EUROPEAN CHEMICALS AGENCY

Helsinki, 07 February 2020

**Addressees**
Registrants of JS_25584-83-2 listed in the last Appendix of this decision

**Date of submission for the jointly submitted dossier subject of this decision**
22/02/2019

**Registered substance subject to this decision, hereafter 'the Substance'**
Substance name: Acrylic acid, monoester with propane-1,2-diol
EC number: 247-118-0
CAS number: 25584-83-2

**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 ***16 May 2022***.

### A. Requirements applicable to 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) in rats, oral route, with the Substance, specified as follows:

   - **Ten weeks premating exposure duration for the parental (P0) generation;**
   - **Dose level setting shall aim to induce systemic toxicity at the highest dose level;**
   - **Cohort 1A (Reproductive toxicity);**
   - **Cohort 1B (Reproductive toxicity) without extension to mate the Cohort 1B animals to produce the F2 generation; 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.

### Conditions to comply with the requests

Each addressee of this decision is bound by the requests for information corresponding to the REACH Annexes applicable to their own registered tonnage of the Substance at the time of evaluation of the jointly submitted dossier.

To identify your legal obligations, please refer to the following:

i. 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 states 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.

**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.

Approved[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 X of REACH**

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

1. **Extended one-generation reproductive toxicity study (Annex X, Section 8.7.3.)**

The basic test design of an Extended one-generation reproductive toxicity (EOGRT) study (OECD TG 443) is a standard information requirement under Annex X to REACH. Furthermore Column 2 of Section 8.7.3. defines when the study design needs to be expanded.

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

You have provided a read-across justification document in IUCLID Section 13.

You predict the properties of the Substance from two structurally similar substances (i.e. source substances):

i. acrylic acid, CAS no. 79-10-7
ii. methyl acrylate, CAS no. 96-33-3.

The source studies that you have used in your read-across approach are, respectively

i. Two-generation reproductive toxicity study in rats, [redacted] 1994 / [redacted] 1997 performed according to the OECD TG 416, oral route, GLP, test material purity not reported
ii. Two-generation reproductive toxicity study in rats, [redacted] 2009, performed according to the OECD TG 416, inhalation route, GLP, test material purity 99.9%.

In your comments, you indicate a test material purity of >98.9% for study (i) above. However, the test material purity is not reported in the technical dossier.

As further support, you have also provided a continuous breeding study in mice (Morrisey 1989) conducted with propylene glycol (i.e. 1,2-Propanediol), CAS No. 57-55-6.

You have provided the following reasoning for the prediction of toxicological properties: "*The target chemical hydroxypropyl acrylate (CAS no. 25584-83-2) and its analogue chemicals 2-hydroxyethyl acrylate (CAS no. 818-61-1), acrylic acid (CAS no. 79-10-7), and methyl acrylate (CAS no. 96-33-3) have a similar molecular structure, i.e. all substances are acrylates. In addition, hydroxypropyl acrylate and 2-hydroxyethyl acrylate contain an alcohol group which only differs in the length of the alcohol being either a propyl or an ethyl. The functional groups of the compounds are the acrylate and, where applicable, the alcohol group. The difference in length of the backbone is toxicologically of lesser importance. In addition, metabolism of the target and source chemicals will be similar. Finally, the substances have similar physico-chemical and toxicological properties.*"

ECHA understands that your read-across justification document intends to cover several endpoints. For the endpoint Reproductive toxicity, more specifically the Extended one-generation reproductive toxicity (EOGRT) study, you propose to use information from the source substances acrylic acid (CAS no. 79-10-7) and methyl acrylate (CAS no. 96-33-3), supported by information from propylene glycol (1,2-Propanediol, CAS no. 57-55-6). In your read-across document you explain that for the source substance 2-hydroxyethyl acrylate (CAS

no. 818-61-1) there is no relevant information available for fertility.

Furthermore, ECHA understands that you predict the properties of the Substance using a read-across hypothesis which is based on the formation of common (bio)transformation products: the Substance and source substance methyl acrylate form a common (bio)transformation product, acrylic acid. Acrylic acid itself is also used as a source substance. The supporting data from propylene glycol represents information on another, non-common (bio)transformation product of the Substance. Overall, your read-across hypothesis assumes that the different compounds have the same type of effects, i.e. you conclude that the information gives no indication of a fertility impairing effect. The properties of your Substance are predicted to be quantitatively equal to those of the source substances.

Annex XI, Section 1.5. specifies two conditions which must be fulfilled whenever a read-across approach is used. Firstly, there needs to be structural similarity between substances which results in a likelihood that the substances have similar physicochemical, toxicological and ecotoxicological properties so that the substances may be considered as a group or category. Secondly, it is required that the relevant properties of a substance within the group may be predicted from data for reference substance(s) within the group.

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

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

A. Existing data on the Substance contradicts with the hypothesis

Annex XI, Section 1.5. provides that "substances whose physicochemical, toxicological and eco-toxicological properties are likely to be similar or follow a regular pattern as result of structural similarity may be considered as a group or 'category' of substances. The ECHA Guidance[2] indicates that "*it is important to provide supporting information to strengthen the rationale for the read-across*". The set of supporting information should allow to verify the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s). The observation of differences in the toxicological properties between the source substance(s) and the Substance is a warning sign. An explanation for such a difference resulting in a contradiction between the similarities in properties claimed in the read-across hypothesis and the observation of different properties needs to be provided and supported by scientific evidence.

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar target and source substances cause the same type of effect(s).

You have provided a sub-chronic toxicity study (OECD TG 408) and a combined repeated dose toxicity study with the reproduction/developmental toxicity screening test (OECD TG 422) with the Substance.

The sub-chronic toxicity study (OECD TG 408) conducted with the Substance showed effects in several organs. In particular, the effects observed in thymus indicate immunotoxicity, which is a particular concern for developmental immunotoxicity (for details, see *Specifications for the study design* section below).

[2] Guidance on information requirements and chemical safety assessment, Chapter R.6, Section R.6.2.2.1.f

The studies provided for the source substances that are mentioned further above did either not examine thymus effects (acrylic acid), or did not show any thymus effects (methyl acrylate).

In your comments you do not agree with ECHA's argumentation and suggest that the decrease in thymus weights in females in the OECD TG 408 study with the Substance is a biologic variation and does not suggest immunotoxicity. As explained in the *Specifications for the study design* section below, a decrease in size (weight) of the lymphoid organs, e.g. thymus, is often the first manifestation of (immuno)toxicity. Hence the available data indicates differences in the toxicological properties of the source and target substances.

Furthermore, you also consider that your read-across approach is strengthened by the sensitising properties of other acrylates such as methyl acrylate and butyl acrylate which have not shown reproductive toxic effects.

Sensitising properties of other acrylates does not support your read-across approach for reproductive toxicity: toxicological similarity in one or multiple endpoints does not necessarily lead to predictable or similar human health properties in other endpoints.

The available set of data on the target and source substances indicates differences in the toxicological properties of the substances. This contradicts your read-across hypothesis whereby the structurally similar target and source substances cause the same type of effect(s). You have not demonstrated and justified that the properties of the source substance(s) and of the Substance are likely to be similar despite the observation of these differences. Therefore, you have not provided sufficient supporting evidence to comply with the requirements of Annex XI, 1.5.

B. Missing information on common/non-common compounds

As indicated under A, supporting information should allow verification of the crucial aspects of the read-across hypothesis and establish that the properties of the Substance can be predicted from the data on the source substance(s).

Supporting information must include toxicokinetic information on the formation of the common compound and/or bridging studies to compare properties of the Substance and source substances, and information on the impact of exposure to the non-common compounds on the prediction.

*B1. Missing information on the formation of common compound*

As indicated above, your read-across hypothesis is based on the (bio)transformation of the Substance and of the source substance(s) to a common compound(s). In this context, information characterising the rate and extent of the (bio)transformation of the Substance and of the source substance(s) is necessary to confirm the formation of the proposed common (bio)transformation product and to assess the impact of the exposure to the parent compounds.

You have not provided any experimental data or other adequate and reliable information about the rate and extent of the (bio)transformation of the source substance methyl acrylate. Furthermore, the toxicokinetics study on the Substance [redacted] 2017) does not address the formation of the proposed common compound acrylic acid.

In your comments you explain that even though the toxicokinetics study on the Substance ([redacted] 2017) measured only the formation of propylene glycol as the ester hydrolysis product, equimolar amounts of acrylic acid has to be formed and therefore the formation of acrylic acid was '*indirectly assessed*'. ECHA acknowledges that the formation of acrylic acid in this study is indirectly addressed.

You also provide *in vitro* hydrolysis data of the Substance and the analogue substance 2-hydroxyethyl acrylate, and information on *in vivo* metabolism of the analogue substance 2-hydroxyethyl acrylate. You conclude that "*Overall, these in vitro metabolism results imply that the acrylate esters can be quickly metabolized through hydrolysis to AA and/or glutathione conjugation in vivo.*". You further refer to the read-across justification document provided in the dossier for further information "*showing that methyl acrylate follows the same metabolic elimination pathways.*"

As explained above, for the analogue substance 2-hydroxyethyl acrylate there is no relevant information available for fertility, and this substance is not part of your read-across approach to address the endpoint Reproductive toxicity. Furthermore, the hydrolysis data of 2-hydroxyethyl acrylate does not provide adequate and reliable information about the rate and extent of the (bio)transformation of the source substance methyl acrylate.

In the absence of this information, you have not provided supporting evidence establishing that the proposed common (bio)transformation product is formed at a similar rate, as assumed in your read-across hypothesis. Therefore, you have not provided sufficient supporting information to strengthen the rationale for the read-across.

*B2. Missing information on the impact of non-common compounds: Adequacy and reliability of the study*

As indicated above, your read-across hypothesis is based on the (bio)transformation of the Substance and of the source substance(s) to a common compound(s). In this context, exposure to the Substance and of the source substance(s) may also lead to exposure to other compounds than the common compound of interest. The impact of exposure to these non-common compounds on the prediction of properties of the target needs to be assessed to ensure that a reliable prediction can be made.

According to Annex XI, Section 1.5., if the grouping concept is applied then in all cases the results to be read across should e.g:

- have adequate and reliable coverage of the key parameters addressed in the corresponding test method referred to in Article 13(3); in this case OECD TG 443
- adequate and reliable documentation of the applied method shall be provided.

You have provided a toxicokinetic study on the Substance ([redacted] 2017), which shows that the major systemic metabolite of the Substance is propylene glycol.

You have provided a study conducted with propylene glycol, which you have used to support your read-across approach: a continuous breeding study in mice (Morrisey 1989) provides information on fertility parameters in multi-generation studies. You have included this supporting study to prove that the non-common compound propylene glycol is "*of negligible concern for reproductive toxicity in humans*".

According to the provisions of Annex X, Section 8.7.3., information on Extended one-generation reproductive toxicity study as specified in the OECD TG 443 shall be provided.

The supporting information with propylene glycol does not provide an adequate and reliable coverage of the key parameters expected to be investigated in a study performed according to the OECD TG 443, such as histopathology of the gonads for both sexes, and reproductive organ weights for the females. Furthermore, the test material purity has not been reported.

In your comments, you indicate a test material purity of >99% for this study. However, the test material purity is not reported in the technical dossier.

In your comments you further explain that the conclusion "*of negligible concern for reproductive toxicity in humans*" for propylene glycol was drawn in a comprehensive assessment by "NTP and CERHR EG/PG Expert Panel". You agree that within this study (Morrisey, 1989) not all parameters of the current OECD TG 443 were examined, but explain that all these parameters were examined in the 90-day study and the OECD TG 422 study conducted with the Substance itself.

As explained above, the missing parameters included e.g. histopathology of the gonads for both sexes, and reproductive organ weights for the females. For example, according to OECD TG 443, organ weights and histopathology is required for both P animals and F1 adults. While organ weight and histopathological analyses have been performed in the 90-day study and the OECD TG 422 study with the Substance, neither of these studies examined organ weights and histopathology of the gonads in the F1 adults. Therefore, the supporting information does not provide an adequate and reliable coverage of the key parameters expected to be investigated in a study performed according to the OECD TG 443.

Furthermore, you explain that acrylic acid did not induce developmental or reproductive toxicity effects in an OECD TG 416 study. ECHA notes that the (absence of) effects in a study performed with acrylic acid does not inform on properties of propylene glycol.

In the absence of such information, you have not established that a reliable prediction of the property under consideration of the Substance can be derived on the basis of your read-across hypothesis. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

**Conclusions on the read-across approach**

As explained above, based on the abovementioned shortcomings with regards to the prediction of toxicological properties under A and B, you have not established that relevant properties of the Substance can be predicted from data on the analogue substances. Therefore, your adaptation does not comply with the general rules of adaptation as set out in Annex XI, Section 1.5. and your grouping and read-across approach is rejected.
Therefore, the information requirement is not fulfilled.

*The specifications for the study design*

*Premating exposure duration and dose-level setting*

The length of premating exposure period must be ten weeks to cover the full spermatogenesis and folliculogenesis before the mating, allowing meaningful assessment of the effects on fertility.

Ten weeks premating exposure duration is required to obtain results adequate for classification and labelling and /or risk assessment. There is no substance specific information in the dossier supporting shorter premating exposure duration[3].

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 shall be included.

*Cohort 3*

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

Existing information on the Substance itself derived from the available OECD TG 408 study shows evidence of immunotoxicity in all treated groups in females:

- Reduced thymus weights (-14.5% in low dose; -14% in mid dose; and -27% in high dose with statistical significance) without significant changes in the body weight.

Furthermore, the Substance has a harmonised classification for Skin Sens. 1.

In your comments you do not agree with ECHA's argumentation. You consider that even with a statistically significant decrease in thymus weight in the high dose females, all thymus weights were within the historical control data, there are no histopathological changes in thymus or other lymphoid organs, there are no similar changes in males, and there is no dose-response. Based on this, you suggest that the decrease in thymus weights in females is a biological variation.

You refer to historical control data and explain that the observed reduction in thymus weights in low, mid and high dose (minus 14% to 27%) result from the study control being at the upper end of the historical control (mean of study control = 404.6 mg vs. mean of historical control = 285.9 mg [range: 175.5 – 481.9 mg]). However, you have not provided any supporting information showing that the studies used to compile the historical control data stems from studies with same exposure duration (90 days) using identical species/strain of same age. Therefore, ECHA cannot conclude if the observed thymus effects are indeed a observation resulting from biological background variation.

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

In your comments you consider that isolated weight alterations of lymphoid organs without histopathological findings are not regarded as indicators of potential immunotoxicity. However, according to the literature you refer to[4], *"The thymus is the first lymphoid organ that shows morphologic alterations after exposure to many immunotoxicagents. A decrease in size (weight) is often the first manifestation of toxicity."* Further literature you refer to[5], lists *"Altered weight or pathology of lymphoid organs"* as triggers for the developmental immunotoxicity cohort.

According to ECHA Guidance[3], one severe statistically and/or biologically significant organ weight finding related to an immunology organ indicates a particular concern justifying inclusion of the developmental immunotoxicity cohort. Even though the effects in thymus, i.e. reduced weights, are observed only in females, it is biologically significant as it is observed in all test groups, and it is also statistically significant at the high dose.

In your comments you also consider that using the sensitising properties of the Substance as supporting evidence for immunotoxicity is scientifically not appropriate. According to ECHA Guidance[3], sensitising properties can be used as a supporting factor to justify the concern for developmental immunotoxicity.

Taken together, the effects observed in thymus in females of all dose groups, supported by the sensitising properties of the Substance, indicate a particular concern.

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

*Species and route selection*

The study must be performed in rats with oral[6] administration.

*Further expansion of the study design*

The conditions to include the extension of Cohort 1B are currently not met. Furthermore, no triggers for the inclusion of Cohorts 2A and 2B (developmental neurotoxicity) were identified. However, you may expand the study by including the extension of Cohort 1B, as well as Cohorts 2A and 2B 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[3].

[4] Kuper C.F. et al.; Histopathologic approaches to detect changes indicative of immunotoxicity, Toxicological Pathology, 28(3), 454-466, (2000)
[5] Moore N.P. et al.; Guidance on the selection of cohorts for the extended one-generation reproduction toxicity study (OECD test guideline 443), Regulatory Toxicology and Pharmacology, 80, 32-40, (2016)
[6] ECHA Guidance R.7a, Section R.7.6.2.3.2.

## Appendix B: Procedural history

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

On 18 December 2017 ECHA issued decision CCH-D-2114382275-45-01/F[7].

On 2 January 2019 and 22 February 2019 the registrant updated the dossier and provided the results of the 90-day sub-chronic toxicity study.

On 15 March 2019 ECHA informed the registrants that the request for an EOGRT study was withdrawn and would be addressed in this separate decision.

The compliance check was initiated on 3 April 2019.

The decision making followed the procedure of Articles 50 and 51 of the REACH Regulation, as described below:

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

ECHA took into account your comments and did not amend the requests.

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.

[7] https://echa.europa.eu/documents/10162/01d74e47-7872-55d6-c3fe-1e207d3f303c

## Appendix C: Observations and technical guidance

1. The substance subject to the present decision is provisionally listed in the Community rolling action plan (CoRAP) for the start of substance evaluation in 2021.

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

3. 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.

4. 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'[8].

5. Test material

   *Selection of the test material(s)*

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

   While selecting the test material you must take into account the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected test material must contain that constituent/ impurity.

   *Technical reporting of the test material*

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

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

Technical instructions are available in the manual "How to prepare registration and PPORD dossiers"[9].

6. List of references of the ECHA Guidance and other guidance/ reference documents[10]

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)[11]

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[12]

[9] https://echa.europa.eu/manuals
[10] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[11] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[12] 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 Mammalian Reproductive Toxicity Testing and Assessment – No 43, referred to as OECD GD 43.

**Appendix D: 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] |
| [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.