Committee for Risk Assessment

RAC

Opinion

proposing harmonised classification and labelling
at EU level of

Dibenzoyl peroxide; benzoyl peroxide

EC Number: 202-327-6
CAS Number: 94-36-0

CLH-O-0000007215-78-01/F

Adopted

1 December 2022

1 December 2022

CLH-O-0000007215-78-01/F

OPINION OF THE COMMITTEE FOR RISK ASSESSMENT ON A DOSSIER PROPOSING HARMONISED CLASSIFICATION AND LABELLING AT EU LEVEL

In accordance with Article 37 (4) of Regulation (EC) No 1272/2008, the Classification, Labelling and Packaging (CLP) Regulation, the Committee for Risk Assessment (RAC) has adopted an opinion on the proposal for harmonised classification and labelling (CLH) of:

Chemical name: **Dibenzoyl peroxide; benzoyl peroxide**

EC Number: **202-327-6**

CAS Number: **94-36-0**

The proposal was submitted by **Ireland** and received by RAC on **23 November 2021.**

In this opinion, all classification and labelling elements are given in accordance with the CLP Regulation.

PROCESS FOR ADOPTION OF THE OPINION

Ireland has submitted a CLH dossier containing a proposal together with the justification and background information documented in a CLH report. The CLH report was made publicly available in accordance with the requirements of the CLP Regulation at ***http://echa.europa.eu/harmonised-classification-and-labelling-consultation/*** on **7 February 2022**. Concerned parties and Member State Competent Authorities (MSCA) were invited to submit comments and contributions by **8 April 2022**.

ADOPTION OF THE OPINION OF RAC

Rapporteur, appointed by RAC: **Anja Menard Srpčič**

The opinion takes into account the comments provided by MSCAs and concerned parties in accordance with Article 37(4) of the CLP Regulation and the comments received are compiled in Annex 2.

The RAC opinion on the proposed harmonised classification and labelling was adopted on **1 December 2022** by **consensus**.

Classification and labelling in accordance with the CLP Regulation (Regulation (EC) 1272/2008)

	Index No	Chemical name	EC No	CAS No	Classification		Labelling			Specific Conc. Limits, M-factors and ATE	Notes
					Hazard Class and Category Code(s)	Hazard statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)	Suppl. Hazard statement Code(s)		
Current Annex VI entry	617-008-00-0	Dibenzoyl peroxide; benzoyl peroxide	202-327-6	94-36-0	Org. Perox. B Eye Irrit. 2 Skin Sens. 1	H241 H319 H317	GHS02 GHS01 GHS07 Dgr	H241 H319 H317	-	-	-
Dossier submitters proposal	617-008-00-0	Dibenzoyl peroxide; benzoyl peroxide	202-327-6	94-36-0	**Add** Aquatic Acute 1 Aquatic Chronic 1	**Add** H400 H410	**Add** GHS09	**Add** H410	-	**Add** M = 10 M = 10	-
RAC opinion	617-008-00-0	Dibenzoyl peroxide; benzoyl peroxide	202-327-6	94-36-0	**Add** Aquatic Acute 1 Aquatic Chronic 1	**Add** H400 H410	**Add** GHS09	**Add** H410	-	**Add** M = 10 M = 10	-
Resulting Annex VI entry if agreed by COM	617-008-00-0	Dibenzoyl peroxide; benzoyl peroxide	202-327-6	94-36-0	Org. Perox. B Eye Irrit. 2 Skin Sens. 1 Aquatic Acute 1 Aquatic Chronic 1	H241 H319 H317 H400 H410	GHS02 GHS01 GHS07 GHS09 Dgr	H241 H319 H317 H410	-	M = 10 M = 10	-

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GROUNDS FOR ADOPTION OF THE OPINION

RAC general comment

Dibenzoyl peroxide is an organic peroxide in the form of a granular powder (crystal) and is used in polymerisation reactions (polymers, resins, rubbers) and as an intermediate, adhesive, sealant, coating resin hardener, and toner by industrial and professional workers. It is also formulated into fillers, adhesives, sealants, cosmetics, and personal care products for use by consumers.

ENVIRONMENTAL HAZARD EVALUATION

RAC evaluation of aquatic hazards (acute and chronic)

Summary of the Dossier Submitter's proposal

The current entry in Annex VI of Regulation (EC) No 1272/2008 of dibenzoyl peroxide does not include harmonised classification for environmental hazards.

The Dossier Submitter (DS) proposed to classify the substance as:

- **Aquatic Acute 1 (H400) with M-factor of 10** based on a 96 h EC_{50} value of 0.0602 mg/L for fish *Oncorhynchus mykiss*.
- **Aquatic Chronic 1 (H410) with M-factor of 10** based on 21 d EC_{10} value of 0.001 mg/L for the invertebrate *Daphnia magna.* The substance has low bioaccumulation potential and is rapidly degradable.

Rapid degradability

Hydrolysis

Two hydrolysis studies according to OECD TG 111 are available. In the first study, dibenzoyl peroxide was determined to be hydrolytically unstable at acidic (pH 4), neutral (pH 7) and alkaline (pH 9) conditions at 50 °C. The rate of hydrolysis increased with increasing pH and at pH 9 resulted in the availability of approximately 20 % of the applied test substance. Greater than 50 % hydrolysis occurred after 2.4 hours, equivalent to a half-life (DT_{50}) of less than 1 day under environmentally relevant condition (25 °C). The principal hydrolysis product, benzoic acid, was detected. Benzoic acid can be considered as readily biodegradable and has a low bioaccumulation potential (log K_{OW} < 2) (REACH registration dossier, ECHA, 2021b). Benzoic acid does not have a harmonised classification entry for environmental hazards. In the second study, dibenzoyl peroxide degraded 93.5, 94.1 and 94.2 % at pH 4, 7 and 9 respectively by day 5 and at 50 °C. The half-life of dibenzoyl peroxide at pH 4 and 7 was determined to be 11.9 and 5.2 hours at 25 °C, respectively, while the half-life at pH 9 and 25 °C could not be determined as dibenzoyl peroxide was not detected. The study is considered not reliable as not enough data is available to verify the validity of the study or the observed results.

Ready biodegradability

There are four ready biodegradability studies with conflicting results and with different reliability available on dibenzoyl peroxide. In the first study (Reliability 1) (Anonymous, 2015b) the biodegradation of dibenzoyl peroxide was determined with ready biodegradability closed bottle test (OECD TG 301 D). Secondary activated sludge (non-adapted, 0.4 g (DW)/L pre-conditioned) obtained from the Nieuwgraaf wastewater treatment plant in Duiven (Netherlands) was exposed

to 2 mg/L dibenzoyl peroxide over 28 days at 22-24 °C. Under the test conditions, dibenzoyl peroxide reported a theoretical oxygen demand (ThOD) of 2.7 mg/L, corresponding to 71 % degradation after 28 days. The validity criteria of the test were fulfilled. Dibenzoyl peroxide can be considered readily biodegradable under test conditions of the study.

In the second OECD TG 301 D test (Reliability 2) (Anonymous, 2009c), activated sludge (concentration equivalent to a maximum of 30 mg/L, pre-conditioned, non-adapted), prepared in the laboratory from secondary effluent from a wastewater treatment plant with activated sludge treating domestic wastewater in the municipality of Abidos (France) was exposed to 4 mg/L dibenzoyl peroxide for 28 days. The oxygen depletion in the inoculum blank did not exceed 1.5 mg/L after 28 days. However, the residual oxygen concentration remained above 0.5 mg/L. The reference substance, sodium benzoate, reached 42 % degradation by Day 14 which is below the validity threshold of ≥ 60 %. The validity criteria of the test were not fulfilled. Under the conditions of the study, dibenzoyl peroxide biodegraded 68 % by Day 28, exceeding the 60 % threshold for this test system. However, this level of biodegradation was not achieved within the 10-day window. Dibenzoyl peroxide demonstrated inherent biodegradability under the conditions of the study.

In a further compliant OECD TG 301 D test (Reliability 2) (Anonymous, 1990), the ready biodegradability of dibenzoyl peroxide, 1.5 mg/L (applied using silica gel), was investigated in secondary activated sludge (non-adapted, pre-conditioned) from an activated sludge plant predominantly treating domestic wastewater in Duiven, Netherlands. After 28 days, dibenzoyl peroxide reportedly degraded by 56 %. The test was extended to 84 days; however, the level of degradation did not exceed 56 %. The inhibitory effects of dibenzoyl peroxide on the micro-organisms of the inoculum were not observed. Considering the extent of degradation, the DS considers that dibenzoyl peroxide did not fulfil the ready biodegradability criteria. Under the conditions of the study, it was concluded that dibenzoyl peroxide can be considered as not readily biodegradable. The DS noted that although the validity criteria of the OECD TG 301 guideline were fulfilled the following deviations were noted: secondary activated sludge was used as inoculum instead of recommended secondary effluent (or surface water). The OECD 301 D guideline recommends for substances with water solubility below 1 g/L that stock solutions are prepared in mineral medium or added directly to the mineral medium rather than in water/solvent as was performed in the study. A test concentration of 1.5 mg/L dibenzoyl peroxide was used instead of recommended test concentration of between 2 and 10 mg/L. It is unclear if these deviations affected the biodegradation potential of the test material or validity of the study.

The ready biodegradability of dibenzoyl peroxide was evaluated in accordance with an OECD Ready Biodegradability modified MITI test (OECD TG 301 C) for 21 days (Anonymous, 1992). Under the conditions of the study, dibenzoyl peroxide reported 88 % degradation after 21 days. The robust study summary concluded that dibenzoyl peroxide was readily biodegradable; however, no further information is reported in the study summary to verify the validity of the study. The study is not considered reliable (Reliability 4) by the DS.

The DS noted that benzoic acid (EC 200-618-2) was considered the main degradation product of dibenzoyl peroxide. The robust study summary for benzoic acid (REACH registration dossier) reports that benzoic acid can be considered as readily biodegradable (ECHA dissemination site, 2021b).

Conclusion on rapid degradability

Overall, the DS concluded that dibenzoyl peroxide is considered to be rapidly degradable in the environment.

Bioaccumulation

For dibenzoyl peroxide, the EPISuite KOWWIN (v1.68) and BCFBAF QSAR models predicted log K_{ow} and BCF values for dibenzoyl peroxide of 3.43 and 89.11 L/kg, respectively.

Measured octanol-water partition coefficient (log K_{OW}) determined according to OECD TG 117 was 3.2 at 22 °C.

Aquatic bioaccumulation studies to determine the bioconcentration of dibenzoyl peroxide in aquatic species were not available.

The DS concluded that dibenzoyl peroxide has a low potential for bioaccumulation.

Aquatic Toxicity

The summary of the relevant information on aquatic toxicity for dibenzoyl peroxide are provided in the following table (the key endpoints used in hazard classification are highlighted in bold). Studies that were considered unreliable by the DS were not provided in the Table.

Table: *Summary of relevant information on aquatic toxicity for dibenzoyl peroxide*

Method/Exposure	Test organism	Endpoint	Toxicity values (mg/L)	Reference/Remarks
Acute aquatic toxicity				
OECD 203; EU Method C.1, GLP Semi-static Purity: 74.6 %	*Oncorhynchus mykiss*	96 h LC_{50}	**0.0602 im***	Anonymous, 2010a. ECHA dissemination site, 2021
OECD 202; EU Method C.2, GLP Static Purity: 74.6 %	*Daphnia magna*	48 h EC_{50}	0.11 im*	Anonymous, 2010b. ECHA dissemination site, 2021
OECD 201, EU Method C.3, GLP Static Purity: 74.6 %	*Pseudokirchneriella subcapitata*	72 h E_rC_{50} 72 h E_bC_{50} 72 h E_yC_{50}	0.0711 im 0.0422 im 0.0724 im	Anonymous, 2010c. ECHA dissemination site, 2021
Long-term toxicity				
OECD 211, GLP Semi-static Purity: 74.2 %	*Daphnia magna*	21 d EC_{10} (reproduction) 21 d NOEC (reproduction)	0.001 TWA mm 0.0011 TWA mm	Anonymous, 2015a. ECHA dissemination site, 2021
OECD 201, EU Method C.3, GLP Static Purity: 74.6 %	*Pseudokirchneriella subcapitata*	72 h NOE_rC	0.02 im	Anonymous, 2010c. ECHA dissemination site, 2021

Notes:
mm - mean measured concentration
im - initial measured concentration
TWA mm - Time-weighted average (TWA) measured concentration
* In the CLH report the endpoints are based on mean measured concentrations but based on comment (No 3) received in public consultation this was changed to initial measured concentrations.

Acute aquatic toxicity data on dibenzoyl peroxide are available for all three trophic levels (fish, invertebrates and algae). One study per trophic level was evaluated in the CLH report as reliable for classification purposes. The most sensitive acute toxicity value for fish is 96 h LC_{50} of 0.0602 mg/L for *Oncorhynchus mykiss,* for invertebrates is 48 h EC_{50} of 0.11 mg/L for *Daphnia magna* and for algae is 72 h E_rC_{50} of 0.0711 mg/L for *Pseudokirchneriella subcapitata.* All aquatic acute toxicity values were below the threshold value of 1 mg/L. The acute aquatic classification proposed by the DS was based on the toxicity value for fish (*Oncorhynchus mykiss*, 96 h LC_{50} of

0.0602 mg/L) which is the most acutely sensitive taxonomic group. The DS proposed **Aquatic Acute 1** (H400) with an acute **M-factor of 10** (0.01 < L(E)C_{50} ≤ 0.1 mg/L).

Chronic aquatic toxicity data on dibenzoyl peroxide is available for invertebrates and algae. One invertebrate and one algae study were evaluated in the CLH report as reliable for classification purposes. The most sensitive chronic endpoint for invertebrates is 21 d EC_{10} value of 0.001 mg/L and 21 d NOEC value of 0.0011 mg/L for *Daphnia magna* and for algae is 72 h NOE_rC value of 0.02 mg/L for *Pseudokirchneriella subcapitata.* The chronic aquatic classification proposed by the DS was based on the toxicity value for invertebrate (*D. magna*, 21 d EC_{10} = 0.001 mg/L) along with the understanding that the substance is rapidly degradable. The DS proposed **Aquatic Chronic 1** (H410) with a chronic **M-factor of 10** (0.0001 < EC_{10} ≤ 0.001 mg/L). Based on the available long-term data and the physical-chemical properties of dibenzoyl peroxide (rapidly degradable; BCF < 500; log K_{OW} < 4) the use of the surrogate approach for chronic classification cannot be applied.

Comments received during consultation

Two Member States (MS), one individual, National Authority and company-importer provided comments.

The MSs agreed with the proposed classification for environmental hazards by DS. One MS provided detailed explanation of agreement with DS proposal.

An individual provided safety data sheet. The DS indicated that no additional hazard data were provided in the safety data sheet and the results of the reported studies in the safety data sheet were reflected in the CLH proposal.

A National Authority asked for clarification whether endpoints from acute toxicity studies with *Oncorhynchus mykiss* (Anonymous, 2010a) and *Daphnia magna* (Anonymous, 2010b) are based on initial measured or mean measured concentrations over the test period. In the CLH report the endpoints were based on mean measured concentrations while in EU REACH registration were based on initial measured concentrations. In addition, the National Authority asked RAC to consider which basis (initial measured or mean measured) is most relevant for the acute endpoints, noting the rapid hydrolysis of the test substance. The DS clarified that reported results are based on initial measured concentrations because in expired samples (at 24 h for fish and 48 h for daphnia) no measurable levels of dibenzoyl peroxide were found at any exposure concentration. DS pointed out that the same applies to acute study with *Pseudokirchneriella subcapitata* (Anonymous, 2010c).

The National Authority indicated that the key chronic endpoint for the proposed classification was *Daphnia magna* EC_{10} of 0.001 mg/L (95 % C.I. 0.00010-0.0018 mg/L) based on reproduction. Whilst within the test guideline recommendation, the National Authority noted that the coefficient of variation (CV) around the EC_{10} endpoint for mean number of living offspring produced per parent in the controls was 13.5 %. As this control CV was above 10 % and given the EC_{10} was below the NOEC (albeit it only slightly), the EC_{10} was likely to reflect considerable uncertainty regarding where a 10 % difference compared to the mean living offspring truly lies – this was also demonstrated by the confidence intervals. The National Authority asked for more information about the individual 10 control replicates to understand the background variation and the dose-response regression, e.g., if there was any outlier. The National Authority wondered if the reproduction NOEC of 0.0011 mg/L from the same study, or an EC_{20}, was more reliable and relevant to hazard classification in this instance. The NOEC value would lead to Aquatic Chronic 1 with M-factor of 1 for rapidly degradable substances. The DS indicated that in line with ECHA guidance R.10 (2017) EC_{10} is preferred over NOEC. Therefore, EC_{10} was considered more

appropriate to derive the classification and M factor. The DS agreed with the National Authority that EC_{10} and NOEC lead to a classification of the substance as Aquatic Chronic 1 but with different M-factors. The DS pointed out that in the robust study summary reported in the registration dossier no information was provided on the individual control replicates or on the dose-response regression and therefore it was not possible to provide any further information, including if there was any outlier in this group. The DS noted that the 95 % CI of the EC_{10} spans across three M factor levels, with only the current proposed M factor of 10 fully covered. The DS noted the difference in the number of decimal places for each value: 0.001 mg/L and 0.0011 mg/L for the EC_{10} and NOEC, respectively. No information is provided in the study summary as to whether the EC_{10} value was rounded up.

Company-importer pointed out that they do not have any toxicological and ecotoxicological studies to improve the proposal to give a support to the higher classification.

Assessment and comparison with the classification criteria

Degradation

The substance is hydrolytically unstable at pH 4-9 and 50 °C. Hydrolysis DT_{50} values are less than 1 day under environmentally relevant condition (25 °C and pH 4-9). The main degradation product was benzoic acid which has not been classified for environmental hazard but can be considered as readily biodegradable and has a low bioaccumulation potential. RAC notes that all reported L(E)C50 and NOEC/EC_{10} for fish, invertebrates and algae available on ECHA dissemination site (registered substances) are above the CLP criterion (acute and chronic) of 1 mg/L for acute and chronic hazard classification for rapidly degradable substance (data for ready biodegradability only are available).

There are three ready biodegradability studies (OECD TG 301D) with different reliability (Reliability 1 or 2) and conflicting results available:

- The study by Anonymous, 2015b (Reliability 1) showing a degradation of 71 % in 28 days. The study is considered the most reliable and best documented of all three (guidance criteria fulfilled, non-adapted inoculum and 10-day window criterion fulfilled).
- The study by Anonymous, 2009c (Reliability 2) did not reach the pass-level for readily biodegradability (10-day window criterion not fulfilled), but there is at least a substantial degradation (68 % in 28 days), which also contributes to the conclusion that the substance will not be persistent.
- The study by Anonymous, 1990 (Reliability 2) showed 56 % degradation after 28 days. This study was considered less reliable due to deviation from test guideline.

In line with the current CLP Guidance (Version 5.0, July 2017) "*positive results in ready biodegradability tests could be considered valid, irrespective of negative results, when the scientific quality is good and the test conditions are well documented, i.e., guideline criteria are fulfilled, including the use of non-pre-exposed (non-adapted) inoculum*". Consequently, RAC is of the opinion that dibenzoyl peroxide should be considered readily biodegradable following the study by Anonymous, 2015b.

RAC agrees with the DS proposal to consider dibenzoyl peroxide as rapidly degradable.

Bioaccumulation

The experimental log K_{OW} of 3.2 and estimated log K_{OW} value of 3.43 are below the CLP trigger value of Log $K_{OW} \geq 4$. The low bioaccumulation potential of dibenzoyl peroxide is also supported by the estimated BCF value of 89.11 L/kg which is below the CLP criterion of BCF ≥ 500. Therefore,

RAC agrees with the DS proposal to consider dibenzoyl peroxide as a substance with a low potential to bioaccumulate.

Acute toxicity

Reliable aquatic acute toxicity data on dibenzoyl peroxide are available for fish, invertebrates and algae. RAC notes that all acute toxicity endpoints ($L(E)C_{50}$) for fish, invertebrates and algae are below the threshold value of 1 mg/L. Fish are the most acutely sensitive group and the lowest toxicity value is the initial mean measured 96 h EC50 value of 0.0602 mg/L for rainbow trout *Oncorhynchus mykiss.* According to Table 4.1.0 (a) and 4.1.3 of the CLP guidance, dibenzoyl peroxide should be classified as Aquatic Acute 1 with an M-factor of 10.

Chronic toxicity

Reliable aquatic chronic toxicity data on dibenzoyl peroxide are available for two trophic levels, invertebrates and algae. Data for fish are lacking.

The lowest chronic effect value is obtained from a test with crustacea *Daphnia magna* and corresponds to the time-weighted mean measured 21 d EC_{10} of 0.001 mg/L. As this value is below the threshold value of 1 mg/L, the substance is considered rapidly degradable and the substance has low potential for bioaccumulation, RAC concludes that a classification as Aquatic Chronic 1 (H410) is justified. As $0.0001 < EC_{10} \leq 0.001$ mg/L, the chronic M-factor is 10.

In line with the CLP guidance section 4.1.3.3 and Table 4.1.0. the surrogate method is not applicable for dibenzoyl peroxide as the substance is considered rapidly degradable and does not fulfil the criteria for bioaccumulation.

In summary, based on the available data, RAC considers that dibenzoyl peroxide should be classified according to CLP as:

Aquatic Acute 1 (H400), M-factor = 10 and

Aquatic Chronic 1 (H410), M-factor = 10

This is consistent with the conclusion of the DS.

ANNEXES:

Annex 1 The Background Document (BD) gives the detailed scientific grounds for the opinion. The BD is based on the CLH report prepared by the Dossier Submitter; the evaluation performed by RAC is contained in 'RAC boxes'.

Annex 2 Comments received on the CLH report, response to comments provided by the Dossier Submitter and RAC (excluding confidential information).