EUROPEAN CHEMICALS AGENCY

Helsinki, 11 February 2020

Addressee
Registrant of [redacted] listed in the last Appendix of this decision

Date of submission for the jointly submitted dossier subject of this decision
12/05/2017

Registered substance subject to this decision, hereafter 'the Substance'
Substance name: Polysulfides, di-tert-dodecyl
EC number: 270-335-7
CAS number: 68425-15-0

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 ***18 August 2021.***

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

1. Skin sensitisation (Annex VII, Section 8.3.):

   - i) *in vitro/in chemico* skin sensitisation information on molecular interactions with skin proteins (OECD TG 442C), inflammatory response in keratinocytes (OECD TG 442D) and activation of dendritic cells (OECD TG 442E) (Annex VII, Section 8.3.1.) with the Substance; and
   - ii) *in vivo* skin sensitisation (Annex VII, Section 8.3.2.; test method: EU B.42./OECD TG 429) with the Substance, in case the *in vitro/in chemico* test methods specified under point i) are not applicable for the Substance or the results obtained are not adequate for classification and risk assessment

2. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.; test method EU C.3./OECD TG 201) with the Substance.

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

1. Transgenic rodent somatic and germ cell gene mutation assays (Annex IX, Section 8.4., column 2; test method: EU B.58/OECD TG 488) in transgenic mice or rats, oral route on the following tissues: liver and glandular stomach with the Substance; duodenum must be harvested and stored for up to 5 years. Duodenum must be analysed if the results of the glandular stomach and of the liver are negative or inconclusive.

   OR

   In vivo mammalian alkaline comet assay (Annex IX, Section 8.4., column 2; test method: OECD TG 489) in rats, oral route, on the following tissues: liver, glandular stomach and duodenum with the Substance.

Conditions to comply with the requested information

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

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

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

Appeal

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

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

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

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

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

1. Skin sensitisation (Annex VII, Section 8.3.);

Skin sensitisation is a standard information requirement under Annex VII. Registrants must submit information allowing a conclusion whether the substance is a skin sensitiser and whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A), and risk assessment, where required.[2]

You have provided the following key study in your dossier: Guinea Pig Maximisation Test (1986).

To fulfil the information requirement, the study has to meet the requirements of OECD TG 406 (1981 and/or 1992). The key parameters of this test guideline include:

a) Positive control to establish the sensitivity and reliability of the experimental technique (OECD TG 406, paragrapgh 11), and
b) Selection of challenge concentration: The concentration used for challenge should be the highest non-irritant concentration (OECD TG 406, paragraph 14).

   In case results from the first challenge needs to be clarified (e.g., dose selected for challenge exposure was too high), a rechallenge with naïve control animals should be considered (OECD TG 406, paragraph 24).

The reported study does not comply with these key parameters for the following reasons:

a) Information on positive control group to establish the sensitivity and reliability of the study is missing,
b) Positive reactions were noted in the negative control group where 50% or 33% of animals showed positive reactions 24h or 48h after challenge, respectively. This shows that the dose selected for challenge exposure was too high but no rechallenge to clarify the results were provided.

Therefore, the information provided does not cover the key parameters required by OECD TG 406. Consequently, the information requirement is not fulfilled, and your conclusion that the Substance does not cause skin sensitisation is rejected.

Further information on the Testing and assessment strategy for skin sensitisation can be found in ECHA guidance R.7a, Section R.7.3.7.

In your comments on the initial draft decision you explain that "The registered substance is an UVCB with an extremely low water solubility (0.00026 µg/mL at 20°C) and a high log Kow value (>6.5), consequently the OECD TG 442C, 442D and 442E are not applicable. Therefore, the registrant propose to perform directly a LLNA assay (OECD TG 429)". A justification for not performing an *in vitro* test needs to be included in your updated dossier.

2. Growth inhibition study aquatic plants (Annex VII, Section 9.1.2.)

[2] ECHA Guidance Chapter R.7a, Section R.7.3.7.2

Growth inhibition study aquatic plants is a standard information requirement in Annex VII to REACH.

You have provided a key study (2000) and a supporting study (2010) with the Substance based on OECD TG 201.

We have identified this information and identified the following deficiency(ies):

Tests on substances must be conducted in accordance with OECD test guidelines or another recognised international test method (Article 13(3) of REACH).

The OECD TG 201, and the OECD GD 23, require(s) that the following conditions are met (among others):

- Analytical monitoring of exposure concentrations.
- If an analytical procedure for determination of the test substance in the concentration range used is available, the test solutions should be analysed to verify the initial concentrations and maintenance of the exposure concentrations during the test (see OECD TG 201, paragraph 36) .
- Chemical analysis to demonstrate attainment of equilibrium in WAF preparation and stability during the conduct of the test (see OECD Guidance 23, paragraph 150).
- Exposure concentrations should be confirmed and their stability demonstrated by analysis unless the dissolved concentration is less than the limit of quantification of the most sensitive analytical method (see OECD Guidance 23, paragraph 162).
- Effect concentrations based on the measured values rather than nominal values unless the test concentrations are maintained within 20% of the measured initial concentrations throughout testing (see OECD TG 201 paragraph 39 and ECHA Guidance R7B, section R.7.8.4.1).

The Substance (reported solubility: 0.26 ug/L) is considered poorly water soluble.

For the supporting study (2010), you did not perform any analytical monitoring of exposure concentrations and and therefore you did not demonstrate the presence of the Substance in test medium.

For the key study (2000), you have used the WAF preparation for poorly soluble substances under OECD GD 23. In this study, the saturation concentration of the test substance was below the detection limit of the analytical method used (HPLC). Therefore you did not demonstrate the attainment of equilibrium in WAF preparation, presence of the Substance in the test medium (i.e. initial concentration), compositional stability and maintenance of exposure concentrations. In addition, you have not demonstrated that the method used is the most sensitive method available for the detemination of the Substance in the concentration range used in the test. However, you have demonstrated in long-term studies on the Substance (OECD TG 211 and 210, 2016) that analytical procedure (i.e. UPLC-MS/MS) for determination of the test substance in the concentration range used is available.

The above conditions are not met, therefore the information provided does not fulfil information requirement. In particular, for the key study, the analytical method is not sensitive enough considering the solubility of the Substance, while more sensitive methods exist (i.e. UPLC-MS/MS), as was used for the long term tests on the Substance in the registration dossier (OECD TG 210 and OECD TG 211, 2016).

Therefore, the data provided is rejected and the information requirement is not fulfilled.

In your comments on the draft decision you provide further information explaning why you believe that there is no need to perform an additional OECD TG 201 test on the Substance.

The new information and your argumentation can be summarised as follows:

- The most suitable analytical method at the time (HPLC) was used in the key study and the detection limit of the method (80 µg/L) was far above the predicated water solubility of the Substance. Thus the condition layed out in paragraph 162 in the OECD GD 23 is met.
- The WAFs were directly transferred from the bottles to the test flasks without any filtering or any other process. In addition, long-term daphnia and fish studies confirms that the Substance stayed relatively stable over a two-day period. As the Substance is considered vP and not volatile, loss from the test solution can be ruled out. Therefore, it is clear that the algae were exposed to the Substance during the experiment. Thus according to paragraph 163 of the OECD DG 201, the effect concentration can be expressed based on the nominal concentrations.
- Based on above, the studies submitted meet the information requirement despite the lack of analytical measurements of the tested concentrations.

ECHA agrees with your line of justification outlined above in your comments. ECHA considers that an update of your registration with the information provided in your comments will enable ECHA to consider your registration compliant with this REACH information requirement. We therefore advise you to update the technical registration dossier with this information. ECHA will then check, and confirm, the compliance of the information in the follow-up evaluation of the updated registration, which ECHA will initiate after the expiry of the deadline set by this decision.

In addition, you propose to waive this endpoint based on an adaptation of Annex VII, Column 2 to REACH. Your justification is based on the facts that:

- The Substance is shown to be highly insoluble in water (0.26 µg/L);
- The Substance is unlikely to cross the biological membrane (demonstrated by the results of the OECD TG 305 study as well as the high logkow (12.5 according to Kowwin).

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

In accordance with 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-IX to REACH.

1. **Transgenic rodent somatic and germ cell gene mutation assays (Annex IX, Section 8.4., column 2)**
   OR
   In vivo mammalian alkaline comet assay (Annex IX, Section 8.4., column 2)

Under Annex IX to REACH, the information requirement for an appropriate in vivo somatic cell genotoxicity study is triggered if there is a positive result in any of the in vitro genotoxicity studies in Annex VII or VIII and there are no appropriate results already available from an in vivo somatic cell genotoxicity study.

You have provided the following studies with the Substance in your dossier:

- An OECD TG 471 study
- An OECD TG 473 study
- An OECD TG 476 study (2010)
- An OECD TG 474 study (2010)

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

Your dossier contains positive results for the *in vitro* gene mutation study in mammalian cells, which raise the concern for gene mutation.

The *in vivo* study provided is addressing cytogenicity and not addressing the gene mutation concern raised by the *in vitro* data. Therefore, the provided *in vivo* test is not appropriate.

You concluded that "*Di-tert-dodecyl polysulfides (TPS 32) induced a biologically significant mutagenic activity being demonstrated at the TK locus in L5178Y mouse lymphoma cell culture either with or without metabolic activation, in two independent assays. The clear increase in the number of small colonies is in favour of a clastogenic activity".*

However, the trigger for the *in vivo* study is met, there is no waiver available under column 2 of the relevant REACH section and you have not provided any adaptation under Annex XI of REACH. In any case, you indicate that the information available "is in favour of a clastogenic activity", so no conclusion can be drawn. Further, an increase in the number of small colonies does not exclude a gene mutation effect.

In your comments on the initial draft decision you provided figures presenting results on the increase in small and large colonies and mutation frequency in the *in vitro* gene mutation study in mammalian cells included in your dossier. These details were not available in the registration dossier submission assessed for this compliance check procedure and hence could not be considered for the compliance of it at this stage. We advice you to update your registration should you consider this relevant for the follow-up evaluation. However, ECHA agrees that the data show that the substance induces mainly an increase in small colonies. However, a slight increase in large colonies is observed in the second assays (with and without S9), which was not observed in the first assays. ECHA considers that the increase in large colonies cannot be explained by a mechanism involving exclusively clastogenicity. Moreover,

the chromosomal aberration test (OECD TG 473) that is optimised to detect structural chromosomal aberrations, i.e. clastogenic effects, was clearly negative. This result is not consistent with your claim that the Substance induces clastogenicity.

In addition, it is noted that strong alkylating agents (e.g. MMS) tested in the mouse lymphoma assay (new OECD TG 490 since 2016) are known to induce an increase in both small and large colonies. This demonstrates that chemicals inducing high levels of gene mutation can also induce small colonies (such substances induce the mutation of both the TK gene and of the gene responsible for modulating the cell growth cycle – small colonies are growing more slowly than non-mutated cells).

In your comments you refer to ECHA Guidance Chapter R.7a[4] and Figure R.7.7-1 therein. Your interpretation of the negative result in the 1st in vivo test was that no further testing is needed and the Substance is not genotoxic. However, as stated in ECHA Guidance Chapter R.7a[4], "*The 2nd in vivo test should only be performed if this test is required to make a conclusion on the genotoxicity of the substance under investigation*". As discussed above, the mechanism leading to mutations in the *in vitro* study remains unclear. To make a conclusion on the genotoxicity of the Substance, the positive results in the *in vitro* gene mutation study in mammalian cells need further investigations and therefore you are requested to perform a second *in vivo* test.

Study selection and study design

According to the ECHA Guidance Chapter R.7a[3], the transgenic rodent somatic and germ cell gene mutation assays ("TGR assay", OECD TG 488) and the in vivo mammalian alkaline comet assay ("Comet assay", OECD TG 489) are suitable to follow up a positive in vitro result on gene mutation. Therefore, the TGR and the comet assay are suitable tests to follow up the concern on gene mutation for the Substance.

In case you decide to perform the comet assay according to the test method OECD TG 489, the test must be performed in rats. Having considered the anticipated routes of human exposure and adequate exposure of the target tissue(s) performance of the test by the oral route is appropriate.

In line with the test method OECD TG 489, the test must be performed by analysing tissues from liver as primary site of xenobiotic metabolism, glandular stomach and duodenum as sites of contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the Substance, and probable different local absorption rates of the Substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to analyse both tissues to ensure a sufficient evaluation of the potential for genotoxicity at the site of contact in the gastro-intestinal tract.

In case you decide to perform the TGR assay, according to the test method EU B.58/OECD TG 488, the test must be performed in transgenic mice or rats and the Substance is usually administered orally.

According to the test method EU B.58/OECD TG 488, the test must be performed by analysing tissues from liver as slowly proliferating tissue and primary site of xenobiotic metabolism, glandular stomach and duodenum as rapidly proliferating tissue and site of direct contact. There are several expected or possible variables between the glandular stomach and the duodenum (different tissue structure and function, different pH conditions, variable physico-chemical properties and fate of the Substance, and probable different local absorption rates

[3] ECHA Guidance Chapter R.7a, Section R.7.7.6.3

of the Substance and its possible breakdown product(s)). In light of these expected or possible variables, it is necessary to analyse both tissues to ensure a sufficient evaluation of the potential for mutagenicity at the site of contact in the gastro-intestinal tract. However, duodenum must be stored (at or below −70 °C) until the analysis of liver and glandular stomach is completed; the duodenum must then be analysed only if the results obtained for the glandular stomach and for the liver are negative or inconclusive.

Germ cells

A subsequent germ cell genotoxicity study (TGR/OECD TG 488, or CA on spermatogonia/OECD TG 483) may still be required under Annex IX of REACH, in case 1) an *in vivo* genotoxicity test on somatic cell is positive, and 2) no clear conclusion can be made on germ cell mutagenicity.

Therefore, in case you decide to perform the comet assay, you may consider to collect the male gonadal cells collected from the seminiferous tubules (as described by e.g. O'Brien *et al.*[4]) in addition to the other aforementioned tissues, as it would optimise the use of animals. You can prepare the slides for male gonadal cells and store them for up to 2 months, at room temperature, in dry conditions and protected from light. Following the generation and analysis of data on somatic cells, in accordance to Annex IX, Section 8.4., column 2, you should consider analysing the slides prepared with gonadal cells. This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

In case you decide to perform the TGR, you // Therefore, you // You may consider to collect the male germ cells at the same time as the other tissues, in order to limit additional animal testing. According to the OECD 488 the tissues (or tissue homogenates) can be stored under specific conditions and used for DNA isolation for up to 5 years (at or below −70 °C). Following the generation and analysis of data on somatic cells, in accordance to Annex IX, Section 8.4., column 2, you should consider analysing the collected germ cells. This type of evidence may be relevant for the overall assessment of possible germ cell mutagenicity including classification and labelling according to the CLP Regulation.

[4] O'Brien, J.M., Beal, M.A., Gingerich, J.D., Soper, L., Douglas, G.R., Yauk, C.L., Marchetti, F. (2014) Transgenic Rodent Assay for Quantifying Male Germ Cell Mutant Frequency. J. Vis. Exp. (90), e51576, doi:10.3791/51576

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Appendix C: Procedural history

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

The compliance check was initiated on 02 October 2018.

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

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

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

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

Appendix D: Observations and technical guidance

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

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

3. Test guidelines, GLP requirements and reporting

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

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

   Under Article 10 (a) (vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide: 'How to report robust study summaries'[5].

4. Test material

   Selection of the test material
   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. Any constituents that have harmonised classification and labelling according to the CLP Regulation (Regulation (EC) No 1272/2008) must be identified and quantified using the appropriate analytical methods.

   The OECD Series on Principles of Good Laboratory Practice and Compliance Monitoring, Number 11 [ENV/MC/CHEM(98)16] requires a careful identification of the test material and description of its characteristics. In addition, the Test Methods Regulation (EU) 440/2008, as amended by Regulation (EU) 2016/266, requires that "*if the test method is used for the testing of a* [...] *UVCB* [...] *sufficient information on its composition should be made available, as far as possible, e.g. by the chemical identity of its constituents, their quantitative occurrence, and relevant properties of the constituents*".

   In order to meet this requirement, all the constituents/group of constituents of the test material used for each test must be identified as far as possible. For each constituent/group of constituents the concentration value in the test material must be reported in the Test material section of the endpoint study record.

   Technical Reporting of the test material for UVCB substances
   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/group of constituents of the test material and their concentration values.

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

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" on the ECHA website[6].

5. Environmental testing on UVCB substances

The purpose of the environmental hazard assessment under REACH is to perform the PBT assessment, to determine classification and labelling of the Substance and to perform the risk assessment (e.g. for PNEC derivation).

Your Substance is a complex UVCB and, as indicated in the ECHA Guidance R.11, to fulfil information requirements for persistency, bioaccumulation and aquatic toxicity, you need to consider the following approaches:
- The "known constituents approach" (by assessing specific constituents), or
- The "fraction/block approach, (performed on the basis of fractions/blocks of constituents), or
- The "whole substance approach", or
- various combinations of the approaches described above.
The selection of the proper approach depends on the purpose of the study and the ability to characterise the Substance i.e. knowledge of constituents and/or fractions of the Substance and differences in the properties amongst them.

Use of Water Accommodated Fraction (WAF) approach for ecotoxicity testing
Before conducting the requested test[s] (x-z) you are advised to consult ECHA Guidance R.11 (Section R.11.4.2.2), R7b (Table R.7.8-3 and Appendix R.7.9-4) and the OECD GD 23 [ENV/JM/MONO(2000)6/REV1] on conducting and reporting the results of ecotoxicity test(s) on difficult to test substances.

If you elect to use the Water Accommodated Fraction (WAF) approach in your ecotoxicity tests, you must conduct chemical analyses of the WAF and the test medium. The following key information must be reported:
- Identity of those constituents to which the test organisms are exposed.
- A demonstration that equilibrium has been obtained in the WAF.
- A demonstration of stability in the exposure concentrations during the conduct of the test.
- Full description of the method used to prepare the WAF.
- Test results expressed in terms of measured concentrations, unless you can demonstrate that exposure concentrations remain within ±20% of the initial loading rate.
In order to be able to provide the above you should:
- Carefully consider and choose the analytical methods relevant for your substance.
- Choose a method for preparing the WAF that is consistent with the conditions applied during the conduct of the test (including e.g. the use of co-solvents or the stirring methods).
If it is not possible to provide the above information when using the WAF approach you should consider the use of newer techniques (e.g. passive dosing) as noted in the revised OECD GD 23 that may be better suited for your Substance.

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

[6] https://echa.europa.eu/manuals

[7] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment

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

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

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

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

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

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

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

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

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

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

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

OECD Guidance documents[9]
Guidance Document on aqueous-phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD23.
Guidance Document supporting the OECD TG 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD151.

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

Appendix E: 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.