~~Confidential~~

Helsinki, 12 November 2021

Addressees
Registrant(s) of JS_EC204-398-9 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
09/07/2018

Registered substance subject to this decision ("the Substance")
Substance name: 1,3-diphenylpropane-1,3-dione
EC number: 204-398-9
CAS number: 120-46-7

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 November 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. Water solubility (Annex VII, Section 7.7.; test method: EU A.6./OECD TG 105/OECD GD 29)

2. Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.; test method: EU C.2./OECD TG 202)

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

4. Ready biodegradability (Annex VII, Section 9.2.1.1.; test method: OECD TG 301A/B/C/D/E/F or OECD TG 310)

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

1. Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.; test method: OECD TG 203)

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

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

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

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

- Appendix entitled "Reasons common to several requests";

- 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.

How to comply with your information requirements

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

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

Appeal

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

Failure to comply

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

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

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

Appendix on Reasons common to several requests

1. **Assessment of the (Q)SAR adaptation under Annex XI, Section 1.3.**

You seek to adapt the following standard information requirements by applying (a) (Q)SAR approach(es) in accordance with Annex XI, Section 1.3:

- Short-term toxicity testing on aquatic invertebrates (Annex VII, Section 9.1.1.)
- Growth inhibition study aquatic plants (Annex VII, Section 9.1.2)
- Short-term toxicity testing on fish (Annex VIII, Section 9.1.3.)
- Long-term toxicity testing on aquatic invertebrates (Annex IX, Section 9.1.5.)
- Long-term toxicity testing on fish (Annex IX, Section 9.1.6.)

ECHA has considered the scientific and regulatory validity of your (Q)SAR adaptation(s) in general before assessing the specific standard information requirements in the following appendices.

Under Annex XI, Section 1.3., the following conditions must be fulfilled whenever a (Q)SAR approach is used:

1. the prediction needs to be derived from a scientifically valid model,
2. the substance must fall within the applicability domain of the model,
3. results need to be adequate for the purpose of risk assessment or classification and labelling, and
4. adequate and reliable documentation of the method must be provided.

With regard to these conditions, we have identified the following issue(s):

1.1 The prediction is not adequate due to low reliability

Under ECHA Guidance R.6.1.3.4 a prediction is adequate for the purpose of classification and labelling and/or risk assessment when the model is applicable to the chemical of interest with the necessary level of reliability. ECHA Guidance R.6.1.5.3. specifies that, among others, the following condition must be met:

- reliable input parameters are used.

Your registration dossier provides the following information:

- You provide QSAR predictions (ECOSAR QSAR, version and submodel used are unclear, see the issue below) for aquatic toxicity endpoints based on a Log Kow of 2.52 estimated by the QSAR, as follows:
  - Short term toxicity to invertebrates predicted 48-h LC50 of 7.519 mg/L
  - Short term toxicity to fish predicted 96-h LC50 of 11.31 mg/L
  - Long term toxicity to invertebrates predicted 21-day ChV of 0.309 mg/L
  - Long term toxicity to fish predicted 30-day ChV of 0.552 mg/L
  - Toxicity to algae predicted EC50 of 2.68mg/L and ChV of 0.814mg/L

The following information for the Substance is also available and is considered relevant for the assessment of the predictions:

- Experimental Log Kow of 4.59 (OECD 117)

The prediction(s) for the properties of the Substance are not reliable because:

- The key input parameter for the ECOSAR QSAR is Log Kow. The experimental Log Kow provided in the dossier (4.59) is different from the Log Kow predicted by the ECOSAR v1.11 QSAR (Log Kow 2.52). The inconsistency between experimental and predicted

Log Kow values is critical given the importance of this parameter in the QSAR predictive calculations. The use of the experimental Log Kow as input to the QSAR results in much more conservative predictions than those provided in the dossier. You have not provided evidence that the predictions are based on a reliable Log Kow value for the Substance.

Therefore, you have not demonstrated that the prediction for the Substance is adequate for the purpose of classification and labelling and/or risk assessment.

1.2 Lack of or inadequate documentation of the model (QMRF) and the prediction (QPRF)

Under Appendix C of the OECD Guidance document on the validation of (Q)SAR models (ENV/JM/MONO(2007)2) and ECHA Guidance R.6.1.6.3., adequate and reliable documentation must include

a. (Q)SAR Model Reporting Format document (QMRF) which reports, among others, the following information:
   - an unambiguous definition of the algorithm, the descriptor(s) of the model and its applicability domain,
   - an estimate of the goodness-of-fit and of the predictivity of the model, including information on training set and validation statistics.

b. (Q)SAR Prediction Reporting Format document (QPRF) which reports, among others:
   - a precise identification of the substance modelled,
   - the identities of close analogues, including considerations on how predicted and experimental data for analogues support the prediction.

You provided the following information:

<u>Information about the model used for the prediction:</u>

- The provided QMRFs refer to ECOSAR v1.11, whereas the provided QPRFs refer to ECOSAR v1.0. It is therefore unclear which version was used for the predictions.
- There is no clear indication in the QMRFs or QPRFs as to which submodel within ECOSAR was used for the predictions (e.g. neutral narcosis model or diketones model).
- The predictive algorithms reported in the QMRFs are different from the algorithms provided in the dossier. For example;
  - In the dossier you provide the following equation for the linear regression QSAR for both acute and chronic toxicity to fish: Log Toxicity (mmol/L) = -0.8981(log Kow) + 1.7108.
  - In the QMRFs different equations are provided. For acute toxicity to fish the QMRF provides: LC50y = -0.1423x - 2.0099 and for chronic toxicity to fish the QMRF provides: LogChV (mmol/L) = -0.4834 (log Kow) - 2.2111.
- You have not reported clearly what data are used in the model, the number of compounds which are used to make the regression model, and the related standard error of estimates that would allow assessment of goodness-of-fit and predictivity of the model.

<u>Information provided about the prediction:</u>

- In the dossier, the conclusion for every predicted aquatic toxicity endpoint refers to coumarin (which is not the registered substance). The accompanying documentation (e.g. QPRF) refers to the Substance.

- You have not provided any additional information on structurally similar analogue substances to establish that the model provides accurate predictions for this Substance.

We have assessed the information provided and identified the following deficiencies:

- You have not clearly indicated which model, and which algorithms, were used for the predictions in the documentation provided (QMRFs and QPRFs). Hence, an unambiguous definition of the algorithm(s), and clear descriptor(s) of the model, and its applicability domain were not provided.
- You have not reported clearly what data are used in the model, the number of compounds which are used to make the regression model, and the related standard error of estimates that would allow assessment of goodness-of-fit and predictivity of the model. Hence the required estimate of the goodness-of-fit and of the predictivity of the model, including information on training set and validation statistics were not provided.
- The results provided in the dossier refer to coumarin (which is not the registered substance), whereas the QPRFs refer to the Substance. The conflicting and inconsistent information provided in the documentation prevents a clear and unambiguous understanding of the modelled substance.
- You do not provide any information on structurally similar analogues to allow ECHA to assess how well the selected model may predict ecotoxicity endpoints for similar substances.

In absence of such information, ECHA cannot establish that the prediction can be used to meet this information requirement.

Therefore, your adaptations are rejected.

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

1. Water solubility

Water solubility is an information requirement in Annex VII to REACH (section 7.7).

You have provided a key study using the flask method described in the OECD TG 105, 2013.

ECHA assessed this information and identified the following issues:

The EU test method A.6 and OECD TG 105 describe two methods (the column elution method and the flask method) for conducting the study. The test method must be selected based on a water solubility estimate obtained in a preliminary study. For substances with preliminary water solubility below 10 mg/L the column elution method must be used.

You have provided a study performed with the flask method and you report a water solubility 0.493mg/L. The reported result falls outside of the applicability domain of the flask method.

Therefore, the provided information does not fulfil the information requirement.

2. Short-term toxicity testing on aquatic invertebrates

Short-term toxicity testing on aquatic invertebrates is an information requirement under Annex VII to REACH (Section 9.1.1.).

You have provided the following information:

- An ECOSAR QSAR (model and version used unclear) predicted value for short term toxicity to invertebrates (48-h LC50) of 7.519 mg/L

As explained in the Appendix on reasons common to several requests, your adaptation is rejected. On this basis, the information requirement is not fulfilled.

Study design

OECD TG 202 would fulfil the information requirement. We note that the current water solubility provided in the dossier (0.493 mg/L) indicates that the Substance may be difficult to test. As noted above, the water solubility data provided is not considered reliable (see A.1). In the case that the water solubility is confirmed to be <100 mg/L you should note that OECD TG 202 specifies that, for difficult to test substances, you must consider the approach described in OECD GD 23 or other approaches, if more appropriate for your substance. In all cases, the approach selected must be justified and documented. Due to the properties of Substance, it may be difficult to achieve and maintain the desired exposure concentrations. Therefore, you must monitor the test concentration(s) of the Substance throughout the exposure duration and report the results. If it is not possible to demonstrate the stability of exposure concentrations (i.e. measured concentration(s) not within 80-120% of the nominal concentration(s)), you must express the effect concentration based on measured values as described in OECD TG 202. In case a dose-response relationship cannot be established (no observed effects), you must demonstrate that the approach used to prepare test solutions was adequate to maximise the concentration of the Substance in the test solution.

3. Growth inhibition study aquatic plants

Growth inhibition study aquatic plants is an information requirement under Annex VII to REACH (Section 9.1.2.).

You have provided the following information:

- An ECOSAR QSAR (model and version used unclear) predicted value for algal toxicity EC50 of 2.68mg/L and ChV of 0.814mg/L, respectively.

As explained in the Appendix on reasons common to several requests, your adaptation is rejected.

On this basis, the information requirement is not fulfilled.

Study Design
OECD TG 201 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained above, if the water solubility is confirmed to be <100mg/L the Substance is difficult to test. In that case, you must fulfil the requirements described in 'Study design' under Appendix [A.2].

4. Ready biodegradability

Ready biodegradability is an information requirement in Annex VII to REACH (Section 9.2.1.1.).

You provided the following information in your dossier:

- OECD TG 301B key study with the Substance, with no confirmation that the study was conducted according to GLP [Test Report: 1,3-DIPHENYLPROPANE-1,3-DIONE", Testing facility [redacted]]. The results indicate 89% degradation at 28 days based on TOC removal.

We assessed the information in your dossier and identified the following issues:

To fulfil the information requirement, a study must comply with the OECD TG 301 (Article 13(3) of REACH). Therefore, for a study according to OECD TG 301, the following requirements must be met:

Key validity criteria for OECD TG 301 tests:
- The degradation of the reference compound reached the pass level by day 14;
- The difference of extremes between replicate values of the removal of the test material at the plateau, at the end of the test or, if appropriate, at the end of the 10-d window is ≤ 20%;
- In the toxicity control, the degradation of the reference substance reached ≥ 35% (based on DOC) or ≥ 25% (based on ThOD or $ThCO_2$) by day 14;

Furthermore, for OECD 301B the following criteria must be met:
- The concentration of the test material is in the range of 10-20 mg DOC (or TOC)/L;
- Biodegradation is followed by monitoring the amount of carbon dioxide produced from the test material (corrected for that derived from the blank inoculum). DOC (or TOC) analysis is only an optional additional parameter;
- Measurements of CO_2 evolution in the test suspensions and inoculum blanks are done in parallel;
- The test temperature and pH is reported;
- The methods of preparation of test solutions/suspensions is reported;
- The results of measurements at each sampling point in each replicate is reported in a tabular form;

Your registration dossier provides an OECD TG 301B study showing the following:

- No results are provided for the degradation of a reference compound hence it is unknown whether a reference substance was used or, if used, it achieved the pass level by day 14.
- The difference of extremes of replicate values of the removal of the test material are not provided hence we cannot confirm that the replicate values did not differ by ≤ 20%;
- No data from a toxicity control was provided, hence the degradation of the reference substance in the toxicity control cannot be confirmed to have reached the pass level (≥ 25%) by day 14;

The above key validity criteria for OECD TG 301 tests cannot be confirmed for the provided test based on the information in the dossier.

Furthermore, we note the following additional methodological deficiencies relevant to OECD TG 301B tests:

- The concentration of the test material was 26.01mg/L TOC which is higher than the range of 10-20 mg DOC (or TOC)/L allowed for in OECD TG 301B;
- Biodegradation was followed by monitoring TOC and not the amount of carbon dioxide produced from the test material. DOC (or TOC) analysis is only an optional additional parameter;
- No measurements of CO_2 evolution in the test suspensions and inoculum blanks are provided;
- No test conditions (i.e. temperature, pH, methods of test solution preparations) or tabulated results are provided.

Therefore, the key validity criteria for OECD TG 301 tests are not met and there are critical methodological deficiencies affecting the reliability of the test results. Therefore, the information provided in the dossier is insufficient to allow an independent assessment of the study's reliability.

In the comments to the draft decision, you have attached a copy of the study report for the OECD TG 301B study (Eurofins, 2014) which includes the information that was identified as missing in the dossier and confirms that the key validity criteria for OECD TG 301 tests are met.

The information provided as part of your comments addresses the incompliances identified above. However, as the information is currently not available in your registration dossier, the data gap remains. You should submit this information in an updated registration dossier by the deadline set in the decision.

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

1. Short-term toxicity testing on fish

Short term toxicity testing on fish is an information requirement under Annex VIII to REACH (Section 9.1.3.).

You have provided the following information:

- An ECOSAR QSAR (model and version used unclear) predicted value for short term toxicity to fish (96-h LC50) of 11.31 mg/L

As explained in the Appendix on reasons common to several requests, your adaptation is rejected. On this basis, the information requirement is not fulfilled.

Study Design
OECD TG 203 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained above, if the water solubility is confirmed to be <100 mg/L the Substance is difficult to test. In that case, you must fulfil the requirements described in 'Study design' under Appendix A.2.

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

1. Long-term toxicity testing on aquatic invertebrates

Long term toxicity testing on aquatic invertebrates is an information requirement under Annex IX to REACH (Section 9.1.5.).

You have provided the following information:

- An ECOSAR QSAR (model and version used unclear) predicted value for long term toxicity to aquatic invertebrates (21-day ChV) of 0.309 mg/L

As explained in the Appendix on reasons common to several requests, your adaptation is rejected. On this basis, the information requirement is not fulfilled.

Study Design
OECD TG 211 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained above, if the water solubility is confirmed to be <100 mg/L the Substance is difficult to test. In that case, you must fulfil the requirements described in 'Study design' under Appendix A.2.

2. Long-term toxicity testing on fish

Long term toxicity testing on fish is an information requirement under Annex IX to REACH (Section 9.1.6.).

You have provided the following information:

- An ECOSAR QSAR (model and version used unclear) predicted value for long term toxicity to fish (30-day ChV) of 0.552 mg/L

As explained in the Appendix on reasons common to several requests, your adaptation is rejected. On this basis, the information requirement is not fulfilled.

Study Design
OECD TG 210 specifies that for difficult to test substances OECD GD 23 must be followed. As already explained above, if the water solubility is confirmed to be <100 mg/L the Substance is difficult to test. In that case, you must fulfil the requirements described in 'Study design' under Appendix A.2.

Appendix D: 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[2].

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[3].

[2] https://echa.europa.eu/practical-guides
[3] https://echa.europa.eu/manuals

Appendix E: Procedure

The information requirement for a Pre-natal developmental toxicity (PNDT) study, one species (Annex IX, Section 8.7.2) is not addressed in this decision due to an ongoing dossier evaluation follow-up process. Similarly, the information requirement for a Screening for reproductive/developmental toxicity (Annex VIII, Section 8.7.1.) is not addressed in this decision as the fulfilment of this information requirement is related to the ongoing process for the PNDT study.

However, 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 the 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[4] 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)[5]

RAAF - considerations on multiconstituent substances and UVCBs (RAAF UVCB, March 2017)[6]

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[7]

[4] https://echa.europa.eu/guidance-documents/guidance-on-information-requirements-and-chemical-safety-assessment
[5] https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across
[6] https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316
[7] 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 G: 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]

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.