~~Confidential~~

Helsinki, 02 February 2022

Addressees
Registrants of DCP_2010_11_02_001 as listed in the last Appendix of this decision

Date of submission of the dossier subject to this decision
16/07/2020

Registered substance subject to this decision ("the Substance")
Substance name: Bis(α,α-dimethylbenzyl) peroxide
EC number: 201-279-3

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 ***7 November 2023***.

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

A. Requirements applicable to all the Registrants subject to Annex VI of REACH

1. Apply the harmonised classification and labelling on the Substance for reproductive toxicity (Annex VI, Section 4.);

B. 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 (EU B.71/OECD TG 442E)(Annex VII, Section 8.3.1.); and

   ii. Only if the *in vitro/in chemico* test methods specified under point B.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);

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

1. Long-term toxicity testing on fish (triggered by Annex VIII, Section 9.1.3., column 2; test method: OECD TG 210)

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

1. 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:

- Appendices entitled "Reasons to request information required under Annexes VI 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 VI and 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 VI to VIII to REACH, for registration at 10-100 tpa;
- the information specified in Annexes VI to 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.

For certain endpoints, ECHA requests the same study from registrants at different tonnages. In such cases, only the reasoning why the information is required at lower tonnages is provided in the corresponding Appendices. For the tonnage where the study is a standard information requirement, the full reasoning for the request including study design is given. Only one study is to be conducted; the registrants concerned must make every effort to reach an agreement as to who is to carry out the study on behalf of the other registrants under Article 53 of REACH.

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 for the requests to comply with Annex VI of REACH

Under Article 10(a) of REACH, a technical dossier must contain information specified in Annex VI to REACH.

1. **Apply the harmonised classification and labelling on the Substance for carcinogenicity and skin sensitisation (Annex VI, Section 4.)**

Classification and labelling of the substance, resulting from the application of Title I, II and III of Regulation (EC) No 1272/2008 (CLP), is an information requirement as specified in Annex VI to REACH, Section 4.

The Substance has a harmonised classification under Annex VI of the CLP Regulation. According to the 15th ATP to the CLP Regulation, this harmonised classification has been modified to include a classification as Repro 1B; "may damage the unborn child". The 15th ATP of the CLP Regulation has been adopted on 19 May 2020 and will apply from 01 March 2022.

The classification of the Substance currently listed in your dossier does not reflect this classification as Repro 1B. Whilst the changes in the harmonised classification arising form this ATP can already be implemented on a voluntary basis, you are requested to classify your Substance as Repro 1B by 01 March 2022 at the latest.

Appendix B: 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.

You have provided the following information in the technical dossier, based on which you conclude that the Substance is not a skin sensitiser:

i. *In vivo* Local Lymph Node Assay (key study), non-guideline, GLP, [redacted], 2010.
ii. Guinea pig maximisation test (supporting study), secondary citation from scientific literature Patty's industrial hygiene and toxicology: 2.5.4 Dicumyl peroxide, Clayton, 1993, reliability index 4;
iii. Human patch test, (supporting study), secondary citation from scientific literature Patty's industrial hygiene and toxicology: 2.5.4 Dicumyl peroxide, Clayton, 1993, reliability index 4;
iv. Publication Clinical and experimental studies on the irritating effect of dicumil peroxide on the skin and the upper respiratory tract, Dermatol i venerol XXIX, No2, 33-36, Madzunov, 1990, reliability index 3.

You have adapted this information requirement under Section 8.3.1, Column 2 using the following justification: adequate *in vivo* study is already available.

We have assessed this information and identified the following issue(s):

A) Assessment whether the Substance causes skin sensitisation

Study not conducted using a recognised test method

Toxicological and eco-toxicological tests on substances must be conducted in compliance with the test methods laid down in a Commission Regulation or in accordance with other international test methods recognised by the Commission or ECHA as being appropriate (Article 13(3) of REACH). According to Article 141(2), Article 13 applies from 1 June 2008.

The provided key study was not based on OECD TG 429. Based on the information provided, ECHA understands that the study was conducted according the Modified LLNA (IMDS = Integrated Model for the Differentiation of Skin Reactions), albeit not specified by you. This IMDS test method has not been validated or considered to be scientifically valid by international bodies. In particular, the nature of the measurements performed in this study and the appropriate cut-off values to consider results positive are not validated.

Since the study that you have provided is neither in compliance with the test methods laid down in a Commission Regulation nor in accordance with other international test methods recognised by the Commission or ECHA as being appropriate, the information obtained from this study is rejected.

In addition, you have provided studies ii. to iv. which you assigned with reliability indexes (Klimisch scores) of 3 (not reliable) or 4 (not assignable). We agree with your assessment of the reliability of this information.

Based on the above, the information submitted does not enable to conclude whether the Substance causes skin sensitisation.

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

No assessment of potency

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

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

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 suggest conducting testing according to the OECD TG 497. You consider that "*the "Integrated Testing Strategy (ITS)" Defined Approach would be the preferred choice. The ITS defined approach allows to assess the potential to produce significant sensitisation in humans (Cat. 1A) (see Appendix B.1.B) of the draft decision), as it allows to discriminate chemicals into the three UN GHS/CLP categories 1A (strong sensitiser), 1B (other sensitiser), and Not Classified (non-sensitiser)*". You also point out that the applicability of the *in chemico-in vitro* test methods listed above might be limited by the physico-chemical properties of the substance.

The information from the OECD TG 497 investigates the elements intended to be tested in the tests requested in the decision. ECHA notes that the ITS defined approaches described in the OECD TG 497 rely, among other sources of information, on results from studies conducted according to the OECD TGs 442C and 442E. These studies are also listed under the request B.1.i of this decision.

While the ITS defined approaches may constitute a scientifically sound alternative to the tests requested in the decision, it is the responsibility of the registrants to ensure that the test item is within the applicability domain of all the applied test methods and that the results of the individual tests are integrated and analysed in accordance with the provisions of the OECD TG 497.

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

1. Long-term toxicity testing on fish

Short-term toxicity testing on fish is an information requirement under Annex VIII to REACH (Section 9.1.3.). Long-term toxicity testing on fish must be considered (Section 9.1.3., Column 2) if the substance is poorly water soluble.

You provided three short-term toxicity studies on fish with the Substance:

- [redacted] (2000) according to OECD TG 203 (96h LC50=0.469 mg/L)
- MITI (1992) according to Japanese Industrial Standard JIS K 0102-1986-71 (48h LC50=4.2 mg/L)
- [redacted] (1990) according to OECD TG 203 (96h LC50=108.45 mg/L)

You provided no information on long-term toxicity on fish for the Substance.

We have assessed this information and identified the following issue:

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 (ECHA Guidance R.7.8.5).

In the provided OECD TG 105 study ([redacted] 2010), the saturation concentration of the Substance in water was determined to be 0.43 mg/L.

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

The examination of the information provided, as well as the selection of the requested test and the test design are addressed under section D.1.

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

1. Long-term toxicity testing on fish

You have provided the following information:

- a justification to omit the study which you consider to be based on Annex IX, Section 9.1., Column 2. In support of your adaptation, you provided the following justification:

  '*According to Annex IX of Regulation (EC) No 1907/2006 chronic fish toxicity tests should be proposed if the chemical safety assessment indicates the need to investigate further the effects on fish. However, overall information is sufficient for risk assessment. Therefore, testing of on chronic fish toxicity is not regarded necessary*.'

We have assessed this information and identified the following issue:

Annex IX, Section 9.1., Column 2 does not allow omitting the need to submit information on long-term toxicity to fish under Column 1. It must be understood as a trigger for providing further information on long-term toxicity to fish if the chemical safety assessment according to Annex I indicates the need (Decision of the Board of Appeal in case A-011-2018).

Your adaptation is therefore rejected.

Study design

To fulfil the information requirement for the Substance, the Fish, Early-life Stage Toxicity Test (test method OECD TG 210) is the most appropriate (ECHA Guidance R.7.8.2.).

The Substance is difficult to test due to the low water solubility (0.43 mg/L) and adsorptive properties (Log kow 5.6). OECD TG 210 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 210. 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.

Appendix E: 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 F: Procedure

The Substance is listed in the Community rolling action plan (CoRAP) for the start of substance evaluation 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 01 February 2021.

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).

Deadline to provide the information

In the comments to the draft decision, you requested an extension of the deadline to provide the information from 12 to 18 months from the date of adoption of the decision. You considered that the extension of six months is needed due to limited capacity of the testing laboratories following a high demand of long-term toxicity testing on fish in Europe.

Based on the provided documentary evidence from laboratories indicating the timelines to conduct the study, ECHA has accepted the request and extended the deadline to 18 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 G: 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 H: 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]
[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.