~~Confidential~~

Helsinki, 4 May 2022

Addressees
Registrant(s) of JS_Fadex HE 1819 PK as listed in Appendix 3 of this decision

Date of submission of the dossier subject to this decision
20/01/2016

Registered substance subject to this decision ("the Substance")
Substance name: 2,2''-dihydroxy-4,4''-(2-hydroxy-propane-1,3-diyldioxy)dibenzophenone
EC number: 424-210-0

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 ***11 May 2023***.

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

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

1. Long-term toxicity testing on aquatic invertebrates (triggered by Annex VII, Section 9.1.1., column 2; test method: EU C.20./OECD TG 211)

The reasons for the decision(s) are explained in Appendix 1.

Information required depends on your tonnage band

You must provide the information listed above for all REACH Annexes applicable to you in accordance with Articles 10(a) and 12(1) of REACH. The addressees of the decision and their corresponding information requirements based on registered tonnage band are listed in Appendix 3.

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 requirements for testing and reporting new tests under REACH, see Appendix 4. In addition, the studies relating to biodegradation and bioaccumulation are necessary for the PBT assessment. However, to determine the testing

needed to reach the conclusion on the persistency and bioaccumulation of the Substance you should consider the sequence in which these tests are performed and other conditions described in this Appendix.

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

Appendix 1: Reasons for the decision
Appendix 2: Procedure
Appendix 3: Addressees of the decision and their individual information requirements
Appendix 4: Conducting and reporting new tests under REACH

[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 1: Reasons for the decision

Contents

Reasons related to the information under Annex VII of REACH

1. Long-term toxicity testing on aquatic invertebrates

1 Short-term toxicity testing on aquatic invertebrates is an information requirement under Column 1 of Annex VII to REACH (Section 9.1.1.). However, long-term toxicity testing on aquatic invertebrates must be considered (Section 9.1.1., Column 2) if the substance is poorly water soluble.

1.1. Information provided

2 You have provided a key study that was performed according to EU Method C.2 (Acute Toxicity for Daphnia) but no information on long-term toxicity on aquatic invertebrates for the Substance.

1.2. Assessment of the information provided

3 We have assessed this information and identified the following issues:

4 Poorly water soluble substances require longer time to reach steady-state conditions. As a result, the short-term tests does not give a true measure of toxicity for this type of substances and the long-term test is required. A substance is regarded as poorly water soluble if, for instance, it has a water solubility below 1 mg/L or below the detection limit of the analytical method of the test material (Guidance on IRs and CSA, Section R.7.8.5).

5 In the provided study EU Method A.6 (1996), the saturation concentration of the Substance in water was determined to be less than 35.2 µg/L.

6 Therefore, the Substance is poorly water soluble and information on long-term toxicity on aquatic invertebrates must be provided.

7 In your comments to the draft decision, you do not agree to perform the requested study based on the following reasons.

8 You state that REACH Annex VII 9.1.1. requires short term toxicity testing on invertebrates as mandatory data and you have performed and reported such valid study in your dossier to address this endpoint.

9 You also state in your comments that your interpretation of column 2 of Annex VII 9.1.1., which says that "a long-term study shall be considered if a substance is poorly water soluble", is that the need to perform such a study requires a case-by-case decision and the wording in the draft decision requesting automatically the long-term testing goes beyond the legally required data set and ECHA has not sufficiently substantiated why such a test is mandatory in this case.

10 You further claim in your comments that an organic vehicle was utilized in the short term toxicity test on invertebrates to "increase" the solubility and to provide immediate and constant bioavailability of the test substance to the test organisms. With this you conclude that a general statement in the draft decision that "poorly water soluble substance require longer time to reach steady-state condition" and " As a result, the short term test does not give a true measure of the toxicity of the type of substance" is not specific for your substance.

11 Finally, you provide a new QSAR (ECOSAR v2.0) prediction on the chronic Daphnia toxicity to fulfil this standard information requirement. You further consider that the predicted ChV of 0.094 mg/L confirms the lack of toxicity up to and above the water solubility limit of the substance (i.e. 0.035 mg/L).

12 We have assessed the information provided in your comments to the draft decision and identified the following issues:

13 As regards your comment of the REACH Annex VII 9.1.1. and the necessity to provide information on long-term toxicity on aquatic invertebrates besides the provided information on short-term toxicity, we refer to our above reasons for why ECHA considers this as a requirement already at Annex VII.

14 As regards your comment of the interpretation of column 2 of Annex VII, 9.1.1., ECHA considers that column 2 indicates that long-term instead of short-term test must be conducted for the poorly water soluble substance. As explained under the Guidance on IRs and CSA, further testing (i.e. long-term testing) is required at Annex VII/VIII if the CSA indicates the need to investigate further the effects on aquatic organisms. The Guidance indicates that such a need to conduct further testing is triggered when due to low water solubility of a substance, short term toxicity tests do not reveal any toxicity.

15 As regards your comments on the Substance specific reasons for considering that "poorly water soluble substance require longer time to reach steady-state condition" ECHA refers to the data provided in the dossier. As indicated in the draft decision above, the reported water solubility of 35.2 µg/L shows that the Substance is poorly water soluble. Using the organic vehicle in the short-term toxicity test allowed to expose the test organisms to a maximum concentration of 0.10 mg/L. This value is above the water solubility limit of the Substance, but still below the limit of poor water solubility of 1 mg/L. However, this does not remove the possibility that longer time is required for such a substance to reach steady-state conditions. ECHA acknowledges that the use of a solubiliser allowed to increase the dissolved, and hence bioavailable, test chemical concentration in the solutions. However, it does not inform on whether the steady state (related to internal concentration) was reached. Since no effects were observed in the available short-term toxicity studies, your comments do not remove the possibility that longer time is required for such a substance to reach steady-state conditions and potentially cause hazardous effects. Therefore, the short-term test showing no effects, even if conducted using organic vehicle and exposure concentrations exceeding the reported water solubility, does not necessarily give a true measure of the toxicity of your Substance and a long-term study is needed.

16 As regards the new QSAR prediction on the chronic Daphnia toxicity, ECHA acknowledges the related QMRF and QPRF documents attached in your comments and in your latest dossier update.

17 ECHA has assessed the QSAR prediction provided in your comments against the requirements of Annex XI, Section 1.3.

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

(1) the prediction needs to be derived from a scientifically valid model.

19 With regard to this condition, we have identified the following issue:

20 Under Guidance on IRs and CSA, Section R.6.1.3., a (Q)SAR model must fulfil the principles described in the OECD Guidance document on the validation of (Q)SAR models (ENV/JM/MONO(2007)2) to be considered scientifically valid. For that purpose, the fourth OECD principle requires that appropriate measures of the internal performance (i.e. goodness-of-fit and robustness using the learning data set) and predictivity (using a test data set) of the model are available.

21 To have appropriate robustness, a model must be built from a training set which includes a sufficient number of substances. The minimum number of substances depends on the

number of variables or descriptors included in the model. The ratio between the number of substances and the number of variables or descriptors must be at least 5.

22 The training set of your model is based on one descriptor and three chemicals.

23 Since the ratio between the number of substances and the number of variables or descriptors is less than five, you have not established the robustness, and thus the scientific validity, of the model.

24 Based on the above, your adaptation is rejected.

25 As a consequence, this QSAR prediction cannot be used to fulfil this standard information requirement and it does not demonstrate lack of chronic toxicity to aquatic invertebrates.

26 Therefore, the information requirement is not fulfilled.

1.3. Study design and test specifications

27 The Substance is difficult to test due to the low water solubility (0.0352 mg/L). OECD TG 211 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 211. 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 solutions.

References

The following documents may have been cited in the decision.

Guidance on information requirements and chemical safety assessment (Guidance on IRs & CSA)

Chapter R.4 Evaluation of available information; ECHA (2011).
Chapter R.6 QSARs, read-across and grouping; ECHA (2008).
Appendix to Chapter R.6 for nanoforms; ECHA (2019).
Chapter R.7a Endpoint specific guidance, Sections R.7.1 – R.7.7; ECHA (2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Chapter R.7b Endpoint specific guidance, Sections R.7.8 – R.7.9; ECHA (2017).
Appendix to Chapter R.7b for nanomaterials; ECHA (2017).
Chapter R.7c Endpoint specific guidance, Sections R.7.10 – R.7.13; (ECHA 2017).
Appendix to Chapter R.7a for nanomaterials; ECHA (2017).
Appendix R.7.13-2 Environmental risk assessment for metals and metal compounds; ECHA (2008).
Chapter R.11 PBT/vPvB assessment; ECHA (2017).
Chapter R.16 Environmental exposure assessment; ECHA (2016).

Guidance on data-sharing; ECHA (2017).

All Guidance on REACH is available online: https://echa.europa.eu/guidance-documents/guidance-on-reach

Read-across assessment framework (RAAF)

RAAF, 2017 Read-across assessment framework (RAAF), ECHA (2017)
RAAF UVCB, 2017 Read-across assessment framework (RAAF) – considerations on multi- constituent substances and UVCBs), ECHA (2017).

The RAAF and related documents are available online:
https://echa.europa.eu/support/registration/how-to-avoid-unnecessary-testing-on-animals/grouping-of-substances-and-read-across

***OECD Guidance documents* (OECD GDs)**

OECD GD 23 Guidance document on aquatic toxicity testing of difficult substances and mixtures; No. 23 in the OECD series on testing and assessment, OECD (2019).
OECD GD 29 Guidance document on transformation/dissolution of metals and metal compounds in aqueous media; No. 29 in the OECD series on testing and assessment, OECD (2002).
OECD GD 150 Revised guidance document 150 on standardised test guidelines for evaluating chemicals for endocrine disruption; No. 150 in the OECD series on testing and assessment, OECD (2018).
OECD GD 151 Guidance document supporting OECD test guideline 443 on the extended one-generation reproductive toxicity test; No. 151 in the OECD series on testing and assessment, OECD (2013).

Appendix 2: 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 25 January 2021.

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

In the comments to the draft decision, the lead registrant ([redacted]), who registered the tonnage band 10-100tpa, informed that it has ceased the manufacturing the substance.

ECHA took into accounts the comments and amended the requests.

The deadline of 36 months initially indicated in the draft decision of this decision took into account requests for the following studies which have been removed from the decision: *In vitro* gene mutation study in bacteria; Growth inhibition study aquatic plants; *In vitro* cytogenicity study in mammalian cells or *In vitro* micronucleus study; Short-term repeated dose toxicity (28 days); Long-term toxicity testing on fish; Simulation testing on ultimate degradation in surface water; Soil simulation testing; Sediment simulation testing; Identification of degradation products; Bioaccumulation in aquatic species.

Following the removal of these aforementioned requests only the request for a study on Long-term toxicity testing on aquatic invertebrates remains in the decision.

ECHA considers that 12 months are sufficient for conducting the study on Long-term toxicity testing on aquatic invertebrates with the Substance. Therefore, ECHA has set the deadline in this decision to 12 months.

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 3: Addressees of this decision and their corresponding information requirements

In accordance with Articles 10(a) and 12(1) of REACH, the information requirements for individual registrations are defined as follows:

- 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.

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

Appendix 4: Conducting and reporting new tests for REACH purposes

1. Requirements when conducting and reporting new tests for REACH purposes

1.1. 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].

1.2. 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