EUROPEAN CHEMICALS AGENCY

Helsinki, 17 June 2020

Addressees
Registrant(s) of JS_BDGMA as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
1 October 2019

Registered substance subject to this decision ("the Substance")
Substance name: 2-(2-butoxyethoxy)ethyl methacrylate
EC number: 230-813-8
CAS number: 7328-22-5

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

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***24 March 2022***.

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

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

1. In vitro cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2.; test method: OECD TG 473) or In vitro micronucleus study (Annex VIII, Section 8.4.2.; test method: OECD TG 487)

2. Only if a negative result in Annex VIII, Section 8.4.2. is obtained, In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.; test method: OECD TG 476 or TG 490)

B. Information required from all the Registrants subject to Annex IX of REACH

1. Sub-chronic toxicity study (90-day) (Annex IX, Section 8.6.2.; test method: OECD TG 408) by oral route, in rats

2. Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.; test method: OECD TG 414) by oral route, in one species (rat or rabbit)

3. Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.; test method: EU C.20./OECD TG 211)

4. Long-term toxicity testing on fish (Annex IX, Section 9.1.6.; test method: OECD TG 210)

The reasons for the request(s) are given in the following appendices:

- Appendix entitled "Reasons common to several requests";

- Appendices entitled "Reasons to request information required under Annexes VIII to IX of REACH", respectively.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you, and in accordance with Articles 10(a) and 12(1) of REACH:

- the information specified in Annexes VII and VIII to REACH, for registration at 10-100 tpa;
- the information specified in Annexes VII, VIII and IX to REACH, for registration at 100-1000 tpa.

You are only required to share the costs of information that you must submit to fulfil your information requirements.

How to comply with your information requirements

To comply with your information requirements you must submit the information requested by this decision in an updated registration dossier by the deadline indicated above. You must also update the chemical safety report, where relevant, including any changes to classification and labelling, based on the newly generated information.

You must follow the general testing and reporting requirements provided under the Appendix entitled "Requirements to fulfil when conducting and reporting new tests for REACH purposes". 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.

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 on Reasons common to several requests

1. Assessment of your read-across approach under Annex XI, Section 1.5.

You propose to provide information on the following standard information requirements of the Substance by using grouping and read-across approach under Annex XI, Section 1.5:

- In vitro cytogenicity study in mammalian cells or in vitro micronucleus study (Annex VIII, Section 8.4.2.)
- In vitro gene mutation study in mammalian cells (Annex VIII, Section 8.4.3.)
- Sub-chronic toxicity study (90-day), (Annex IX, Section 8.6.2.)
- Pre-natal developmental toxicity study (Annex IX, Section 8.7.2.)

ECHA has considered the scientific and regulatory validity of your read-across approach(es) in general before assessing the specific standard information requirements in the following appendices.

Grouping of substances and read-across approach

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 (read-across approach). Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance[2] and related documents[3, 4].

You read-across between the structurally similar substances

- 2-[2-(2-ethoxyethoxy)ethoxy]ethyl methacrylate, EC No. 254-588-0 (CAS No. 39670-09-2) (for the *in vitro* micronucleus study and *in vitro* gene mutation study in mammalian cells)
- 2-(2-butoxyethoxy)ethanol (DEGBE), EC No. 203-961-6 (CAS No. 112-34-5) (for the sub-chronic toxicity (90 day) and pre-natal developmental toxicity (PNDT) studies)
- methacrylic acid EC No. 201-204-4 (CAS No. 79-41-4) (for the pre-natal developmental toxicity (PNDT) study)

as source substances and the Substance as target substance.

You have provided the following reasoning for the prediction of toxicological properties: The analogues chosen are *"structurally similar members of the methacrylate esters category"* and/or *"primary metabolites"* of the Substance.

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance.

[2] ECHA Guidance R.6
[3] RAAF
[4] RAAF UVCB

Read-across hypothesis

A read-across hypothesis needs to establish why a prediction for a toxicological or ecotoxicological property is reliable. This hypothesis should be based on recognition of the structural similarities and differences between the source substance(s) and your Substance[5]. It should explain why the differences in the chemical structures should not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern.

Your read-across hypothesis is that the structural similarity between the source substance(s) and your Substance is a sufficient basis for predicting the properties of your Substance.

While structural similarity is a prerequisite for applying the grouping and read-across approach, it does not necessarily lead to predictable or similar (eco)toxicological properties. You have not provided a well-founded hypothesis to establish a reliable prediction for a toxicological or ecotoxicological property, based on recognition of the structural similarities and differences between the source substance(s) and your Substance.

In your comments you state that you "*are convinced that the current read-across approach is ethically and scientifically justified*". You state that "*the existing read-across approach follows basically the category approach = scenario 4/6 ("different compounds have the same type of effect") of the current RAAF guidance, with several hydroxyl and ether methacrylates as category members*" and that "*considering the well-known hydrolysis of the methacrylate esters to their primary metabolites by ubiquitous carboxylases*" you see "*a high probability to replace the existing read-across approach [...] by a new approach based on the progress in understanding the methacrylate metabolism. [...] This approach complies with scenario 1 of the RAAF guidance ("transformation to common compounds").*

Supporting information

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*"[6]. 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).

Missing supporting information to compare properties of the substances

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar substances cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary to confirm that both substance cause the same type of effects. Such information can be obtained, for example, from bridging studies of comparable design and duration for the Substance and of the source substance(s).

The data reported in the dossier, nor your comments to the draft decision, do not include relevant, reliable and adequate information for the Substance and of the source substance(s) to support your read-across hypothesis.

[5] ECHA Guidance R.6.
[6] ECHA Guidance R.6., Section R.6.2.2.1.f

Missing information on the formation of the metabolite /on the impact of the parent compound

Your read-across hypothesis for some analogue substances is also based on the (bio)transformation of the Substance to a metabolite which is considered to be the source substance. In this context, information characterising the rate and extent of the transformation of the Substance is necessary to confirm the formation of the proposed metabolite and to assess the impact of the exposure to the parent compound. In addition, information on the relevance of the metabolite for the toxicological effects of the Substance has to be provided.

The data set reported in the technical dossier does not include information for the Substance and of the source substance(s) to support your read-across hypothesis. You have not provided any experimental data or other adequate and reliable information, about the formation about the metabolite from the Substance. The study available gives information on the hydrolysis of the analogue substance 2-[2-(2-ethoxyethoxy)ethoxy]ethyl methacrylate, not the Substance. It must be shown that this hydrolysis study is adequate and applicable to the Substance. In addition, you have not provided information characterising the exposure to the parent compound while reading across from the metabolite. No experimental data or other adequate and reliable information addressing the impact of exposure to the parent compound is included in the documentation of your read-across approach.

In your comments you state that "*the rapid ester cleavage as the first step in methacrylate ester metabolism was confirmed by recently performed tests on structurally similar (meth)acrylate esters*" and that based on "*an improved data base we will confirm the rapid cleavage of the paranet ester BDGMA and investigate the hydrolysis rate of the substance and thus gain information on systematic availability of the parent ester BDGMA and its metabolities Butyldiglycol and Methacrylic acid (MAA). The new read-across approach will then evaluate effects of BDGMA by assessment of the properties of its metabolites once the assumed rapid hydrolysis rate is experimentally confirmed with the new TK study. [...] The dossier will be updated with the new TK study and the new read-across approach (scenario1).*"

ECHA notes, that the new data may or may not confirm your hypothesis. As you did not provide any new studies on the target and source substances, currently there is no information which could be used to support your hypothesis.

In the absence of such information, you have not established, neither in your dossier nor in your comments to the draft decision, that the Substance and of the source substance(s) are likely to have similar properties and that a reliable prediction of the property under consideration of the Substance can be derived on the basis of your read-across hypothesis.

Therefore your read-across adaptations are rejected.

Appendix A: Reasons to request information required under Annex VIII of REACH

1. In vitro cytogenicity study in mammalian cells or In vitro micronucleus study

An *in vitro* cytogenicity study in mammalian cells or an *in vitro* micronucleus study is a standard information requirement in Annex VIII, Section 8.4.2 to REACH.

You have provided the following key study in your dossier:

i. [redacted] 2012, according to OECD TG 487 with the analogue substance 2-[2-(2-ethoxyethoxy)ethoxy]ethyl methacrylate (EC No. 254-588-0, CAS No. 39670-09-2).

We have assessed this information and identified the following issues:

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

As explained in the *Appendix on Reasons common to several requests* your adaptation, based on the information from the evaluated registration dossier and your comments, is rejected.

Therefore, the information requirement is not fulfilled.

Information on the study design

To fulfil the information requirement for the Substance, both *in vitro* cytogenicity study in mammalian cells (Annex VIII, Section 8.4.2., test method OECD TG 473) and *in vitro* micronucleus study (Annex VIII, Section 8.4.2., test method OECD TG 487) are considered suitable.

2. In vitro gene mutation study in mammalian cells

An *in vitro* gene mutation study in mammalian cells is a standard information requirement in Annex VIII, Section 8.4.3 to REACH in case of a negative result in the *in vitro* gene mutation test in bacteria and the *in vitro* cytogenicity test.

For Annex VIII, 8.4.3., you have not provided a study with the Substance in your dossier. However, you provided an adaptation according to the general rules for adaptation of Annex XI, Section 1.5 (Grouping of substances and read-across), with a key study ([redacted], 2012, OECD TG 476) conducted with the analogue substance 2-[2-(2-ethoxyethoxy)ethoxy]ethyl methacrylate.

We have assessed this information and identified the following issues:

Your dossier contains:
(i) for Annex VIII, Section 8.4.1 - a negative result for an *in vitro* gene mutation study in bacteria ([redacted] 1999, OECD TG 471, with the Substance), and
(ii) for Annex VII, Section 8.4.2 - inadequate data for an *in vitro* micronucleus study.

The *in vitro* micronucleus study provided in the dossier is rejected for the reasons provided in Section A.1 above. The result of the request A.1 will determine whether the present

requirement for an *in vitro* mammalian cell gene mutation study in accordance with Annex VIII, Section 8.4.3 is triggered.

Your adaptation, based on the information from the evaluated registration dossier and your comments, is rejected for the reasons provided in the *Appendix on Reasons common to several requests*.

Consequently, you are required to provide information for this endpoint, if the *in vitro* cytogenicity study in mammalian cells or *in vitro* micronucleus study provides a negative result.

Information on the study design

To fulfil the information requirement for the Substance, both the *in vitro* mammalian cell gene mutation tests using the hprt and xprt genes (OECD TG 476) and the thymidine kinase gene (OECD TG 490) are considered suitable.

Appendix B: Reasons to request information required under Annex IX of REACH

1. Sub-chronic toxicity study (90-day)

A Sub-chronic toxicity study (90-day) is a standard information requirement in Annex IX, Section 8.6.2. to REACH.

You have provided the following key studies in your dossier:

i. Auletta, 1993, according to OECD TG 411 with the analogue substance 2-(2-butoxyethoxy)ethanol (DEGBE), EC No. 203-961-6 (CAS No. 112-34-5);

ii. [redacted] 2014, according to OECD TG 422 with the Substance;

We have assessed this information and identified the following issues:

A. Study (i.) listed above was conducted with the analogue substance 2-(2-butoxyethoxy)ethanol. ECHA thus understands that you have adapted the information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

As explained in the *Appendix on Reasons common to several requests*, your adaptation, based on the information from the evaluated registration dossier and your comments, is rejected.

In addition, the following endpoint-specific deficiency has been identified in your read-across adaptation:

B. To fulfil the information requirement, the sub-chronic toxicity study must be conducted with the most appropriate route of administration, having regard to the likely route of human exposure (Annex IX, Section 8.6.1, Column 1).

The study (i.) you submitted was performed with dermal administration.

However, referring to the criteria in Annex IX, Section 8.6.1, Column 2, ECHA considers that the dermal route is not the most appropriate for this analogue substance, because it is not proven that dermal aborption is higher than oral absorption. In addition, the oral route is considered the most appropriate route of administration to investigate repeated dose toxicity for the Substance.

C. Regarding study (ii.), to be considered compliant and enable concluding whether the Substance has dangerous properties and supports the determination of the No-Observed Adverse Effect Level (NOAEL), a study has to meet the requirements of OECD TG 408. The key parameters of this test guideline include, among others, the dosing of the Substance daily for a period of 90 days until the scheduled termination of the study.

The study (ii.) you have provided does not have the required exposure duration of 90 days as required in OECD TG 408.

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

Information on the design of the study to be performed

Referring to the criteria provided in Annex IX, Section 8.6.2, Column 2, the oral route is the most appropriate route of administration to investigate repeated dose toxicity, because the absorption rate of the Substance through human skin was predicted to be moderate only. Therefore, the sub-chronic toxicity study must be performed according to the OECD TG 408, in rats and with oral administration of the Substance.

2. Pre-natal developmental toxicity study in one species

A Pre-natal developmental toxicity (PNDT) study (OECD TG 414) in one species is a standard information requirement under Annex IX, Section 8.7.2 to REACH.

You have provided the following key and supporting studies and information in your dossier:

i. [redacted] 2014, according to OECD TG 422 with the Substance;

ii. Auletta, 1993, according to OECD TG 411 with the analogue substance 2-(2-butoxyethoxy)ethanol (DEGBE), EC No. 203-961-6 (CAS No. 112-34-5);

iii. Saillenfait, 1999, according to OECD TG 414 (via inhalation) with the analogue substance methacrylic acid, EC No. 201-204-4 (CAS No. 79-41-4);

iv. ECETOC, 2005, and MAK, 2008, 1993, with the analogue substance DEGBE, referring to a number of different studies with different analogue substances.

We have assessed this information and identified the following issues:

A. In order to be considered compliant and enable assessing if the Substance is a developmental toxicant, the information provided has to meet the requirements of OECD TG 414.

   You have not provided information following OECD TG 414 with the Substance. Instead, with study (i.) you have provided a "combined repeated dose toxicity study with the reproduction/developmental toxicity screening test" (OECD TG 422). In this study, structural malformations and variations are not investigated as required in the PNDT study (OECD TG 414).

B. Furthermore, Studies (ii., iii. and iv.) listed above were conducted with analogue substances and ECHA understands that you have adapted the information requirement by using a Grouping of substances and read-across approach under Annex XI, Section 1.5.

   As explained in the *Appendix on Reasons common to several requests* your adaptation, based on the information from the evaluated registration dossier and your comments, is rejected.

   In addition, the following endpoint-specific deficiencies have been identified in your read-across adaptation:

   A robust study summary must be provided for the sole study available or, if more than one is available, for the study/ies giving rise to the highest concern (Articles 3(28) and 10(a)(vii) and Annex I, Section 1.1.4 of REACH).

   The references provided for (iv.) are review reports based on several studies with the

analogue substance DEGBE, with different species (mouse, rat, rabbit), routes of administration and study guidelines. No robust study summaries were provided for the information referred to under iv. above. Therefore, it is not possible to make an independent assessment of the studies.

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

Specifications for the test method or study conditions

A PNDT study according to the test method OECD TG 414 must be performed in rat or rabbit as preferred species with oral[7] administration of the Substance.

3. Long-term toxicity testing on aquatic invertebrates

Long-term toxicity testing on aquatic invertebrates is a standard information requirement in Annex IX, Section 9.1.5 to REACH.

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

i. [redacted] (2012) conducted with the analogue substance 1,4-Butanediol dimethacrylate (CAS No 2082-81-7);
ii. [redacted] (2012) conducted with the analogue substance benzyl methacrylate (EC No 219-674-4, CAS No 2495-37-6);
iii. [redacted] (2012) conducted with the analogue substance ethane-1,2-diyl bis(2-methylacrylate) (EC No 202-617-2, CAS No 97-90-5).

You predict the properties of the Substance from the analogue substances: 1,4-Butanediol dimethacrylate (CAS No 2082-81-7), benzyl methacrylate (EC No 219-674-4, CAS No 2495-37-6), ethane-1,2-diyl bis(2-methylacrylate) (EC No 202-617-2, CAS No 97-90-5).

You have provided a read-across justification that addresses the current endpoint in the Endpoint Summary of IUCLID Section 6.1.4. with the following reasoning for the prediction of long-term toxicity on aquatic invertebrates: "*EC10 21 d to daphnia magna (reproduction) of the structurally related substance Ethyltriglycol methacrylate was 77.1 mg/l. Aquatic toxicity of the most methacrylates is known to be based on narcosis which correlates with log Pow. There are data on 21d daphnia magna reproduction available for two methacrylates with the same log Pow of 3.1 as for Butyldiglycol methacrylates.*
EC10 daphnia magna (21d) for Benzyl methacrylates is 3.34 mg/l [redacted] *2012) and EC10 daphnia magna (21d) for 1,4 Butanediol dimethacrylates is 7.51 mg/l* [redacted] *2012). As 1,4 - Butanediol dimethacrylate has structurally higher correlation with Butyldiglycol methacrylate than Benzyl methacrylate, 7.51 mg/l will be used for PNEC derivation.*"

ECHA understands that you predict the properties of the Substance using a read-across hypothesis which assumes that different compounds have the same type of effects. The properties of your Substance are predicted to be quantitatively equal to those of the source substance(s).

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

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

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 (read-across approach).

Additional information on what is necessary when justifying a read-across approach can be found in the ECHA Guidance[8] and related documents[9,10].

ECHA notes the following shortcoming(s) with regards to prediction(s) of ecotoxicological properties.

A. Read-across hypothesis

A read-across hypothesis needs to be provided, establishing why a prediction for a toxicological or ecotoxicological property is reliable. This hypothesis should be based on recognition of the structural similarities and differences between the source substance(s) and your Substance[8]. It should explain why the differences in the chemical structures should not influence the toxicological/ ecotoxicological properties or should do so in a regular pattern.

Your read-across hypothesis is that the similarity in chemical structure and in some of the physicochemical and ecotoxicological properties between the source substance(s) and your Substance is a sufficient basis for predicting the properties of your Substance for other endpoints.

Nevertheless, similarity in chemical structure and similarity of some of the physicochemical and ecotoxicological properties does not necessarily lead to predictable or similar ecotoxicological properties in other endpoints. As described above, a well-founded hypothesis is needed to establish a reliable prediction for ecotoxicological properties, based on recognition of the structural similarities and differences between the source substance(s) and your Substance. In the present case, there are structural differences between the source substances and the Substance and you have neither described them nor considered the impact of these structural differences on the prediction.

Therefore, you have not provided a well-founded hypothesis to establish a reliable prediction for a long-term toxicity on aquatic invertebrates property.

B. Lack of supporting information

Annex XI, Section 1.5 of the REACH Regulation states that "*physicochemical properties, human health effects and environmental effects or environmental fate may be predicted from data for reference substance(s)*". For this purpose "*it is important to provide supporting information to strengthen the rationale for the read-across*"[11]. 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). Supporting information must include bridging studies of comparable design and duration for the Substance and source substance(s), evidence to confirm similar mode of action, etc.

[8] ECHA Guidance R.6
[9] RAAF
[10] RAAF UVCB
[11] ECHA Guidance R.6, Section R.6.2.2.1.f

As indicated above, your read-across hypothesis is based on the assumption that the structurally similar substances cause the same type of effect(s). In this context, relevant, reliable and adequate information allowing to compare the properties of the Substance and of the source substance(s) is necessary to confirm that both substance cause the same type of effects.

The data set reported in the technical dossier does not include any bridging studies for the Substance and the source substances to compare properties and support your read-across hypothesis.

Furthermore, you claim that the Substance and the source substances have the same mode of action (narcosis, driven by LogKow). However, no evidence is provided to support the claimed similar mode of action for the substances.

In your comments you state that you will "*amend the read-across justification by considering additional information regarding physico-chemical properties as well as ecotoxicological properties of the target and source substances [...].*"

You did not provide any new studies on the target and source substances nor any other evidence to address the issues identified above. As a consequence, currently there is no additional information which could be used to support your hypothesis.

In the absence of such information, you have not established, neither in your dossier nor in your comments to the draft decision, that the Substance and the source substance(s) are likely to have similar properties. Therefore you have not provided sufficient supporting information to strengthen the rationale for the read-across.

As a consequence, your adaptation is rejected and the information requirement is not fulfilled.

4. Long-term toxicity testing on fish

Long-term toxicity testing on fish is a standard information requirement at Annex IX, Section 9.1.6.1 of REACH.

You have adapted the standard information requirement based on column 2 of Annex IX, Section 9.1. with the following: "*The risk characterisation shows that the PEC/PNECaqua ratio for the aquatic environment is <1, indicating no need for further information or testing. According to REACH regulation Annex IX, 9.1. column 2, long-term toxicity testing shall only be considered when the chemical safety assessment indicates the need for further investigations. Because there is no indication of major differences in sensitivity between trophic levels and in the absence of any significant long-term bioaccumulation potential it is not necessary to perform further chronic fish tests with the substance. The environmental risk assessment can be performed with sufficient reliability with the available long-term ecotoxicity data. Thus, no long-term toxicity testing in fish is required for BDGMA*"

As specified in Annex IX, Section 9.1., Column 2, a long-term toxicity study on fish must be performed unless the Chemical Safety Assessment demonstrates that risks towards the aquatic compartment arising from the use of the Substance are controlled (as per Annex I, section 0.1). The justification must be documented in the Chemical Safety Assessment.

In particular, the Chemical Safety Assessment must take into account the following elements to support that long-term toxicity testing is not required:

- all relevant hazard information from your registration dossier;
- the outcome of the risk assessment in relation to the uses of the Substance.

Regarding long-term toxicity testing, there are no further requirements for fish testing if there is compelling evidence to suggest that the fish is likely to be at least a factor of about 10 less sensitive than invertebrates or algae. In case the relative sensitivity of fish cannot be predicted, further testing is needed.[12]

Compelling evidence to compare the species sensitivites must be based on reliable data and on data that is relevant to the effect endpoints foreseen to be investigated in an OECD TG 210 study (stage of embryonic development, hatching and survival, appearance, behaviour, weight, length).

As specified in requests B.3, the data on long-term toxicity to *Daphnia* is not compliant. Hence, your dossier currently does not include adequate information to characterise the hazardous property of the Substance to aquatic organisms.

You have not provided an exposure assessment and related risk characterisation for the Substance. Hence, you have not demonstrated that risks are controlled.

Regarding your above quoted claim that in the absence of major differences in sensitivity and in the absence of any significant long-term bioaccumulation potential further testing could be omitted, ECHA notes the following. First, the long-term *Daphnia* study is not compliant and you have not justified based on which compelling evidence fish is likely to be at least a factor of about 10 less sensitive than invertebrates or algae in chronic studies[12]. Second, lack of bioaccumulation is not a basis, in accordance with Annex IX, Section 9.1., Column 2, to adapt the information requirement.

In your comments you reiterate that long-term toxicity testing in fish is not needed since 1) you consider that the information requirement for long-term *Daphnia* (request B.3) can be fulfilled by updating the read-across justification; 2) "*there is no indication of major differences in sensitivity between trophic levels in tests on BDGMA itself as well as structurally similar substances. The substance does not reveal a long-term bioaccumulation potential*". However, as explained in request B.3 above, based on the information provided in the dossier and in your comments, the standard information requirement for long-term toxicity to Daphnia is not fulfilled. Furthermore, as explained above, compelling evidence to compare species sensitivity has not been provided and a lack of bioaccumulation does not form a basis to adapt the information requirement in accordance with Annex IX, Section 9.1, Column 2.

In conclusion, in the absence of all this information, your Chemical Safety Assessment does not demonstrate that the risks of the Substance are adequately controlled. As a consequence, your adaptation is rejected as it does not meet the specific rules for adaptation of Annex IX, Section 9.1., Column 2.

Based on the above, the information requirement is not fulfilled.

[12] ECHA Guidance R.7b, Section R.7.8.5.3

Appendix C: Requirements to fulfil when conducting and reporting new tests for REACH purposes

A. Test methods, GLP requirements and reporting

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

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

3. Under Article 10(a)(vi) and (vii) of REACH, all new data generated as a result of this decision must be reported as study summaries, or as robust study summaries, if required under Annex I of REACH. See ECHA Practical Guide on How to report robust study summaries[13].

B. Test material

Before generating new data, you must agree within the joint submission on the chemical composition of the material to be tested (Test Material) which must be relevant for all the registrants of the Substance.

1. Selection of the Test material(s)

   The Test Material used to generate the new data must be selected taking into account the following:
   - the variation in compositions reported by all members of the joint submission,
   - the boundary composition(s) of the Substance,
   - the impact of each constituent/ impurity on the test results for the endpoint to be assessed. For example, if a constituent/ impurity of the Substance is known to have an impact on (eco)toxicity, the selected Test Material must contain that constituent/ impurity.

2. Information on the Test Material needed in the updated dossier
   - You must report the composition of the Test Material selected for each study, under the "Test material information" section, for each respective endpoint study record in IUCLID.
   - The reported composition must include all constituents of each Test Material and their concentration values and other parameters relevant for the property to be tested.

This information is needed to assess whether the Test Material is relevant for the Substance and whether it is suitable for use by all members of the joint submission.

Technical instructions on how to report the above is available in the manual on How to prepare registration and PPORD dossiers[14].

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

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

Appendix D: General recommendations when conducting and reporting new tests for REACH purposes

A. Testing strategy for aquatic toxicity testing

You are advised to consult ECHA Guidance R.7b, (Section R.7.8.5) which describes the Integrated Testing Strategy, to determine the sequence of aquatic toxicity tests and testing needed.

Appendix E: Procedure

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

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

The compliance check was initiated on 19 June 2019.

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

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.

Appendix F: List of references - ECHA Guidance[15] and other supporting documents

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

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

Read-across assessment framework (RAAF, March 2017)[16]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[16]

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.

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

[16] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

OECD Guidance documents[17]
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.

[17] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Appendix G: Addressees of this decision and the corresponding information requirements applicable to them

You must provide the information requested in this decision for all REACH Annexes applicable to you.

Registrant Name	Registration number	Highest REACH Annex applicable to you
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

Where applicable, the name of a third party representative (TPR) may be displayed in the list of recipients whereas ECHA will send the decision to the actual registrant.