~~Confidential~~

Helsinki, 10 January 2022

Addressees
Registrant(s) of JS_70356-09-1 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
30/06/2020

Registered substance subject to this decision ("the Substance")
Substance name: 1-[4-(1,1-dimethylethyl)phenyl]-3-(4-methoxyphenyl)propane-1,3-dione
EC number: 274-581-6
CAS number: 70356-09-1

Decision number: Please refer to the REACH-IT message which delivered this communication (in format CCH-D-XXXXXXXXXX-XX-XX/F)

DECISION ON A COMPLIANCE CHECK

Under Article 41 of Regulation (EC) No 1907/2006 (REACH), you must submit the information listed below, by the deadline of ***17 April 2023***.

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

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

1. Skin sensitisation Annex VII, Section 8.3.; test method:

   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.); and

   ii. Only if the in vitro/in chemico test methods specified under point 1.i.) are not applicable for the Substance, or the results obtained are not adequate for classification and risk assessment, in vivo skin sensitisation (Annex VII, Section 8.3.2.; test method: EU B.42./OECD TG 429) with the Substance.

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

1. Long-term toxicity testing on terrestrial invertebrates (test method: OECD TG 222 or 220 or 232) or long-term toxicity testing on terrestrial plants (OECD 208 or ISO 22030) (triggered by Annex IX, Section 9.4.1., column 2)

2. Effects on soil micro-organisms (Annex IX, Section 9.4.2.; nitrogen transformation test, test method: EU C.21/OECD TG 216)

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

- Appendices entitled "Reasons to request information required under Annexes VII 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 Annex VII to REACH, for registration at 1-10 tonnes per year (tpa), or as a transported isolated intermediate in quantity above 1000 tpa;
- 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". For references used in this decision, please consult the Appendix entitled "List of references".

Appeal

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

Failure to comply

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

Authorised[1] under the authority of Mike Rasenberg, Director of Hazard Assessment

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

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

1. Skin sensitisation

Skin sensitisation is an information requirement under Annex VII to REACH (Section 8.3.). Under Section 8.3., Column 1, the registrants must submit information allowing (1) A) a conclusion whether the substance is a skin sensitiser and B) whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A), and (2) risk assessment, where required.

To fulfil the information requirement, information from *in vitro/in chemico* studies needs to address each of the key events of skin sensitisation (a) molecular interaction with skin proteins, (b) inflammatory response in keratinocytes, and (c) activation of dendric cells (Annex VII, Section 8.3.1.).

In case *in vitro/in chemico* methods are not suitable for the Substance or the results cannot be used for classification and risk assessment an *in vivo* skin sensitisation study (Annex VII, Section 8.3.2.) must be performed.

In your comments to the draft decision, you propose to adapt the information requirement by applying a weight of evidence approach in accordance with Annex XI, Section 1.2.

In the dossier, you have provided the following information:

i. In vivo guinea pig maximization test (key study, similar to OECD TG 406, non-GLP, [redacted] 1982) conducted with the Substance.

In your comments to the draft decision, you have provided the following information on the Substance:

ii. Open Epicutaneous Test (OET, [redacted], 1982b) conducted on guinea pigs.
iii. Freund's complete adjuvant test (FCAT, [redacted], 1982c) conducted on guinea pigs.
iv. Human Repeated Insult Patch Test (HRIPT) ([redacted], 1979)
v. *in silico* assessment using the OECD QSAR Toolbox (version 4.2) and Derek Nexus (version 6.1.0)

You justify the weight of evidence as follows: "*based on the concordant results available from the three animal tests and one human study, as well as predictions generated in silico by two different QSAR systems, the registrants are convinced that a weight of evidence provides sufficient information for decision-making in regard to the skin sensitisation potential of BMDBM addressing the human health aspects of BMDBM. All available data confirm that BMDBM is not a skin sensitiser*.".

Annex XI, Section 1.2 states that there may be sufficient weight of evidence from several independent sources of information leading to assumption/conclusion that a substance has or has not a particular dangerous (hazardous) property, while information from a single source alone is insufficient to support this notion.

According to ECHA Guidance R.4, a weight of evidence adaptation involves an assessment of the relative values/weights of the different sources of information submitted. The weight given is based on the reliability of the data, consistency of results/data, nature and severity of effects, and relevance and coverage of the information for the given regulatory information requirement. Subsequently, relevance, reliability, coverage, consistency and results of these sources of information must be balanced in order to decide whether they together provide

sufficient weight to conclude that the Substance has or has not the (dangerous) property investigated by the required study.

Annex XI, section 1.2 requires that adequate and reliable documentation is provided to describe your weight of evidence approach.

In your comments to the draft decision, you have summarised the sources of information for each endpoint in relation to the reliability, coverage of key parameters, consistency and results and conclude that as a weight of evidence based on the available sources of information, no further studies are needed.

ECHA has assessed the provided sources of information in a weight of evidence approach.

A) Assessment whether the Substance causes skin sensitisation

Information that can be used to support weight of evidence adaptation for information requirement of Section 8.3 of Annex VII includes similar information that is investigated by *in vitro*, *in chemico* and/or *in vivo* test methods. These key investigations include:

- investigation of cell proliferation in the draining lymph nodes (local lymph node assay), investigation of local responses in animals or human studies (guinea pig assays or human studies), or investigation of molecular interaction with proteins, inflammatory response in keratinocytes and activation of dendritic cells (in vitro and in chemico assays).

The sources of information (i to v.) provide relevant information, as they aim to provide information on these key investigations. However, these sources of information have the following deficiencies affecting their reliability.

i. Adequacy of the studies for hazard identification (sources of information i-iv)

According to the ECHA Guidance[2], "*The evaluation of data quality includes assessment of adequacy of the information for hazard/risk assessment and C&L purposes*". The ECHA Guidance defines adequacy as "*the usefulness of data for hazard/risk assessment purposes*". In the context of a weight of evidence adaptation of standard information requirements, the set of information provided must be adequate for hazard identification.

To be adequate for hazard identification, particular attention should be paid to the quality of the tests including, but not limited to, the concentrations of test material that have been used (dose level selection), and the use of appropriate positive and negative controls.

You have provided three studies (i to iii) which provide information on local responses in animals (guinea pigs). Concerning these studies you claim that based on the local effects seen in the study (ii) following induction exposure, the dose level selection for induction for the other studies (20%) is considered adequate. Furthermore, you indicate that while no negative controls were identified for study (i), negative control groups were included in studies (ii) and (iii). Based on this, you consider that these studies together provide a valuable information to be considered while determining a skin sensitisation potential of the Substance. In addition, you consider that the study (iv) performed in humans confirms that the Substance is not a skin sensitiser.

ECHA has evaluated if these studies provide adequate information for the hazard identification:

[2] ECHA Guidance R.4

In the studies (i to iii) the doses selected for induction and challenge cause major concern. In study (i) the induction and challenge concentrations were 20% and no local effects were reported. This already provides information that the induction concentration was not the concentration causing mild-to-moderate irritation, as required by the test method[3]. In the study (iii), 5% solution was used in the intradermal induction and 20% for the challenge. No reactions after induction were reported, indicating that the concentration selected for induction was not appropriate, as required by the test method. Moreover, , the studies (i and iii) do not contain positive control group, which is needed for the verification of proper functioning of the test method. As a conclusion, these studies (i and iii) do not do not allow a reliable conclusion of the hazardous properties of the Substance at the higher concentrations.

In the study (ii) it is stated that 20% induction did cause irritation following 15 days of treatment (detailed results not provided e.g. number of animals showing local reactions and the grade of reactions). In the study (ii) topical induction treatment was given 15 times, and in the study (i) topical induction was given two times, which may cause the difference in the local reactions observed. Due to the differences in exposure duration, the effects noted in the study (ii) do not justify the dose level selection for the other studies (i and iii). Moreover, the study (ii) does not contain positive control group, which is needed for the verification of proper functioning of the test method. Therefore, while the findings in study (ii) suggest that the dose selection was appropriate for that particular study, and that the Substance was not a skin sensitiser, the results are unreliable due to lack of positive controls in the study, and the study does not allow a reliable conclusion of the hazardous properties of the Substance.

In addition, you considered that the study (iv) performed in humans confirms that the Substance is not a skin sensitiser. ECHA notes that the study (iv) is part of a "*Clinical safety evaluation of eight products*" (title of the publication), and therefore, seems to have been conducted on humans for the purpose of risk assessment and with the objective of identification of safe levels for specific intended uses. The concentrations tested were up to 10% and aimed for identification of safe levels for specific intended uses of the Substance in a formulation, and not for hazard identification at higher concentrations.

Therefore, while this source of information (iv) indicates that the Substance does not have the hazardous property of skin sensitisation when tested up to 10%, it does not inform on the hazardous properties of the Substance at the higher concentrations, and cannot support the conclusion that the Substance is a non-sensitiser.

ii. *Reliability of the provided information (source of information v)*

ECHA Guidance R.6.1.5.3. specifies that, among others, the following conditions impact the reliability of the model prediction:

- a substance must fall within the applicability domain specified by the model developer;
- the prediction is consistent with information available for other related endpoint(s).

To further support your weight of evidence conclusion that the Substance is a non-sensitiser, you have provided *in silico* assessment for the Substance using the OECD QSAR Toolbox (version 4.2) and Derek Nexus (version 6.1.0) and indicate that both Toolbox and Derek predict the Substance to be a non-sensitiser (source of information v).

Furthermore, the Derek report provided in the comments specify that the Substance may photodegrade and result with degradation products that can be classified as strong allergens.

ECHA has evaluated the reliability of the provided information for the weight of evidence:

[3] OECD TG 406, versions 1981, 1992 and 2021

First, the Derek Nexus predicts the Substance as a non-sensitiser. However, the prediction report provided in the comments indicates that the Substance (input structure) "contains misclassified features". This indicates that the Substance structure contains fragments that have been observed in sensitisers.These structural fragments do not match skin sensitisation structural alerts in Derek, and therefore, the Substance may be misclassified as a non-sensitiser (negative prediction).

According to the publicly available information in Derek QMRF, the applicability of "the negative prediction to the query compounds can be determined by an expert, if required, by investigating the presence (or absence) of misclassified and/or unclassified features". Therefore, in presence of misclassified features in the input structure and in absence of further explanations, the Substance is considered to fall outside the applicability domain of the model, further reducing the reliability of the prediction obtained from this model.

Second, the results provided from the OECD Toolbox in your comments contradicts the negative prediction for the Substance as the following were reported:

- a protein binding alert via Schiff-base formation for the profiler "Skin Sensitisation by OASIS" identified for the Substance (target structure); and
- a prediction of weak sensitiser as a result from an *in vivo* guinea pig study (GPMT).

Therefore, the prediction provided from the OECD Toolbox is not consistent with information provided to support predictions, adding uncertainty and further reducing the reliability of the prediction.

Finally, you have explained that the Substance may photodegrade to metabolites of concern. This indicates that the Substance has a potential to be transformed to sensitisers. However, you have not further considered the (a)biotic activation of the Substance or the impact of potential (a)biotic activation including photodegradation on the predictions or on the weight of eveidence approach.

Based on above, the *in silico* predictions for the Substance (v) are not reliable and therefore, do not support the conclusion of your weight of evidence. Most importantly, the information provided from the *in silico* models indicate a skin sensitisation hazard potential for the Substance, which warrant consideration in a weight of evidence.

iii. Conclusion

Taken together, the provided information indicate that the Substance may have a potential for skin sensitisation hazard (information from in silico models). Due to the uncertainty in the *in vivo* testing (guinea pig studies and HRIPT), this potential for skin sensitisation hazard cannot be excluded by the experimental information (guinea pig studies and HRIPT) provided in the dossier and in the comments to the draft decision. Furthermore, you have not considered the potential of (a)biotic activation including photodegradation into sensitising metabolites and the impact of this on the weight of evidence approach. Therefore, it is not possible to conclude, based on any source of information alone or considered together, whether your Substance has or has not the particular dangerous properties foreseen to be investigated in skin sensitisation studies.

B) Assessment whether the Substance can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

i. No assessment of potency

To be considered compliant and enable a conclusion in cases where the substance is considered to cause skin sensitisation, the information provided must also allow a conclusion whether it can be presumed to have the potential to produce significant sensitisation in humans (Cat. 1A).

As the currently available data does not allow to conclude whether the Substance causes skin sensitisation (see section A above), this condition cannot be assessed.

Conclusion on your weight of evidence approach

Therefore, your adaptation is rejected and the information requirement is not fulfilled.

C) Information on the study design

To fulfil the information requirement for the Substance for skin sensitisation, *in vitro/in chemico* studies (OECD TG 442C, OECD TG 442D and EU Method B.71/OECD TG 442E) are considered suitable.

In case *in vitro/in chemico* methods are not suitable for the Substance or the results cannot be used for classification and risk assessment an *in vivo* skin sensitisation study must be performed and the murine local lymph node assay (LLNA) (EU Method B.42/OEDC TG 429) is considered as the appropriate study.

In your comments to the draft decision, you explained that due to physico-chemical properties of the Substance, the currently available *in chemico/in vitro* methods are not applicable. More specifically, you referred to the LogP value of the Substance (6.1) and poor water solubility (ca. 30 µg/L) and the limitations in respect to DPRA method (OECD TG 442C), Keratinosens method (OECD TG 442D) and h-CLAT method (OECD TG 442E). No considerations on the suitability of other available *in chemico/in vitro* methods were provided.

ECHA has assessed your comments, as follows.

<u>OECD TG 442C</u>

The available methods included in the OECD TG 442C (Direct Peptide Reactivity Assay (DPRA), the Amino Acid Derivative Reactivity Assay (ADRA) and the kinetic Direct Peptide Reactivity Assay (kDPRA)) specify the test conditions in respect to solubility.

For the DPRA (Appendix I, OECD TG 442C), it is stated that in case precipitation is noted at the desired concentration of 100 mM, only positive results should be used. The ADRA (Appendix II, OECD TG 442C) has been designed for poorly soluble substances.

<u>OECD TG 442D</u>

The OECD TG 442D (2018) contains currently two different methods i.e. keratinosens (Appendix IA) and Lusens (Appendix IB). For both of the test methods following statements are given in paragraph 4 of the respective Appendices "*In general mono constituent substances with a LogP above 7 may be insoluble in the exposure medium, however, if solubility or stable dispersion can be obtained and documented, testing may still be conducted*."

Based on the currently available methods, there are no LogP specific limitations, even if there are issues with solubility, but a stable dispersion can be obtained. If solubility limits are not met, or if it is not possible to obtain stable dispersion, positive results could still be used.

OECD TG 442E

The OECD TG 442E (2018) contains currently three methods i.e. Human Cell Line Activation test (h-CLAT), U937 cell line activation Test (U-SENS™), and Interleukin-8 Reporter Gene Assay (IL-8 Luc assay). For the h-CLAT method only there are LogP specific limitations, as the methods states in Annex I, paragraph 4 "*Test chemicals with a Log Kow greater than 3.5 tend to produce false negative results (14). Therefore, negative results with test chemicals with a Log Kow greater than 3.5 should not be considered. However, positive results obtained with test chemicals with a Log Kow greater than 3.5 could still be used to support the identification of the test chemical as a skin sensitiser.* The other methods do not contain LogP specific limitations, however the substance needs to be solubilised at appropriate concentrations, or to form a stable dispersion, as specified in the individual methods.

Conclusion

The current *in chemico/in vitro* test guidelines (OECD TGs 442C, D and E) contain multiple methods in addition to the ones indicated by you in your comments to the draft decision. It is not possible for ECHA to conclude that currently available *in vitro/in chemico* methods are not suitable for the Substance without any evidence, e.g. in the form of pre-tests with suitable vehicles as described in the corresponding test guidelines.

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

1. **Long-term toxicity on terrestrial invertebrates or Long-term toxicity on terrestrial plants**

Effects on terrestrial organisms is an information requirement under Annex IX to REACH (Section 9.4.1.). Long-term toxicity testing must be considered (Section 9.4., column 2) if the substance has a high potential to adsorb to soil or is very persistent.

A substance is considered to be very persistent in soil if it has a half-life >180 days or, in absence of specific soil data, if it is not readily biodegradable (ECHA Guidance R.7.11.5.3., page 149).

According to the provided information, the Substance is considered to be very persistent in soil as it is not readily biodegradable (4% in a study according to OECD 302C and 0% in a study according to ISO 11734). Therefore, long-term testing is triggered.

You have provided an adaptation omitting the information based on Annex IX, Section 9.4., Column 2 with the following justifications:

a. *"the study does not need to be conducted because direct and indirect exposure of the soil compartment is unlikely"*
b. *"According to the outcome of the chemical safety assessment, which is based on the EM method by applying aquatic toxicity data, the PEC/PNEC ratio for the soil compartment is smaller than 1, so that no risk for terrestrial organisms at any substance life cycle stage from the stage of formulation up to the stage of its intended use is likely"*;

ECHA has assessed this information and identified the following issues:

a. Arguments based on unlikely exposure

Under Section 9.4., Column 2, paragraph 1 of Annex IX to REACH, these studies do not need to be conducted if direct and indirect exposure of the soil compartment is unlikely.

Exposure based adaptation based on column 2 of Annexes VIII-X requires that a qualitative argumentation can be applied when it is argued that exposure is absent or not significant, e.g. due to the specific uses of a substance (ECHA Guidance R.5.1.2). Such qualitative risk characterisation establishes control of risk by demonstrating that i) strictly controlled conditions apply or ii) that no releases are to be expected, and thus the likelihood of exposure is negligible (ECHA Guidance R.5.1.3.2).

In your registration dossier you have indicated the following uses of the Substance: formulation of cosmetic products and consumer use of cosmetic products.

In your exposure assessment you state that the greatest portion of emissions from private use of cosmetics will be released to the public sewerage system and that "*it is anticipated that a larger fraction of the substance is going to bind to sludge during the sewage treatment*". You indicate that the Predicted Environmental Concentrations (PECs) in grassland from use of cosmetics is predicted to be 1.7 mg/kg wet weight and 0.00938 mg/kg wet weight based on "modified PEC".

You have thus not demonstrated that i) strictly controlled conditions would apply or ii) that no releases are to be expected. In contrast, the uses of the substance and the information in

your exposure assessment indicate that the Substance is likely to reach STP sludge (which can be applied to agricultural or grassland soil as indicated in ECHA Guidance R.16.4.3.5).

Therefore your arguments to adapt this information requirement based on unlikely exposure are rejected.

b. Arguments based on Equilibrium Partitioning Method (EPM)

Under Section 9.4., Column 2, paragraph 2 of Annex IX to REACH, in the absence of data for soil organisms, the equilibrium partitioning method may be applied to assess the hazard to soil organisms. In this context, ECHA Guidance R.7.11.6. describes an integrated testing strategy (ITS) for soil toxicity which rely on the assignment of the Substance to a "soil hazard category" in order to decide what confirmatory toxicity tests must be conducted.

Soil hazard category 3 applies for substances that are very persistent in soil (DT50 > 180 days, and in the absence of specific soil data, persistence would be assumed, unless the substance is readily degradable) and the aquatic toxicity data does not screen for being very toxic to aquatic organisms (EC/LC50 < 1 mg/L for algae, daphnia or fish). In this hazard category, at least the following must be provided to fulfil the information requirements on terrestrial toxicity (ECHA Guidance, Table R.7.11—2):

- $PNEC_{screen}$ as a screening assessment (using PNEC for aquatic organisms), and
- a confirmatory long-term terrestrial toxicity test (either on terrestrial invertebrates or on plants) and toxicity testing on soil micro-organisms to confirm the outcome of the screening assessment.

If there is no indication of risk from neither of these methods, no further toxicity testing for soil organisms need to be conducted.

Based on the information provided in the registration dossier, the Substance is potentially very persistent in soil (no soil simulation study provided but it is not readily biodegradable: 4% degradation in 28 days, [redacted] 2010), and not toxic to aquatic organisms (no effects in saturation concentration in short-term studies). Hence soil hazard category 3 applies.

You have not provided an initial screening assessment based on a $PNEC_{screen}$ using the EPM and a quantitative exposure assessment for the soil compartment (PEC_{soil}) in your Chemical Safety Report. We note that in the absence of effects observed in the aquatic toxicity studies provided in your dossier, it is unlikely that $PNEC_{screen}$ would indicate a risk to the soil compartment. However you have also not provided any confirmatory test (no short or long term toxicity test(s) on terrestrial organisms) to support the outcome of the screening assessment.

As you have not provided any confirmatory long-term toxicity test to terrestrial organisms to support the outcome of the screening assessment, you have not demonstrated that toxicity to terrestrial organisms can be safely excluded. Therefore, your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

Study design

The earthworm reproduction test (OECD TG 222), Enchytraeid reproduction test (OECD TG 220), and Collembolan reproduction test (OECD TG 232) are considered adequate to fulfil the information requirement on long-term toxicity testing to terrestrial invertebrates. ECHA is not in a position to determine the most appropriate test protocol, since this decision is dependent upon species sensitivity and substance properties.

The OECD TG 208 (Terrestrial plants, growth test) considers the need to select the number of test species according to relevant regulatory requirements, and the need for a reasonably broad selection of species to account for interspecies sensitivity distribution. For long-term toxicity testing, ECHA considers six species as the minimum to achieve a reasonably broad selection. Testing must be conducted with species from different families, as a minimum with two monocotyledonous species and four dicotyledonous species, selected according to the criteria indicated in the OECD TG 208 guideline.

It is in your discretion to choose and justify the most appropropriate confirmatory long-term test for the Substance. While testing on invertebrates is preferred (ECHA Guidance R.7.11.5.3.), we note that there has been some statistically insignificant effects observed in the fresh water algae test and terrestrial plants may therefore be considered for testing.

In the comments to the draft decision you agree to choose the most appropriate test and to perform the requested study.

2. **Effects on soil micro-organisms (Annex IX, Section 9.4.2.)**

Effects on soil micro-organisms is an information requirement under Annex IX to REACH (Section 9.4.2.).

You have provided an adaptation omitting the information based on Annex IX, Section 9.4., Column 2 with the following justifications:

a. *"the study does not need to be conducted because direct and indirect exposure of the soil compartment is unlikely"*
b. *"According to the outcome of the chemical safety assessment, which is based on the EM method by applying aquatic toxicity data, the PEC/PNEC ratio for the soil compartment is smaller than 1, so that no risk for terrestrial organisms at any substance life cycle stage from the stage of formulation up to the stage of its intended use is likely"*;

As already explained in Appendix B.1, your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

Study design

According to ECHA Guidance R.7.11.3.1, the nitrogen transformation test (EU C.21/OECD TG 216) is suitable for most non-agrochemicals.

In the comments to the draft decision you agree to perform the requested study.

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[4].

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[5].

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

Appendix D: Procedure

The Substance is listed in the Community rolling action plan (CoRAP) and substance evaluation was initiated in 2015.

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 16 November 2020.

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

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

ECHA 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 E: List of references - ECHA Guidance[6] 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)[7]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, 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.

Data sharing
Guidance on data-sharing (version 3.1, January 2017), referred to as ECHA Guidance on data sharing in this decision.

OECD Guidance documents[9]

[6] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[7] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[8] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[9] http://www.oecd.org/chemicalsafety/testing/series-testing-assessment-publications-number.htm

Guidance Document on aqueous–phase aquatic toxicity testing of difficult test chemicals – No 23, referred to as OECD GD 23.

Guidance document on transformation/dissolution of metals and metal compounds in aqueous media – No 29, referred to as OECD GD 29.

Guidance Document on Standardised Test Guidelines for Evaluating Chemicals for Endocrine Disruption – No 150, referred to as OECD GD 150.

Guidance Document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test – No 151, referred to as OECD GD 151.

Appendix F: Addressees of this decision and their corresponding information requirements

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

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