set of animals to be tested at adolescence and the other set of animals at young adulthood.

Cohort 3

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

The Substance itself shows anti-androgenic activity both *in vitro* and *in vivo*, as described under 'Cohorts 2A and 2B' above, which is considered a specific mechanism/mode of action with an association to developmental immunotoxicity for the following reasons. (1) androgen receptors are expressed by almost all immune cells (2) since androgens influence the sexual dimorphism of the immune system, it is possible that hormonally active substances can contribute to the development of immune related disorders (3) the immune system can be a relevant target for hormonally active compounds with anti-androgenic activities, especially following perinatal exposure. Specifically, the anti-androgen DEHP causes developmental immunotoxicity (Tonk EC, Verhoef A, Gremmer ER, van Loveren H, Piersma AH. Relative sensitivity of developmental and immune parameters in juvenile versus adult male rats after exposure to di(2-ethylhexyl) phthalate. Toxicol Appl Pharmacol. 2012 Apr 1;260(1):48-57). These considerations give rise to a particular concern that anti-androgenic substances (such as the Substance) have developmental immunotoxic properties.

[11] In OECD TG 443 adverse effects on sexual function and fertility may limit the number of offspring available for developmental investigations. However, the dosing should not be lowered in order to get a sufficient number of offspring. The priority of the OECD TG 443 test is to identify potential effects on sexual function and fertility.

In your comments on the proposed amendments, you consider that the Substance does not have anti-androgenic activity, and therefore additional investigations for developmental immunotoxicity are not justified. These considerations are rejected for the same reasons as set out under 'Cohorts 2A and 2B' above.

Therefore, the developmental immunotoxicity Cohort 3 needs to be conducted.

Species and route selection

The study must be performed in rats with oral[12] administration.

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

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[13].

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[14].

[13] https://echa.europa.eu/practical-guides
[14] 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 18 September 2020.

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

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

Deadline

In your comments to the draft decision, you requested ECHA "*to postpone the communication of the final decision (CCH) only after the PBT assessment is completed*" in the context of the ongoing substance evaluation (CoRAP) for the Substance. Please note that the study requested in this decision has been identified on the basis of the information gap related to the information requirement for an EOGRT study at the tonnage band specified in this decision. The obligation to provide this information is independent of the outcome of the ongoing substance evaluation for PBT concerns and thus, your request to postpone the communication of the final decision cannot be accepted.

Furthermore, in your comments on the draft decision, you requested an extension of the deadline to provide information from 24 to 36 months from the date of adoption of the decision. In support of your request you have provided information from a CRO/the performing laboratory which confirms your request.

Therefore we granted the request and extended the deadline to 36 months.

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

ECHA received proposal(s) for amendment and modified the draft decision.

ECHA invited you to comment on the proposed amendment(s) and referred the modified draft decision to the Member State Committee.

Your comments on the proposed amendment(s) were taken into account by the Member State Committee.

Deadline

In your comments on the proposal for amendment, you requested a further extension of the deadline to provide information from 36 to 42 months from the date of adoption of the decision. You provided a letter from the test laboratory, justifying the extension with planning and evaluating of the additional tests, as well as reduced testing capacity due to safety measures required by the COVID19 pandemic.

ECHA considers that the study designs including the additional tests can be conducted within the standard timelines. ECHA further notes that the normally applicable timeline

has already been extended due to reduced testing capacity. Therefore, ECHA has not extended the deadline further.

The Member State Committee reached a unanimous agreement on the draft decision during its MSC-76 meeting and ECHA took the decision according to Article 51(6) of the REACH Regulation.

Appendix D: List of references - ECHA Guidance[15] 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)[16]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[17]

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[18]

[15] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[16] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[17] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[18] 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 their corresponding information requirements

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.