~~Confidential~~

Helsinki, 03 May 2021

Addressees
Registrant of 271-360-6 Joint Subm. EM Lead as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
13/05/2020

Registered substance subject to this decision ("the Substance")
Substance name: Alcohols, C9-11-branched
EC number: 271-360-6
CAS number: 68551-08-6

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 ***10 May 2023***.

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

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

1. **Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.; test method: OECD TG 443) by oral route, in rats, specified as follows:**

   - **At least two 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; and**
   - **Cohorts 2A and 2B (Developmental neurotoxicity).**

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 Annexes VII to X 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 to X to REACH, for registration at more than 1000 tpa.

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". In addition, you should follow the general recommendations provided under the Appendix entitled "General recommendations when conducting and reporting new tests for REACH purposes". For references used in this decision, please consult the Appendix entitled "List of references".

Appeal

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

Failure to comply

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

Authorised[1] under the authority of Christel Schilliger-Musset, Director of Hazard Assessment

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

Appendix A: Reasons to request information required under Annex X 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 X to REACH. Furthermore Column 2 of Section 8.7.3. defines when the study design needs to be expanded.

You have provided a reference to an earlier decision[2] requesting the EOGRT study, stating that "*This information will be submitted later based on ECHA decision number CCH-D-2114342397-45-01/F.*". In the document attached to IUCLID section 7.8.1, you provide your considerations on the study design, proposing "*to execute the EOGRTS basic study design as outlined in the compliance check letter*".

The proposed study design requires modification to fulfil the information requirement.

The following refers to the specifications of this required study.

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.

A 2-week premating exposure duration for P0 animals is sufficient for your Substance, because the F1 animals of Cohort 1B are mated to produce the F2 generation and, thus, the premating exposure duration will be 10 weeks for these Cohort 1B animals.

Therefore, the requested premating exposure duration is at least two 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 X 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 X) and there are indications of one or more relevant modes of action

[2] https://echa.europa.eu/documents/10162/21e3150a-0831-2ade-6502-98211de23e9f

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 X).

As you have also indicated in the document attached to IUCLID section 7.8.1, the use of the Substance is leading to significant exposure of professionals and consumers. The Substance is used by professionals in oil and gas field drilling and production operations, metal working fluids/rolling oils and coatings (PROCs 1, 2, 3, 4, 5, 8a, 8b, 9, 10, 11, 13, 15, 17, 19, 28). In addition, exposure to consumers may arise e.g. in the following product categories: adhesives and sealants, anti-freeze and de-icing products, biocidal products, coatings and paints, thinners, paint removes, fillers, ink and toners, lubricants and greases, and textile dyes.

Furthermore, there are indications of one or more modes of action related to endocrine disruption because changes in organs/parameters sensitive to endocrine activity are observed. More specifically, the OECD TG 408 study showed

- Dose-dependent increase in the incidence of thyroid follicular cell hyperplasia in both sexes
- Increased thyroid weights (absolute and relative) at all dose levels in both sexes: the increase of absolute weight was up to 22% in males, and up to 58% in females
- Decreased levels of T3 in both sexes at all dose levels
- Decreased levels of T4 in males at high dose, and in females at all dose levels
- Increased levels of TSH in males at all dose levels, and in females at high dose
- Changes in HDL/LDL ratio

According to OECD GD 150[3], the above-mentioned effects are indicative of thyroid disruption.

In the study report you consider these thyroid-related changes to be non-adverse, representing '*an adaptive change secondary to test substance-related hepatic microsomal enzyme induction*'. In the document attached to IUCLID section 7.8.1 you also question the human relevance of these findings, based on '*quantitative differences in thyroid homeostasis and function between rats and humans*'.

According to the ECHA/EFSA Guidance for the identification of endocrine disruptors[4], '*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).*'. You have not provided substance-specific data which would provide proof that the observed thyroid-related effects would not be relevant to humans.

In your comments on the draft decision, you argue that the thyroid effects are to be considered secondary to the liver enzyme induction. You postulate a mode of action (MoA) which starts with hepatocellular hypertrophy, which through increased clearence of thyroid hormones (TH) by the liver results in lower T3/T4, leading to increased production of TSH and eventually to follicular cell hypertrophy/hyperplasia and increased thyroid weights. You refer to literature[5,6,7,8] comparing hepatic clearance of T3 and T4, half-life of T4, and TSH levels between rats and humans. To further support the MoA, you refer to measurements of liver

[3] https://www.oecd-ilibrary.org/docserver/9789264304741-en.pdf?expires=1590588065&id=id&accname=guest&checksum=E35A4458AB8BAC1C4A0145EFCCDE304B
[4] https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2018.5311
[5] Dohler et al. (1979). The rat as a model for the study of drug effects on thyroid function: Consideration of methodological problems. Pharmacol. Ther. 5:305-318
[6] Meek ME et al (2003). A framework for human relevance analysis of information on carcinogenic modes of action. Crit Rev Toxicol. 33(6):591-653
[7] McClain RM et al (1992). Thyroid gland neoplasia: Non-genotoxic mechanisms. Toxicol. Lett. 64/65:397-408.
[8] Liu et al (1995). Alteration of thyroid hormone homeostasis by UDP-glucuronosyltransferase inducers in rats: A dose-response study. J. Pharmacol. Exp. Ther. 273:977-985.

enzymes for the Substance [redacted] study ongoing) and the analogue substance [redacted]; data provided in IUCLID 7.8.1 and in the comments), with an expectation that the the results of liver enzyme induction between [redacted] and [redacted] will be highly concordant. To justify the read-across from [redacted] you refer to the read-across justification document in IUCLID Section 13.

Based on the above, you argue that the thyroid-related changes indicate a non-adverse adaptive set of changes that are not human relevant, but rather a reflection of quantitative differences in thyroid homeostasis and function between rats and humans. In addition, you consider the changes in LDL and HDL to be non-adverse.

Firstly, ECHA notes that the effects on the thyroid outlined in your proposed MoA are adverse in the rat; they ultimately result in thyroid cancer[6].

Secondly, the non-human relevance argumentation applies to the ultimate adverse outcome, i.e. carcinogenicity[6]. Following sustained substance-induced reduced TH levels (irrespective of cause), and a compensatory increase in THS levels, rats ultimately develop thyroid cancer. However, this adverse effect can be considered not relevant to humans if it can be demonstrated that it is caused by liver enzyme induction due to quantitative differences in thyroid homeostasis and function between rats and humans.

ECHA wants 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, 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[9]. 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 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 TH synthesis should also be excluded, e.g. by evaluating *in vitro* the potential for inhibition of the sodium–iodide symporter and thyroid peroxidase.

ECHA emphasises 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.

Regarding point 1., ECHA notes that existing studies have investigated TSH, T3 and T4 levels.

[9] 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.

Regarding point 2., you indicate that a study comparing liver enzyme induction in rats between [redacted] (i.e. the Substance) and the analogue substance [redacted] is ongoing and that the results are expected by August 2020. As explained in the notification letter to the draft decision, ECHA does not take dossier updates into account after the notification of the draft decision, and notes that by end of 2020 this information has not been provided. This information may be useful to support read-across within the category outlined in the read-across justification as it allows comparison of the toxicity profile of some of the category members. However, data on liver enzyme induction of [redacted] becomes redundant once the results with the Substance-specific data become available. Therefore, ECHA have not assessed the proposed read-across in detail. The data on [redacted] indicate liver enzyme induction in the rat. 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.

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[10]. 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 (DNT).

Existing information on the Substance itself derived from available OECD TG 408 study shows evidence of thyroid disruption as indicated further above under 'Extension of Cohort 1B'.

In the document attached to IUCLID section 7.8.1 you question the human relevance of these findings, as well as the link between thyroid hormones and function, and neurodevelopmental outcomes.

As explained above, you have not provided substance-specific data which would provide proof that the observed thyroid-related effects would not be relevant to humans. Therefore, these effects are to be regarded as relevant to humans.
Furthermore, according to the ECHA/EFSA Guidance for the identification of endocrine disruptors[4], '*Substances inducing histopathological changes (i.e. follicular cell hypertrophy*

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

and/or hyperplasia and/or neoplasia) in the thyroid, with or without changes in the circulating levels of THs, would pose a hazard for human thyroid hormone insufficiency in adults as well as pre- and post-natal neurological development of offspring'.

In your comments to the draft decision, you provided several lines of arguments, questioning the plausibility of the link leading from liver enzyme induction to reductions in maternal serum TH levels and ultimately to child neurodevelopmental impairment in humans. You concluded that '*Using a weight of evidence approach and incorporating read-across principles, the addition of Cohorts 2A and 2B are not scientifically justified, and hence should not be included in the study design*.' ECHA has evaluated and weighed these arguments as addressed below.

As explained above under '*Extension of Cohort 1B*', you have not provided the information needed to conclude on whether or not there are qualitative and quantitative differences in TH homeostasis between rats and humans following exposure to the Substance, nor have you provided any information which excludes other possible MoAs.

In this context you refer to a study on fipronil which assessed thyroid function in 159 workers (Herin, 2011[11]). Fipronil is known to cause liver enzyme induction. You state that chronic occupationl exposure to fipronil in this study did not show an increase in thyroid abnormalities. ECHA notes that epidemiological studies are to be considered as supportive evidence for the evaluation of whether a substance is likely to have adverse effects for humans. However, they cannot be used to override or dismiss evidence of adversity found in laboratory studies, nor can they replace laboratory studies[4].

The basic physiological processes regulating TH synthesis and release are qualitatively similar across species. The TH system is to be regarded as a network of interconnected MoAs which share the intermediate key events, e.g. reduced serum TH levels. However, there are quantitative species-specific differences[12]. Therefore, the relationship between changes in circulating THs, including the ones mediated by differences in metabolism, and downstream adverse effects are very complex and additional elements, for example species-specific metabolic capacity and age specific differences in sensitivity, have to be taken into consideration. Therefore, species differences in the sensitivity of specific neurodevelopmental outcomes as a result of Substance-induced changes of circulating levels of THs during gestation and early post-natal development cannot be ruled out at this time.

You argue that there is no established link between liver enzyme induction through reduced maternal serum TH levels to neurodevelopmental impairment in humans. The nature and severity of any adverse effects depends on the lifestage exposed. Reduced TH levels in the mother may be reversible in nature, however, for the developing foetus which is dependent on maternal TH for its brain development the effects are irreversible. As stated above, the thyroid MoAs are an interconnected network that share intermediate key events; one of these events is reduced TH levels. The fact that there is a different non-human relevant MoA leading to cancer in rats is not relevant in this context. Irrespective of cause, reduced TH levels during critical windows of development will cause developmental neurotoxicity.

You consider that the only molecular initiating event related to adverse outcomes in neurodevelopment in mammals is direct inhibition of thyroperoxidase (AOP 42 in the AOP Wiki[13]). AOPs are linear in nature, starting with a molecular initiating event and ending in an adverse outcome. Also the non-human relevant MoA in your comments can be visualised as

[11] Herin F et al. (2011) Thyroid function tests in persons with occupational exposure to fipronil. Thyroid. 21:701–706
[12] Janssen and Janssen (2017) Directional thyroid hormone distribution via the blood stream to target sites. Mol Cell Endocrinol. 458:16-21.
[13] https://aopwiki.org/aops/42

a linear AOP, starting with liver enzyme induction and ending in cancer. As stated above, both these AOPs are part of a larger thyroid related AOP/MoA network which share a intermediate key event; i.e. reduced TH levels. Another example is iodine deficiency, too little iodine in the diet impair thyroglobulin synthesis resulting in reduced TH levels and adverse outcome(s). Any mechanism which caused the common intermediate key event, i.e. reduced TH levels have the capacity to cause any of the subsequent adverse outcomes.

Finally, you refer to a publication which summarises current testing strategies on rodent models and discusses new approaches for evaluation the developmental neurotoxicity of thyroid disruptors[14]. ECHA agrees that there are uncertainties in all test systems; however, uncertainties in the test method is not a reason not to test. In addition, you raise the fact that serum T3 and/or T4 does not necessarily correlate with thyroid activity within tissues; this is clinically referred to as peripheral hypothyroidism. ECHA fails to understand why peripheral hypothyroidism is relevant in this case. THs are released form the thyroid gland mainly as T4 which is then de-iodinised to the more potent T3 in peripheral tissues where TH exerts its action. If there are defects in TH metabolism, transport and/or receptor signalling in a peripheral tissue then this tissue may appear resistant to TH action despite the fact that serum T3/T4 are in the normal range.

In this case, the OECD TG 408 study with the Substance shows clear indications of thyroid disruption; i.e. changes in histopathology and changes in T3, T4 and TSH supported by changes in LDL and HDL (cholesterol synthesis is primarily regulated by THs). This pattern of effects can be summarised as systemic hypothyroidism. According to the ECHA Guidance R.7a, Appendix R.7.6-2, such signs of thyroid toxicity constitute particular concern related to developmental neurotoxity (Annex X, Column 2 of Section 8.7.3).

Based on the above, ECHA considers that adverse neurodevelopmental outcomes as a result of Substance-induced changes of circulating levels of THs during gestation and early post-natal development cannot be ruled out at this time.

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 the developmental neurotoxicity cohorts 2A and 2B.

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

Species and route selection

The study must be performed in rats with oral[15] administration.

Further expansion of the study design

No triggers for the inclusion of Cohort 3 (developmental immunotoxicity) were identified. However, you may expand the study by including 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 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[16].

[14] O'Shaughnessy KE and Gilbert ME. (2019). Thyroid disrupting chemicals and developmental neurotoxicity – New tools and approaches to evaluate hormone action. Mol and Cell Endocrin in press, corrected proof: https://doi.org/10.1016/j.mce.2019.110663
[15] ECHA Guidance R.7a, Section R.7.6.2.3.2.
[16] ECHA Guidance R.7a, Section R.7.6.

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[17].

B. Test material

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 the careful identification and description of the characteristics of the Tests Materials in accordance with OECD GLP (ENV/MC/CHEM(98)16) and EU Test Methods Regulation (EU) 440/2008 (Note, Annex), namely all the constituents must be identified as far as possible as well as their concentration. Also any constituents that have harmonised classification and labelling according to the CLP Regulation must be identified and quantified using the appropriate analytical methods.

With that detailed information, ECHA can confirm 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[18].

[17] https://echa.europa.eu/practical-guides
[18] 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.

On 14 October 2016 ECHA issued decision CCH-D-2114342397-45-01/F.

On 18 June 2018 and 31 July 2018 the registrant updated the dossier. ECHA assessed the information provided and concluded that the information did not comply with the information requirement addressed in the compliance check decision.

On 25 September 2019 ECHA issued decision CCH-D-2114482409-39-01/F according to Article 42(1) of the REACH Regulation.

On 8 April 2020 and 13 May 2020 the registrant updated the dossier and provided a sub-chronic toxicity study (90-day).

On 29 May 2020 ECHA informed the registrant that the request for an EOGRT study was withdrawn and would be addressed in this separate decision.

The compliance check of the information requirement for an extended one-generation reproductive toxicity study was initiated on 1 June 2020.

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

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

As no amendments were proposed, ECHA adopted the decision under Article 51(3) of REACH.

Appendix D: List of references - ECHA Guidance[19] 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)[20]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[20]

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[21]

[19] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[20] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[21] 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]

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.