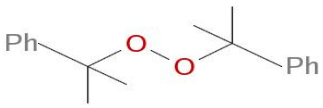
# SUBSTANCE EVALUATION CONCLUSION and EVALUATION REPORT

**For**

# Bis(α,α-dimethyl benzyl) peroxide

**EC No. 201-279-3**

**CAS RN 80-43-3**




**Evaluating Member State Competent Authority:**
**Norwegian Environment Agency**

Dated: 14 September 2023

# Evaluating Member State Competent Authority



| | |
|---|---|
| **MSCA name:** | Norwegian Environment Agency |
| **Address:** | Postboks 5672 Torgarden<br>7485 Trondheim, Norway |
| **Telephone Number:** | +47 73 58 05 00 |
| **Email address:** | post@miljodir.no |
| **Web:** | Miljodir.no |



## Year of evaluation in CoRAP: 2015

**Further information on registered substances here:**

http://echa.europa.eu/web/guest/information-on-chemicals/registered-substances

**Further information on the substance evaluation process here:**

https://echa.europa.eu/regulations/reach/evaluation/substance-evaluation

# Foreword

This Conclusion document, as required by Article 48 of the REACH Regulation, provides the outcome of the Substance Evaluation carried out by the evaluating MSCA. The document consists of two parts i.e. A) the conclusion and B) the evaluation report.

With this Conclusion document the substance evaluation process is finished and the Commission, the Registrant(s) of the Substance and the Competent Authorities of the other Member States are informed of the considerations of the evaluating MSCA. In case the evaluating MSCA proposes further regulatory risk management measures, this document shall not be considered initiating those other measures or processes. Further analyses may need to be performed which may change the proposed regulatory measures in this document. Since this document only reflects the views of the evaluating MSCA, it does not preclude other MSCAs or the European Commission from initiating regulatory risk management measures which they deem appropriate.

# Contents

## List of Tables

## List of Figures

# Part A. Conclusion

## 1. Scope of the evaluation

Bis(a,a-dimethylbenzyl) peroxide (dicumyl peroxide) was originally selected for substance evaluation to clarify concerns about:

- PBT/vPvB
- Consumer use
- Exposure of environment
- High (aggregated) tonnage
- Wide dispersive use
- Exposure of workers
- High RCR

During the evaluation the following additional concern was identified: reproductive toxicity.

## 2. Overview of other processes / EU legislation

**Table 2-1 Overview of other processes / EU legislation**

| No other processes | CCH | TPE | GMT | Previously on CoRAP | Annex VI (CLP) | Annex XVII (Restriction) | Candidate List/Annex XIV (Authorisation) |
|---|---|---|---|---|---|---|---|
| ☐ | ☒ | ☒ | ☒ | ☐ | ☒ | ☐ | ☐ |

| Other EU legislation | Previous legislation | Stockholm convention | Other |
|---|---|---|---|
| PPP/BPR | NONS/RAR | POP | (e.g., UNEP) |
| ☐ | ☐ | ☐ | ☐ |

For further details, please refer to PACT (https://echa.europa.eu/pact).

## 3. Conclusion and regulatory follow-up action

The evaluation of the available information on the Substance has led the evaluating MSCA to the following conclusions.

Dicumyl peroxide has been classified during the substance evaluation process as Repr 1 B (H360D), see section 5.1.

**Table 3-1 Conclusion and regulatory follow-up action**

| Initial and additional concern | Conclusion on concern | Regulatory follow-up action |
|---|---|---|
| PBT/vPvB | Concern removed (clarification of hazard/exposure) | No need for regulatory follow-up at EU level |
| Persistence | Concern confirmed.<br><br>Based on the new information generated via the substance evaluation procedure, bis(α,α-dimethylbenzyl) peroxide fulfills the criterion for persistent and very | No need for regulatory follow-up at EU level |

| | | |
|---|---|---|
| | persistent substances (P/vP) with an aqueous half-life of 142 days at 12 °C. | |
| Bioaccumulation | Concern removed.<br><br>Although the substance has been seen to accumulate in fish to some degree, the B/vB-criteria is not fulfilled. | No need for regulatory follow-up at EU level |
| Toxicity | Concern confirmed.<br><br>The toxicity criteria (T) are fulfilled based on the harmonized classification as Repr. 1B. | Identification as SVHC (authorisation) |
| Reproductive toxicity | Concern confirmed.<br><br>The substance has received recently a harmonized classification as Repro 1B (ATP 15). | Identification as SVHC (authorisation) |
| Consumer use | Concern removed (Registrant actions to ensure safety)<br><br>Following harmonised classification as Repro 1B, the substance is now restricted under Annex XVII entry 30 | No need for regulatory follow-up at EU level |
| Exposure of environment | Concern removed (clarification of hazard/exposure) | No need for regulatory follow-up at EU level |
| High (aggregated) tonnage | Concern confirmed | Not applicable |
| Wide dispersive use | Concern confirmed | Not applicable |
| Exposure of workers | Concern confirmed | Not applicable |
| High RCR | Concern confirmed | Not applicable |

**Table 3-2 Additional endpoint evaluated (outside scope of initial/additional concern)**

| **Additional endpoint** | **Conclusion** | **Regulatory follow-up action** |
|---|---|---|
| Specific target organ toxicity (repeated) | Concern confirmed | No need for regulatory follow-up at EU level |
| Mobility | Concern removed | No need for regulatory follow-up at EU level |
| Aquatic toxicity (chronic) | Concern confirmed | No need for regulatory follow-up at EU level |

# 4. Regulatory follow-up actions at EU level

## 4.1 Harmonised Classification and Labelling

Not applicable

## 4.2 Identification as a substance of very high concern, SVHC (first step towards authorisation)

Bis(α,α-dimethylbenzyl) peroxide fulfills the criteria for identification as a SVHC according to Article 57(c).

## 4.3 Restriction

Not applicable.

## 4.4 Other EU-wide regulatory risk management measures

Not applicable.

# 5. Currently no need for regulatory follow-up at EU level

## 5.1 No need for regulatory follow-up at EU level

The eMSCA submitted in 2017 a CLH dossier proposing classification of bis(a,a-dimethylbenzyl) peroxide as Repr. 2 (H361D). The Risk Assessment Committee agreed on a stronger classification as Repr. 1B (H360D, may damage the unborn child), see section 14.7 for details. The resulting harmonised classification according to the entry in Annex VI of CLP Regulation (Regulation (EC) 1272/2008), ATP 15 is as follows:

**Table -5-1 Harmonised classification**

| HARMONISED CLASSIFICATION ACCORDING TO ANNEX VI OF CLP REGULATION (REGULATION (EC) 1272/2008) | | | | | | | |
|---|---|---|---|---|---|---|---|
| **Index No** | **International Chemical Identification** | **EC No** | **CAS No** | **Classification** | | **Spec. Conc. Limits, M-factors** | **Notes** |
| | | | | **Hazard Class and Category Code(s)** | **Hazard statement code(s)** | | |
| 617-006-00-X | | 201-279-3 | 80-43-3 | Org. Perox. F | H242 | | |
| | | | | Skin Irrit. 2 | H315 | | |
| | | | | Eye Irrit. 2 | H319 | | |
| | | | | Aquatic Chronic 2 | H411 | | |
| | | | | Repr. 1B | H 360D | | |

The more stringent classification as Repr. 1 B gives considerable downstream effects on other regulatory frameworks protecting workers, consumers and exposure of workers and the environment. Furthermore, the aggregated tonnage and exposure from wide dispersive use will likely be reduced.

## 5.2. Other actions

Not applicable.

# 6. Tentative plan for follow-up actions

Bis(α,α-dimethylbenzyl) peroxide fulfills the criteria for identification as a SVHC according to Article 57(c).

**Table 6-1 Follow-up actions**

| Follow-up action | Date for intention | Actor |
|---|---|---|
| SVHC identification | By 31.12.2023 | NO CA |

# Part B. Substance evaluation report

In the substance evaluation report (part B), the document provides explanation how the evaluating MSCA assessed and drew the conclusions from the information available.

## 7. Overview of the Substance Evaluation Process

In accordance with Article 45(4) of the REACH Regulation, the evaluating MSCA evaluated the Substance based on the information in the registration dossier(s) and on other relevant and available information.

Before concluding the substance evaluation, a Decision to request further information was issued according to Article 46 on 30 May 2017 requesting the following information:

1) Simulation testing on ultimate degradation of dicumyl peroxide in surface water (test method: Aerobic mineralisation in surface water — simulation biodegradation test, EU C.25/OECD 309, pelagic test — without additional suspended solids/sediment, containing a natural concentration of 15 mg SPM dw/l) as specified in Appendix I, section 1. The study shall be performed at 12 °C.
2) In case the study requested under point 1 results in the registered substance to meet the criteria for a persistent (P) or very persistent (vP) substances under REACH Annex XIII, the following study is required: Bioaccumulation of bis(a,a dimethylbenzyl) peroxide in aquatic species (Annex IX, Section 9.3.2.; test method Bioaccumulation in Fish: Aqueous Exposure Bioaccumulation Fish Test, OECD 305).

A dossier update containing the requested information on degradation and bioaccumulation was received on 29 November 2022 and the eMSCA considered the dossier update as compliant.

During the SEV process, bis(α,α-dimethylbenzyl) peroxide was classified as Repr. 1B H360D after a proposal from the eMSCA. This classification fulfills the criteria for identification as a SVHC according to Article 57(c).

## 8. Substance identity

The information on the Substance, including identifiers and structural formula, can be found on the cover page. For more details see ECHA: https://echa.europa.eu/home

Synonyms: Dicumyl peroxide, DCP

### 8.1. Type of Substance

Mono-constituent.

# 9. Physicochemical properties

**Table-9-1 Overview of physicochemical properties**

| Property | Value |
|---|---|
| Molecular weight/weight range | 270.3661 |
| Physical state at 20°C and 101.3 kPa | White, granular solid |
| Vapour pressure | (EU Method A.4 (Vapour Pressure)<br>< 10 Pa at 60 °C,<br><10 Pa at 70 °C,<br><10 Pa at 80 °C,<br>10 Pa at 90 °C,<br>29 Pa at 100 °C,<br>71 Pa at 110 °C, (*interpolation)*<br>146 Pa at 120 °C.*(interpolation)* |
| Water solubility | 0.43 mg/L at 20 °C (OECD 105) |
| Partition coefficient n-octanol/water (Log $K_{ow}$) | 5.6 at 25 °C (EU method A.8 (partition coefficient) and OECD guideline 117 |
| Partition coefficient organic carbon/water (Log $K_{oc}$) | log Koc 3.98 (9550) at 25 °C ("OECD 121) |
| Flash point | *130.7* °C at 101300 Pa (ISO 2592) |
| Explosive properties | Non-explosive |
| Oxidising properties | Data waiving: a study on oxidising properties does not need to be conducted, as the substance is an organic peroxide. |
| Granulometry | 1700 µm (Mass median diameter) (OECD 110) |
| Stability in organic solvents and identity of relevant degradation products | bis(α,α-dimethylbenzyl) peroxide is reported to be stable in toluene for 1 week in a refrigerator (Reliability 4 (not assignable)) |
| Dissociation constant | Data waiving |
| Melting point | 39.8 °C at 101325 Pa (EU Method A.1), |

# 10. Manufacture and uses

## 10.1. Quantities

The aggregated tonnage (per year) of the Substance is 1,000 - 10,000 tonnes.

## 10.2. Overview of uses

**Table-10-1 Overview of uses**

| Main uses | Key information |
|---|---|
| **Manufacture** | Manufacture of organic peroxides |
| **Formulation** | Formulation and (re)packaging of polymers.<br>Industrial formulation of organic peroxides in materials and formulation of mixtures |
| **Uses at industrial sites** | Industrial use of organic peroxides in polymer industry<br>Manufacture of plastic products, chemicals, and rubber products.<br>Industrial use of reactive processing aid in the production of articles |
| **Uses by professional workers** | Articles used by professional workers, see article service life. According to Spin database use by professional workers can be expected (SPIN). |
| **Consumer Uses** | Articles used by consumers, see article service life. According to Spin database use by consumers is demonstrated (SPIN). |
| **Article service life** | Outdoor and indoor use in long-life materials with low release rate (e.g., metal, wood and plastic articles, flooring, furniture, toys, construction materials, curtains, footwear, leather products, paper and cardboard products, electronic equipment). |

In the assessment of regulatory needs for organic hydroperoxides and aliphatic/cumyl peroxides, professional and consumer uses have been reported in the past (ECHA (2023)). Even though these uses are not registered currently, it cannot be excluded that such uses might take place again in the future. According to the database on substances in preparations in Nordic countries (SPIN), bis(α,α-dimethylbenzyl) peroxide has been used in considerable amounts (1->2000 t/a) in preparations in the recent years (2015-2021) and exposure of workers, consumers and the environment is likely.

# 11. Classification and labelling

**Table 11-1 Classification of the Substance**

| Harmonised classification (Annex VI of CLP) | | Self-classification in registrations | Self-classification in C&L notifications | |
|---|---|---|---|---|
| **Org. Perox. F** | H242 | Org. Perox. Type F | Org. Perox. Type E | H242 |
| **Skin Irrit. 2** | H315 | Skin Irrit. 2 | Self-React. F | H242 |
| **Eye Irrit. 2** | H319 | Eye Irrit. 2 | | |
| **Aquatic Chronic 2** | H411 | Aquatic Chronic 2 | Aquatic Acute 1 | H400 |
| **Repr. 1B** | H360D | Repr. 1B | Repr. 1B | H360 |

# 12. Environmental fate properties

## 12.1. Degradation

### 12.1.1. Abiotic degradation

12.1.1.1. Hydrolysis

According to disseminated data, the hydrolysis of bis(α,α-dimethylbenzyl) peroxide was investigated in an OECD TG 111 guideline study (Hydrolysis as a Function of pH*):* Registrants explain "*In the preliminary test (incubation at 50 °C for 5d) degradation of the test item of more than 10 % was observed at all pH values. The test item was considered hydrolytically unstable, and the full test was performed. In the full test, duplicate samples prepared in three buffer solutions were incubated at 10, 25 and 50 °C at pH 4,7, and 9. Samples were taken at 0d, 6h, 12h, 1d, 2d, 3d, 4d, 5d, 7d, 14d and analysed by HPLC-UV/Vis. To derive reaction rate constants the logarithms of the concentrations were plotted against time and reaction rate constant k and half-life times were calculated by regression analysis or from the slope. DT50 values from plots of logarithms of concentrations against time indicate only moderate degradation of bis(α,α-dimethylbenzyl) peroxide, with values ranging from about 12 d (50 °C at pH9) to about 228 d (10 °C at pH7)*."

**Table 12-1 Hydrolysis data**

| pH | Temperature | Half-life (days) | Equivalent first order rate constant $k_{obs}$ ($day^{-1}$) |
|---|---|---|---|
| 4 | 10 | 90,55 | 0,0077 |
| | 25 | 25,36 | 0,0273 |
| | 50 | 11,72 | 0,0591 |
| 7 | 10 | **228,41** | 0,003 |
| | 25 | 31,35 | 0,0221 |
| | 50 | 12,8 | 0,0542 |
| 9 | 10 | 78,48 | 0,0088 |
| | 25 | 31,9 | 0,0217 |
| | 50 | 11,55 | 0,06 |

The reaction rate constants calculated within this study show dependency from the temperature, as expected, but no significant influence of the different pH values could be observed at 25°C and 50°C. However, there was a marked effect at 10°C, with a hydrolysis half-life of 228 days at pH7. No degradation products could be found and analytically identified throughout the study. The study does not have a mass balance and the data should therefore be interpreted with care.

### 12.1.2. Biotic degradation

12.1.2.1. Biodegradation in water

#### 12.1.2.1.1. Estimated data

The fragment-based models such as ACD, EPISUITE (BIOWIN), OASIS and ECOSAR do not consider the peroxide bond (Canada, 2009). Estimated data on degradation is therefore given very little weight but is still mentioned for the sake of transparency.

The probability for biodegradation has been assessed using BIOWIN (v4.10) and this indicated that according to BIOWIN 2 (non-linear model) the probability of bis(α,α-dimethylbenzyl) peroxide biodegrading fast is 0.3365 and the time until ultimate biodegradation as predicted by BIOWIN 3 is 2.2215 months, see Table 12-2Table 12-2. This would indicate that the Substance fulfils the screening criteria for persistency (Biowin 2 = probability <0.5 and ultimate biodegradation timeframe prediction Biowin 3 >2.2 months) as detailed in the REACH PBT guidance.

**Table 12-2 Biowin estimations**

| **Probability of Rapid Biodegradation (BIOWIN v4.10):** | |
|---|---|
| Biowin1 (Linear Model): | 0.5071 |
| Biowin2 (Non-Linear Model): | 0.3365 |
| **Expert Survey Biodegradation Results:** | |
| Biowin3 (Ultimate Survey Model): | 2.2215 (months) |
| Biowin4 (Primary Survey Model): | 3.1606 (weeks) |
| **MITI Biodegradation Probability:** | |
| Biowin5 (MITI Linear Model): | 0.1268 |
| Biowin6 (MITI Non-Linear Model): | 0.0391 |
| **Anaerobic Biodegradation Probability:** | |
| Biowin7 (Anaerobic Linear Model): | -0.6686 |
| **Ready Biodegradability Prediction:** | NO |

### 12.1.2.1.2. Screening tests

OECD TG 301 F: *Ready Biodegradability: Manometric Respirometry Test*

According to disseminated data the ready biodegradability of bis(α,α-dimethylbenzyl) peroxide was investigated in a study conducted according to OECD Guideline 301 F , indicated as key study (Ready Biodegradability: Manometric Respirometry Test). The test spanned over a period of 28 days with an initial concentration of 20 and 100 mg/L using activated sludge obtained from the STP Ruhrverband in Schmallenberg, Germany as the inoculum. The tests were conducted in darkness, at 22 °C ± 1 °C and pH 7.4 ± 0.2. The biodegradation rate was determined by measurement of oxygen consumption. Inoculum blank, abiotic sterile control, procedural/functional control with sodium benzoate and toxicity control were performed. Validity criteria are fulfilled by the registrant, but available data is not sufficient to confirm this assumption. No inhibitory effects of the registered substance were reported for the toxicity control (35 % degradation in 14 days). This exceeds the threshold value of 25 % and bis(α,α-dimethylbenzyl) peroxide is assumed to be non-toxic in the test system. Sodium benzoate was degraded by 89 % within the first 14 days. No significant degradation of bis(α,α-dimethylbenzyl) peroxide was observed in the abiotic control during the test (only 1 %).

The biodegradation of bis(α,α-dimethylbenzyl) peroxide in the static test was found to be on average 20 % at 100 mg/L and, on average, 44 % at 20 mg/L after 28 days. There appears to be a correlation between reduced degradation and higher concentrations of test

substance in these tests. This may be a result of reduced availability of the substance at higher concentrations. A similar problem was noted in the preparatory stages of the simulation study (OECD TG 309) for concentrations at 100 mg/L, but at a lower temperature: 12°C vs 22°C. Thus, the degradation behaviour between the replicates showed a considerable variability but did not exceed the 60% required to meet the criteria for "readily biodegradable".

The eMSCA therefore agrees with the registrant's conclusion that "According to the test guideline, bis(α,α-dimethylbenzyl) peroxide must be considered as not readily biodegradable under the corresponding test conditions."

OECD TG 301D: *Ready Biodegradability: Closed Bottle Test*

According to disseminated data the ready biodegradability of bis(α,α-dimethylbenzyl) peroxide was investigated in a study conducted according to OECD TG 301 D (Ready Biodegradability: Closed Bottle Test) over a period of 28 days. The test was extended to 57 days with an initial concentration of 1000 mg/L and using activated sludge obtained from the RZWI Nieuwgraaf sewage treatment plant (STP) in Duiven as the inoculum. Inoculum was obtained from an activated sludge plant treating predominantly domestic wastewater. The biodegradation rate was determined by measurement of oxygen consumption. Inoculum blank, abiotic sterile control, procedural/functional control with acetic acid, sodium salt and vehicle control with silica gel were performed. The use of silica gel is not mentioned in OECD guideline for the test (OECD guideline 301D) but is in line with the ISO (1995) recommendation for *preparation and treatment of poorly water-soluble organic compounds for the subsequent evaluation of their biodegradability in an aqueous medium*. However, a toxicity control was not performed and hence the bis(α,α-dimethylbenzyl) peroxide may have been toxic to the micro-organisms although the reported no observed effect concentration (NOEC) for STP is 1000 mg/L. Validity criteria are fulfilled based on dissolved $O_2$ not falling below 1,5 mg/L and differences in extremes being less than 20% of removal.

The results of the study indicated that after 28 days bis(α,α-dimethylbenzyl) peroxide was biodegraded to only 18%. However, after 57 days bis(α,α-dimethylbenzyl) peroxide was biodegraded to 60% as calculated by BOD/ThOD indicating that considerable biodegradation may occur eventually. Overall registrants concluded that bis(α,α-dimethylbenzyl) peroxide is regarded as not readily biodegradable based on this test. The eMSCA notes that the delayed onset of degradation is also observed in the OECD TG 309 aquatic simulation study.

OECD TG 301C: *Ready Biodegradability: Modified MITI Test*

An additional study indicated that the biodegradation of bis(α,α-dimethylbenzyl) peroxide in a test corresponding to OECD 301C: "Ready Biodegradability: Modified MITI Test (I)" showed 0% degradation after 28 days at 25°C with an initial concentration of 100 mg/L. No toxicity control was performed but the reported NOEC for STP is 1000 mg/L according to an OECD TG209 study. The control sample with aniline reached a degradation of more than 60 % after 14 d and the validity criteria is therefore fulfilled. Bis(α,α-dimethylbenzyl) peroxide is considered as not readily biodegradable.

Overall, results from three screening test for ready biodegradability (OECD TG 301 C, D and F) showed 0-44% biodegradation at 25° C within 28 days demonstrating no ready biodegradability. The eMSCA therefore considers that the Substance fulfils the screening criteria for persistency according to the PBT guidance (R.11).

### 12.1.2.1.3. Simulation tests (water and sediments)

*OECD TG 309: Aerobic mineralization in surface water*

To address the requirement of the substance evaluation decision dated 30 May 2017, the registrants submitted an OECD TG 309 study (aerobic mineralization in surface water). This was conducted using radiolabeled [14C] bis(α,α-dimethylbenzyl) peroxide (specific

activity 52 mCi/mmol) with a radiochemical purity of 98.4%. The label was introduced in one of the two benzyl rings of the compound, but the exact position is not indicated. The study used aerobic surface water collected from the river 'Leine,' collected from the surface of the river (approx. upper 20 cm water) at an undisturbed recess. The characteristics of the water sample are provided in Table 12-3 .

Water was filtered (0.2 µm and 0.45 µm membrane) after collection. Aliquots of 80 mL were transferred to exposure vessels for each replicate. 120 ml glass bottles were used for testing mineralization and transformation of the test item and reference control. 150 ml glass bottles were used for controls and for internal CO2-traps at selected timepoints and at low concentrations. bis(α,α-dimethylbenzyl) peroxide was applied at nominal concentrations of 0.5 or 50 µg/L to the low and high dose vessels, respectively. The test material was supplied as a solution in toluene and was further diluted in acetonitrile to an application solution with 6.72 MBq. Further, vessels were prepared for untreated controls, sterile controls (14C-bis(α,α-dimethylbenzyl) peroxide at a concentration of 50 µg/L) and reference control (14C radiolabeled aniline sulphate at a concentration of 10 µg/L) were also included.

Preliminary tests showed challenges with the solubility of the substance and its solvent. It had been supplied in toluene, which is a poorly water-miscible solvent, and the concentrations were unstable in the tests. The test was further complicated by the tendency of the substance to absorb to the walls of the test vessel. A comparison between 20°C and 12°C showed that the concentration also significantly decreased over time in the lower concentration. Together this made it challenging to perform a test that would give reliable degradation kinetics, resulting in a significant delay for performing the study. The concentrations used in the study were therefore lowered from the originally planned 10 - 100 µg/L to 0.5 and 50 µg/L. Duplicate vessels were sacrificed for each sampling interval. Mineralization and transformation were studied at the high concentration, while only mineralization was studied at the low concentration. Sterile controls were also run at 50 µg/L and included analysis of mineralization and transformation. Several iterations of the analytical setup were attempted using a solid phase extraction (SPE), but the analytical recoveries were too low (60-70%). Analysis showed that the loss of substance occurred during the sample preparation due to evaporation of the substance along with the extraction solvent. The water samples were therefore not extracted, and bis(α,α-dimethylbenzyl) peroxide and the main transformation products were analyzed by HPLC with fraction collector and offline liquid scintillation counting (LSC) after stabilization and filtration. Radioactive contents in each test vessel and associated volatile traps were analyzed by LSC. Analysis of bis(α,α-dimethylbenzyl) peroxide and the metabolite 2-Phenyl-2-propanol was performed using LSC and combination of HPLC, fraction collector and offline LSC. Evolved $^{14}CO_2$ was determined by purging the headspace through sodium hydroxide traps. Additionally, a sample of water was acidified to pH 2 – 3 followed by shaking to determine dissolved $^{14}CO_2$. Test vessels were incubated in the dark under aerobic conditions at 12±2°C however, no temperature records were reported to verify this.

**Table 12-3 Summary of water sample characteristics**

| Characteristics | Value at first sampling | Value at second sampling |
|---|---|---|
| Oxygen concentration (mg/l) | 9.93 | 9.43 |
| Water total suspended solids (ppm) | 6.5 mg/L*<br>7.5 mg/L# | 3.5 mg/L*<br>4.0 mg/L# |
| Dissolved organic carbon (%) | 6,04 | 5,24 |
| Water pH | 8,04 | 7,64 |

* determined with membrane filter with pore size 0.45 µm
# determined with membrane filter with pore size 0.20 µm

Dissolved oxygen during the test ranged between an average of 10.18 to 6.97 mg/L across the low and high dose samples. pH measurements ranged from an average of 6.76 to 8.00, and the temperature was maintained at 12±2°C. Based on $^{14}CO_2$ measurements, the reference control substance achieved >60% mineralization by day 7 days and 12 days in the high and low concentration tests, respectively, confirming the viability of test system. The mass balance based on applied radioactivity (AR) was 84.7 to 120.3% for the high dose samples and 80,4 to 100.8% for the low dose samples. Losses were due to the substance absorbing to the vessel walls and volatilization of the test substance in addition to transformation products.

The registrants report that major transformation products detected were $CO_2$ and 2-phenyl-2-propanol, with maximum 2-phenyl-2-propanol (CAS number: 617-94-7) concentrations of 9.8 % of the applied amount, observed on 37 days of incubation. The corresponding concentration at the end of the study period was 0.4 % of the applied amount. Minor transformation products were not detected. At study termination, evolved $^{14}CO_2$ in solution and in headspace accounted for 13 % of the applied radioactivity. The metabolite 2-phenyl-2-propanol was also formed in the sterile (autoclaved) control replicates. This metabolite was detected in samples analyzed at day 64, 70 and at test end with 9.2–9.9 % of applied radioactivity, respectively. The concentration of this metabolite remained constant over this time course and its concentration was very similar to the maximum determined concentration in the test item replicates. No formation of $^{14}CO_2$ was observed in the sterile controls. These observations suggest that the test item is first degraded by hydrolysis, followed by microbial degradation of the metabolite 2-phenyl-2-propanol. Details of the mass balance at study termination are provided in Table 12-4.

**Table 12-4 Mass balance for bis(α,α-dimethylbenzyl) peroxide and metabolites at study termination**

| MASS BALANCE FOR LOW AND HIGH DOSE SYSTEMS IN THE OECD 309 STUDY AT STUDY TERMINATION | | | |
|---|---|---|---|
| Source | Low dose (0,5µg/L) as a % of applied radioactivity (97 days) | High dose (50µg/L) as a % of applied radioactivity (90 days) | Sterile control (50µg/L) as a % of applied radioactivity (90 days) |
| bis(α,α-dimethylbenzyl) peroxide - Water layer | | 79.4 | 72.9 |
| 2-phenyl-2-propanol-Water layer | | 0.4 | 9.3 |
| $^{14}CO_2$ dissolved | | 5.7 | - |
| bis(α,α-dimethylbenzyl) peroxide - Headspace | | 11.4 | 9.4 |
| $^{14}CO_2$Headspace | | 7.2 | - |
| Total Radioactivity Headspace | | 11.4 | 9.4 |
| % Total $^{14}CO_2$ | 60.21 | | |
| % AR Test Solution/acidified | 26.1 | 83.5 | 87.4 |
| Mass Balance | 86.3 | 102.1 | 96.9 |

Kinetic Analysis

The results were evaluated by the registrants based on the FOCUS guidance, Single First order (SFO) as well as Hockey-stick (HS) were used to calculate the DT50. The data used for calculation in the high concentration test was the %-amount of radioactivity applied as bis(α,α-dimethylbenzyl) peroxide that was still present as the parent substance. The transformation half-lives of the degradants were not calculated. In the low concentration test, the data used for the kinetics were the applied radioactivity as bis(α,α-dimethylbenzyl) peroxide minus the evolved $^{14}CO_2$. The eMSCA notes that this assumes that all radioactivity in the low concentration test would be bis(α,α-dimethylbenzyl) peroxide unless transformed to $^{14}CO_2$. Whether or not this is the case is difficult to assess for the low concentration but based on the appearance of the degradation product 2-Phenyl-2-propanol in the high concentration test and sterile control, it does not seem to be likely. The eMSCA considers the use of HS kinetics in the low-test concentration to be reasonable as the mineralisation starts after an adaptation phase of 78 days and then proceeds very rapidly. This acceleration of degradation is however not apparent at the high-test concentration. The registrants indicate that this may be an artefact.

**Table 12-5 DT50 values from kinetics**

| | **50 µg/L, Primary Transformation** | **0,5 µg/L Mineralisation at low concentration** | |
|---|---|---|---|
| Model | SFO | SFO | Hockey-stick |
| DT50 | 142 | 164 | 92.2 (overall) |

The study report documented that the kinetic modelling was performed using CAKE v3.3. SFO and HS modelling was chosen as the best fit. This results in a transformation half-life for bis(α,α-dimethylbenzyl) peroxide (DT50) of 142 days in the high concentration test and 164 days in the low concentration test with SFO and 92.2 days overall DT50 for the HS model at 12°C.

Overall, the eMSCA considers that the study was performed to acceptable standards for the purpose of persistence assessment of bis(α,α-dimethylbenzyl) peroxide. The eMSCA would like to note that the kinetics modelling on the low concentration is less certain than the high dose, as the $CO_2$-evolution in the test system is used as a marker for degradation of bis(α,α-dimethylbenzyl) peroxide, and will not reflect the presence of metabolites. This is therefore likely an underestimation of the degree of degradation, as the formation of 2-phenyl-2-propanol through hydrolysis has been demonstrated in both the sterile and high concentration test. The DT50 is also longer for the low concentration test, as would be expected for this approach. It should also be noted that there is an apparent accelerated degradation in the low concentration test at day 97. This datapoint is after the recommended test duration of maximum 90 days, and there are no other data points between days 78, where degradation seems to start, and 97. The datapoints for that day also have a large spread (59 and 20% AR). The degradation based on this datapoint therefore have an increased uncertainty. The eMSCA therefore puts more weight on the results from the high concentration test, with a half-life of 142 days. Interestingly, in the OECD TG 301D-screening biodegradation test, a similar effect was observed with degradation speeding up after a long lag-period.

The eMSCA re-performed the kinetics as per the FOCUS guidance documents using CAKE v3.6 software and has recreated the same results as the registrant. The results are presented in the figures and tables below. The visual fit for the SFO kinetics is acceptable for the high concentration test, see Figure 12-1, while the HS is clearly better for the low dose test, see Figure 12-2. The $Chi^2$-error is acceptable for all fits. The k- and k1-parameters are significantly different from zero as p-values are >0,1, however, the k2-

parameter from the HS-fit on the low concentration is not significant, see **Error! Reference source not found.**.

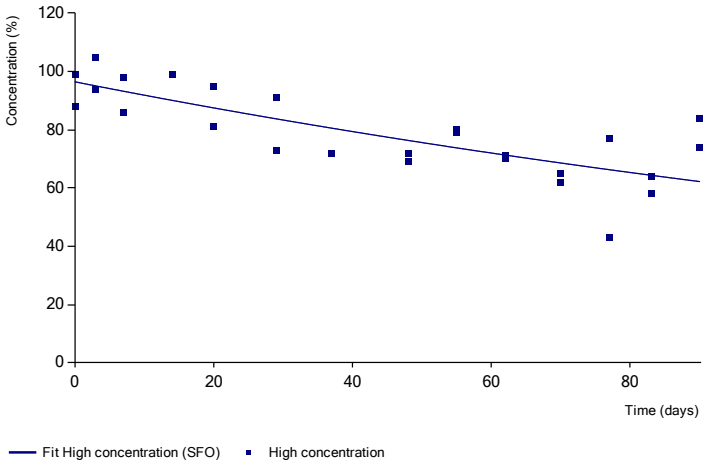



**Figure 12-1 SFO kinetics for the high concentration test**

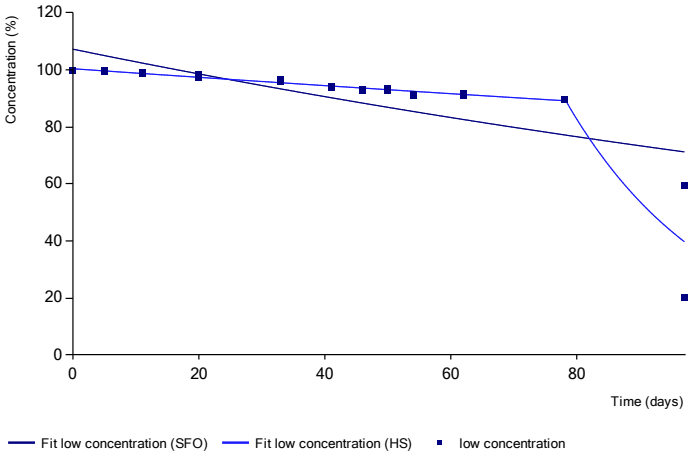



**Figure 12-2 SFO and HS kinetics for the low concentration test**

**Table 12-6 Fit summaries for kinetics**

| Soil | | Kinetic Model | DT50 | M0 | Parameter (k, k1, k2, g, tb, α, β) | Chi²-error | Prob >t | Lower 95% CI | Upper 95% CI |
|---|---|---|---|---|---|---|---|---|---|
| High concentration | | Parent: SFO | 142 | 96,5 | k: 0,00487 | 6,8 | 5,95E-07 | 0,00328 | 0,006 |
| Low concentration | | Parent: SFO | 164 | 107 | k: 0,00422 | 9,81 | 0,000184 | 0,00212 | 0,006 |
| Low concentration | | Parent: HS | 92.2 (overall) 457 (K1) 14.3 (K2) | 100 | k1: 0,00152 k2: 0,043 tb: 78,2 | 0,479 | 0,00593 0,39 N/A | 0,000371 -0,273 -64,8 | 0,003 0,359 221 |

### 12.1.2.1.3.1. Summary and discussion of biodegradation in water and sediment

According to the described tests, bis(α,α-dimethylbenzyl) peroxide is not readily biodegradable. The three screening tests show none or low biodegradation after the standard test duration. The OECD TG 301C showed 0%, OECD TG 301D showed 18%

(increased to 60% after 57 days) and 301F showed up to 44 %. The reported tests are in agreement with each other and indicate that the substance will not biodegrade rapidly.

There is also an OECD TG 309 surface water simulation study on bis(α,α-dimethylbenzyl) peroxide available, showing that the substance has a long DT50 in surface water. The eMSCA considers that the most reliable value is a half-life of 142 days at 12◦C based on single-first order (SFO) kinetics in the high dose concentration.

#### 12.1.2.2. Biodegradation in soil

No experimental data is available.

#### 12.1.2.3. Summary and discussion of persistence

No data are available for photodegradation or fate in soil. In a hydrolysis study bis(α,α-dimethylbenzyl) peroxide was stable at high pH and low pH but was even more stable at low temperatures. The reaction was first order with a half-life of 228 days at pH 7, 78 days at pH 9 and 91 days at pH 4 at 10 °C.

Estimated data with Biowin indicate that the Substance fulfils the screening criteria for persistency (Biowin 2 = probability <0.5 and ultimate biodegradation timeframe prediction Biowin 3 >2.2 months) as detailed in the REACH PBT guidance.

Results from three screening tests for ready biodegradability (OECD TG 301 C, D and F) showed 0-44% biodegradation at 25 °C within 28 days, demonstrating that the substance is not readily biodegradable. The substance fulfils the screening criteria for persistency according to the PBT guidance.

In an aerobic surface water simulation study conducted at 12 °C, bis(α,α-dimethylbenzyl) peroxide showed slow transformation and mineralisation. Kinetic calculations indicate that the transformation DT50 of bis(α,α-dimethylbenzyl) peroxide are between 142 and 164 days based on SFO. The hockey-stick model was also used for the low-concentration test, and indicated an overall DT50 of 92 days, but a slow-phase DT50 based on k1 of 457 days. Considering the uncertainties of the data from the low concentration test, the eMSCA considers the DT50 of 142 days value to be more reliable.

This exceeds the criteria for persistent (P) and very persistent (vP) substances, with half-lives at 40 and 60 days in fresh water, respectively.

The eMSCA therefore considers that the substance is persistent and very persistent according to Reach annex XIII.

## 12.2. Environmental distribution

#### 12.2.1.1. Distribution modelling

According to disseminated data, the log $K_{OC}$ was 3.98 ($K_{OC}$ 9549.93) in a HPLC study performed according to EU Method C.19 and OECD Guideline 121. The substance can be assumed to absorb very strongly to particles.

The eMSCA has modelled the distribution in the environment and in a sewage treatment plant (STP) for bis(α,α-dimethylbenzyl) peroxide using Epiweb v4.1 and using measured values for user input to the model for log$K_{OW}$, boiling point, melting point, and water solubility[1]. Based on the level III Fugacity model, most of the substance is likely to be

[1] Physical Property user-input to model based on dissemination page data:
Log $K_{OW}$ (octanol-water): 5.60
Boiling Point (deg C): 341.08
Melting Point (deg C): 39.80
Water Solubility (mg/L): 0.43

retained in sewage treatment plants, with an estimated 22% entering the environment, see **Error! Reference source not found.**. When in the environment, bis(α,α-dimethylbenzyl) peroxide will be most likely to partition into soil and sediment, see **Error! Reference source not found.**.

**Table 12-7 Distribution modelling for STP, Epiweb v4.1**

| Fraction of emission directed to: | % |
|---|---|
| Total removal | 77,87% |
| Total biodegradation | 0,67% |
| Total sludge adsorption | 76,78% |
| Total to air | 0,42% |

**Table 12-8 Distribution modelling for environment, Epiweb v4.1**

| Fraction of emission directed to: | % |
|---|---|
| Air | 0,294 |
| Water | 3,24 |
| Soil | 40,2 |
| Sediment | 56,3 |

## 12.3. Mobility

On the disseminated page, an experimental study according EU Method C.19 and OECD TG 121 (Estimation of the Adsorption Coefficient (Koc) on Soil and on Sewage Sludge using High Performance Liquid Chromatography (HPLC) is available. The study was run twice at 25 °C and compared to a suite of well-known reference substances. The test substance has an average $K_{OC}$ of 9550 based on the two trials, corresponding to a log Koc 3.98 at 25°C. The substance can be regarded as adsorptive and likely to distribute in sediment and soil.

The eMSCA therefore considers that the substance has a low potential for mobility in the environment.

## 12.4. Bioaccumulation

According to the disseminated data, bis(α,α-dimethylbenzyl) peroxide has been determined to have a log $K_{ow}$ of 5.6. This would indicate that bis(α,α-dimethylbenzyl) peroxide is likely to partition in the lipids of aquatic organisms. These data were also backed up by the supporting studies which reported an octanol water partition coefficient of 5.5. In the updated version of EPIsuite (BCFBAF v3.01) BCF from regression-based method is estimated at 2301[2]. Using the Arnot-Gobas method, which also includes

[2] Physical Property user-input to model based on dissemination page data:
Log Kow (octanol-water): 5.60

biotransformation, BCF is estimated to be 384 for high trophic level, 515 for mid trophic level and 565 for lower trophic.

### 12.4.1.1. Aquatic bioaccumulation study 1: OECD TG 305 C with *Cyprinus carpio*

There are two studies available for the substance where bioaccumulation has been studied. The oldest test is a Japanese MITI BCF test (OECD Guideline 305 C (Bioaccumulation: Test for the Degree of Bioconcentration in Fish)). 15 -20 Fish (carp, *Cyprinus carpio*) per test concentration were exposed to test substance concentrations of 0.01 and 0.001 mg/L at 25°C for 56 d under flow through conditions. Recovery rates were used as correction factors for the determination of test substance concentration in fish samples. Test substance concentrations were determined by GC and BCF values of 137 - 1470 (10 µg/L) and 181 - 667 (1 µg/L) were reported, see Table 12-9Table 12-9. The values do not seem to have been lipid normalized, although the average lipid content of the fish is reported as 4.6%.

The eMSCA has had the original study translated from Japanese, and important information is still missing. It is reported that there was a problem with the initial dosing during the pre-exposure of the fish. The subsequent 8 weeks exposure seem to have relatively stable water concentrations for bis(α,α-dimethylbenzyl) peroxide, although some fluctuations of the water level during the test are reported. The depuration rates seem to be relatively swift in the 1st concentration part (top concentration) getting below 90% after 7 days but the 2nd concentration part does not seem to depurate below 20-30% over the 7 days, but this may be due to the concentration levels being close to the LOQ (the report only seems to give the LOD).

**Table 12-9 Reported BCF values from MITI BCF test**

| | 1 week | 2 weeks | 4 weeks | 6 weeks | 8 weeks |
|---|---|---|---|---|---|
| 10 µg/L | 137<br>468 | 654<br>720 | 1470<br>1440 | 501<br>328 | 711<br>703 |
| 1 µg/L | 364<br>181 | 520<br>404 | 667<br>609 | 404<br>505 | 337<br>438 |

The study appears not to have determined a steady state BCF or performed a depuration phase and a kinetic BCF cannot be calculated. Also, only two fish were sampled per data point, leading to low confidence level. In addition, some details of the study have not been reported and a reliability factor of 2 has been assigned. However, since this study was performed to an older version of the OECD 305 test guideline and has a poor study design, it may be more appropriate with a reliability factor of 3 or 4. However, if the 4$^{th}$ week data at the high dose is removed as an outlier/contamination the BCF would be in accordance with the QSAR data reported by the registrant.

The limited details available and the experimental design used for determining the bioconcentration potential makes it difficult to conclude with confidence whether bis(α,α-dimethylbenzyl) peroxide will bioconcentrate in the environment. Of highest concern is the lack of growth correction and lipid normalization. Food was given twice daily in significant amounts, totalling 4%. Fish growth is expected to be extensive at 3% feeding rate[3] and may have had a significant effect on the reported values through growth dilution.

---

Boiling Point (deg C): 341.08
Melting Point (deg C): 39.80
Water Solubility (mg/L): 0.43

[3] http://www.oecd.org/chemicalsafety/testing/49190726.pdf

### 12.4.1.2. Aquatic bioaccumulation study 2: OECD TG 305 *C with Oncorhynchus mykiss*

Since the uncertainties attached to the above study are substantial, a new bioaccumulation study (OECD TG 305) was performed using rainbow trout (*Oncorhynchus mykiss*) in an aqueous exposure under flow-through conditions. An exposure (uptake) phase of 28 days was carried out. The following depuration phase lasted 21 days. A flow-through test with 3 groups (one solvent (methanol) control group and two exposure groups of nominally 3 and 15 µg test item/L) was carried out. During the uptake phase, two groups of fish were exposed to the test item at nominal concentrations of 3 and 15 µg test item/L, corresponding to a time-weighted arithmetic mean concentration of 1.73 and 8.25 µg/L, respectively. The measured concentrations were maintained within ± 20% of the mean measured value during the uptake phase for both the low and high concentration. Five fish samples were taken from each tank on days 0.3, 1, 2, 4, 7, 14 and 28 of the uptake phase as well as on days 0.3, 1, 2, 4, 8 and 14 of the depuration phase.

After 28 days of uptake the fish were transferred to a medium free of the test item (depuration phase) for 21 days. In parallel, a solvent (methanol) control was performed containing the same solvent concentration as the test concentrations during uptake phase. No steady-state phase was reached for either of the concentrations.

A depuration phase of 21 days was conducted. The concentrations of the test item in fish decreased over time and the depuration rate constants were calculated. For the low-test concentration, the concentration in the fish began to fall below LOQ already as of depuration day 0.3 and was completely below LOQ on depuration day 4 and completely below LOD on depuration day 14. For the high-test concentration, concentration in the fish fell below LOD on day 14. Therefore, further samplings were not carried out and the depuration phase was terminated on day 21.

The test substance was not radiolabelled but was quantitatively analysed via LC-MS analyses. Test media samples were stabilized with acetonitrile and cleaned up via SPE cartridges. Afterwards the extracts were evaporated to dryness on a rotary evaporator at 40 °C and dissolved with 2 mL acetonitrile. The measurement was carried out via LC-MS/MS on a Zorbax RRHD Eclipse Plus C18 column in gradient mode. A dual jet stream electrospray ionization source was used for ionization. Detection by high-resolution quadrupole time of flight (QToF) mass spectrometer operating in positive ion scan mode. The quality control of the chemical measurement seems robust and solid.

For the test organism samples homogenized fish samples were extracted with 15 mL acetonitrile, treated for 15 min on an overhead shaker and afterwards centrifuged for 5 min at 4000 rpm. The extract was collected in a centrifuge vial. Fish extract samples were analysed using LC-MS/MS on a reversed phase column in gradient mode. Detection by electrospray tandem mass spectrometer operating in positive ion mode.

No fish died during the test, and no unusual behaviour was observed. The validity criteria for oxygen saturation and temperature were met. The fish had an initial lipid content of 4,72 %, measured in the control group. At the end of the study the lipid content was 5,19-5,62%, measured in the two exposed groups. Considerable growth was observed during the study. The mean weight and length at the start were 2.17 g and 5.99 cm, respectively. At the end of the study the mean values were 6.61 g and 8.68 cm.

**Figure 12-3 Uptake of dicumyl peroxide at the low test concentration, eMSCA has plotted data and line-fit using r-script bcmfr.**

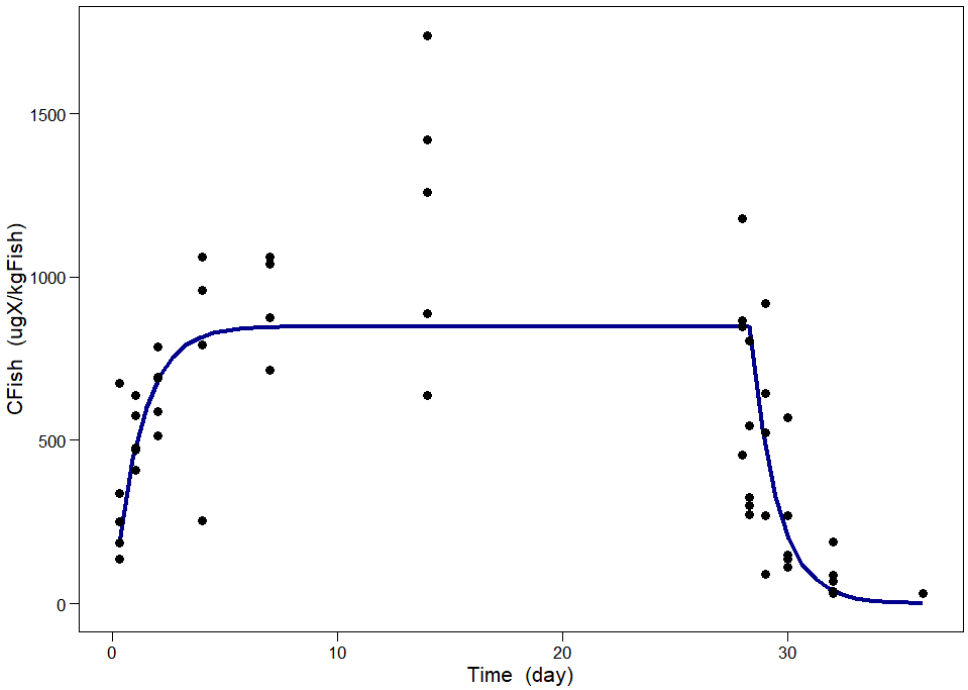
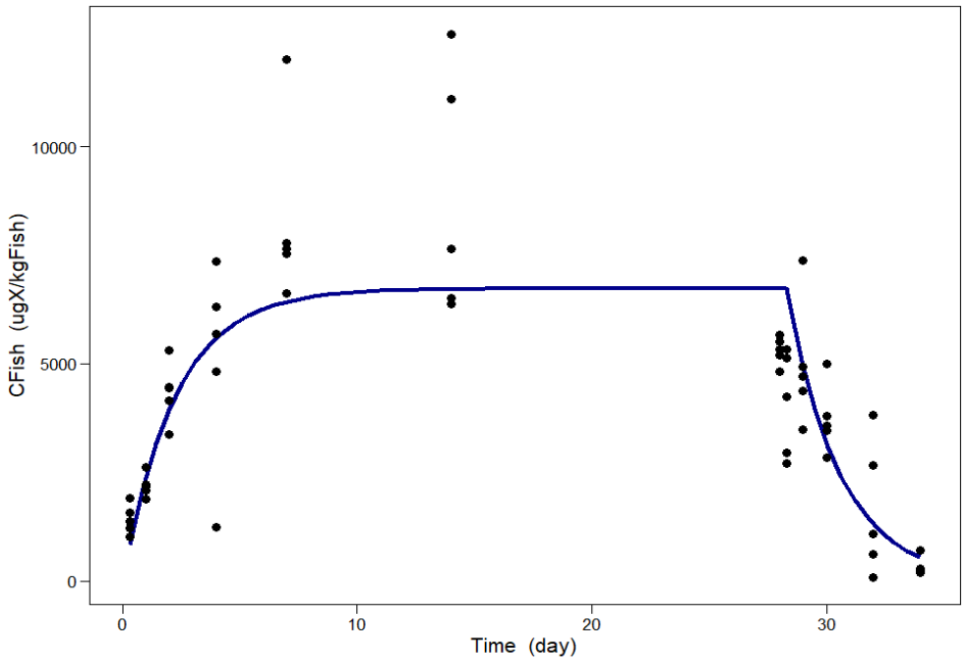



**Figure 12-4 Uptake of dicumyl peroxide at the high-test concentration, eMSCA has plotted data and line-fit using r-script bcmfr**




Based on the uptake and depuration shown in Figure 12-3 and Figure 12-4, the registrant has calculated the kinetic BCF with lipid and growth corrections. These are given in Table 12-11 . The numbers used in these calculations are given in Table 12-10Table . Based on the raw data supplied in the study report, the eMSCA has reperformed the analysis of the study using the R-script *bcmfr* (v.0.4-18). The BCF values are slightly (2-8%) lower in the eMSCA calculation.

**Table 12-10 Overview of Uptake and Depuration Rates, Growth Rate, Growth Corrected Depuration Rates, Lipid Normalization Factor and Depuration Times**

| Nominal test conc. (µg/L | Growth rate $k_g$ ($day^{-1}$) | Uptake rate $k_1$ ($L \times kg^{-1} \times day^{-1}$) | Depuration rate $k_2$ ($day^{-1}$) | Growth-corrected depuration rate $k_{2g}$ ($day^{-1}$) | Lipid normalization factor | Depuration time $DT_{50}$ (days) | Depuration time $DT_{90}$ (days) |
|---|---|---|---|---|---|---|---|
| 3.00 | 0,0195 | 373,1 | 0,7143 | 0,694 | 0,0545 | 1,00 | 3,32 |
| 15.0 | | 357,4 | 0,4249 | 0,405 | 0,0590 | 1,71 | 5,68 |

**Table 12-11 Bioconcentration factors of dicumyl peroxide**

| Test concentration nominal (µg/L) | TWA (µg/L) | BCFK[1)] ($L * kg^{-1}$) | BCFKGL[2)] ($L * kg^{-1}$) |
|---|---|---|---|
| 3.00 | 1.73 | 523 (441-605) | 493 |
| 15.0 | 8.25 | 841(737-946) | **747** |

[1)] = Kinetic BCF, [2)] = Kinetic BCF, with lipid and growth correction

Conclusion bioaccumulation

There are two OECD TG 305 studies of fish bioaccumulation of dicumyl peroxide in the registration dossier. The oldest study has a low reliability, but the newest can be regarded as reliable. Based on the bioaccumulation study in rainbow trout, dicumyl peroxide has a lipid and weight corrected BCF of 747, well below the B- criteria of 2000 in Reach Annex XIII. Although dicumyl peroxide has been seen to accumulate in fish to some degree, the B-criteria according to annex XIII is not fulfilled.

# 13. Environmental hazard assessment

## 13.1. Aquatic compartment (including sediment)

### 13.1.1. Fish

Short term

Three short-term toxicity studies for fish are available for dicumyl peroxide.

The first study was performed according to the Japanese Industrial Standard JIS K 0102-1986-71 "Testing methods for industrial wastewater" with the fish species medaka (*Oryzias latipes*). The test did not have detailed documentation or analytical control. The nominal 48 h lethal concentration 50 (LC50) was reported to be 4.2 mg/L. However, it should be noted that this value is above the water solubility limit of 0.43 mg/L and that the study is indicated as not reliable by the registrant.

The second study was conducted with guppies (*Poecilia reticulate*) in accordance with OECD Test Guideline 203 (1984). Four nominal concentrations (10, 21, 46 and 100 mg/L) were

tested in a semi-static system for 96 h. Acetone was used as solvent for preparing the stock solution of the two lowest concentrations, whereas the two higher concentrations were obtained by adding the test substance directly into the diluting water of the definitive test. The 96 h LC50 was calculated to 108.45 mg/L and the NOEC was estimated to approximately 5 mg/L. Serious deviations in behaviour (such as reduced swimming activity, bad reaction to mechanical stimuli, and fast breathing) was observed after 48 h in the test concentrations 21-100 mg/L. However, it was reported that the substance remained visible at the surface of the test media as a fine layer of solids at all test concentrations. Therefore, the test was regarded as not reliable by the registrants.

The third study was a 96h short-term toxicity test using medaka fish (*Oryzias latipes*) in accordance with OECD TG 203 performed in 2000. Dicumyl peroxide was dissolved in acetone, afterwards acetone was removed by distillation with a rotary evaporator. The measured concentrations (0.386, 0.513, 0.721, 1.01 and 1.44 mg/L) were tested under semi-static conditions. The 96 h LC50 was reported to be 0.469 mg/L (measured) and the 96 h LC0 value was 0.386 mg/L. Sublethal effects of abnormal breathing, abnormal behaviour, swimming disabilities, and specific symptoms were observed in the groups exposed to 1.44 mg/L after 3 hours and for concentrations of 0.513 -1.01 mg/L after 24 hours. No abnormal symptoms were observed in the control group during the exposure period. The applicant concluded that the study was not reliable due to the use of acetone as solvent. However, the use of solvents is commonly accepted, although recommended to be avoided where possible. The study was performed according to good laboratory practice (GLP) and with analytical chemistry and should therefore be assigned a higher reliability factor.

Registrants have used the three short-term toxicity studies for fish in a weight of evidence approach that dicumyl peroxide showed no effects at maximum water solubility.

Long term

There are no data available for the long-term toxicity to fish. A long-term toxicity test on fish has been requested in compliance check decision sent in February 2022. The requested information shall be provided by 7 November 2023.

### 13.1.2. Aquatic invertebrates

Short term

Three short-term toxicity tests for aquatic invertebrates are available. All three used *Daphnia magna* and were performed according to OECD Test Guideline 202, with analytical chemistry and in compliance with GLP.

The key study was performed using a water accommodated fraction (WAF) of bis(α, α-dimethylbenzyl) peroxide which had been prepared following a 72-h stirring period. *D. magna* were exposed to nominal concentrations (1, 10 and 100 mg/L) under semi-static conditions for 48 h. The 48 h half maximal effective concentration (EC50) was reported to be > 100 mg/L (nominal) and > 0.397 mg/L (measured). The registrants concluded that the results of the study indicate no acute toxic effects at the highest concentration tested (i.e., the limit of solubility).

The supporting study was also performed using a WAF. The exposure lasted for 48 h under static conditions with concentrations of 0.11 mg/L, 0.22 mg/L, 0.43 mg/L, 0.87 mg/L and 1.74 mg/L. According to registrants the substance concentration was monitored via analysis of non-purgeable organic carbon. Since the non-purgeable organic carbon analysis is not a specific analysis for the test compound, the results can only be used as an indication of the concentration. The 48 h EC50 and NOEC was reported to be > 1.74 mg/L. The results of this study also indicated that there were no acute toxic effects at the limit of solubility.

Another study was performed using test solutions of bis(α, α-dimethylbenzyl) peroxide dissolved in solvent (dimethyl sulfoxide). The test was conducted under semi-static

conditions for 48 h with nominal concentrations of 0.198, 0.296, 0.444, 0.667 and 1.00 mg/L. The 48 h EC50 was reported to be 0.262 mg/L and the NOEC to be 0.202 mg/L. However, the applicant concluded that the effects may have been due to higher amounts of impurities present in the solutions due to the use of a solvent. This is considered unlikely, particularly considering the level of impurities reported and the fact that the test was run below the level of solubility.

In summary, the WAF studies performed using bis(α, α-dimethylbenzyl) peroxide exposed to *D. magna* showed that the EC50 was greater than the limit of water solubility. The test using solvent revealed a dose response relationship with an EC50 of 0.262 mg/L.

Long term

One long-term toxicity test on aquatic organisms has been reported. The available test is a reproduction test performed for 21 days according to OECD TG 211 using *D. magna*. The study was given a reliability factor of 1 and appears to have been performed well. *D. magna* were exposed to control, solvent control, and measured concentrations of 0.0187, 0.0331, 0.0600, 0.117 and 0.247 mg/L under semi-static conditions.

The most sensitive endpoint reported was the effect on reproduction. NOEC and lowest observed effect concentration (LOEC) for the study were reported to be 0.117 and 0.247 mg/L, respectively.

### 13.1.3. Algae and aquatic plants

Two studies on green algae are available on the dissemination pages.

The key study was a 72-hour toxicity study using the green algae *Pseudokirchnerella subcapitata* performed according to the OECD TG 201. *P. subcapitata* was exposed to bis(α, α-dimethylbenzyl) peroxide at nominal concentrations of 0 (control, solvent control), 0.512, 1.28, 3.20, 8.00, 20.0 mg/L under static conditions. The measured concentrations were below 80% nominal, hence mean measured concentrations should have been used for the calculation of the effect concentrations. This is particularly important as the tests were also performed above the limit of solubility. Nevertheless, the cell density data indicated EC50 values of >20 mg/L (measured initial was 17.2 mg/L and final was 12.2 mg/L) and NOEC values of 3.20 mg/L (measured initial was 2.68 mg/L and final was 1.68 mg/L) after 72 h. The growth rate data were slightly less sensitive with a 72 h EC50 of >20 mg/L (measured initial was 17.2 mg/L and final was 12.2 mg/L) and NOEC of 8 mg/L (measured initial was 6.51 mg/L and end was 4.53 mg/L).

This indicates that there is no effect of bis(α, α-dimethylbenzyl) peroxide at the limit of solubility.

The supporting study was performed similarly to the key study but at significantly higher concentrations than the limit of solubility (up to 1000 mg/L). There was no analytical chemistry performed during the study, so an accurate assessment of the chemical concentrations could not be verified. Nevertheless, the study indicated that the EC50 for growth and biomass was >1000 mg/L (nominal). The NOEC for growth was reported to be 10 mg/L. However, it is unclear from the data presented how this was calculated.

Overall, no effects on algae growth rate were observed at the limit of solubility for dicumyl peroxide.

### 13.1.4. Sediment organisms

No data available.

A decision on testing proposal requesting long term toxicity testing on sediment organisms has been sent to the registrants in February 2022. The requested information shall be submitted by 9 May 2024.

### 13.1.5. Other aquatic organisms

No data available.

## 13.2. Terrestrial compartment

No data available.

## 13.3. Microbiological activity in sewage treatment systems

An activated sludge respiration inhibition test is available. The test was performed according to OECD TG 209 using 1000 mg/L (nominal) bis(α, α-dimethylbenzyl) peroxide applied to silica gel using a solvent. No toxicity was observed at this concentration after 30 min. A positive control was performed using 2,4,5 trichlorophenol and the results showed an EC50 between 10-20 mg/L which indicates accurate performance of the test. Therefore, the study indicates that bis(α, α-dimethylbenzyl) peroxide is not toxic to microorganisms and should not cause toxicity to microorganisms in sewage treatment systems.

## 13.4. PNEC derivation and other hazard conclusions

**Table 13-1 PNEC derivation and other hazard conclusions**

| Compartment | Hazard conclusion | Remarks/Justification |
|---|---|---|
| Freshwater | Hazard assessment conclusion: PNEC Freshwater: 2.34 µg/L | Assessment factor: 50<br>Obtained from NOEC *D. magna* 0.117 mg/L |
| Marine water | Hazard assessment conclusion: No hazard identified | Direct release to marine environment is not expected. |
| Intermittent releases to water | No data. | Aquatic toxicity unlikely |
| Sediments (freshwater) | Hazard assessment conclusion: PNEC Sediments freshwater: 2.24 mg/kg sediment dw | Extrapolation method: Partition coefficient as outlined in TGD part II chapter 3, page 117, using a PNEC water of 2.34 µg/L |
| Sediments (marine water) | Hazard assessment conclusion: No exposure expected | Direct release to marine environment is not expected. |
| Sewage treatment plant | Hazard assessment conclusion: PNECSTP: 100 mg/L | Assessment factor: 10<br>NOEC from OECD TG 209 |
| Soil | Hazard assessment conclusion (soil): PNECsoil 0,447 mg/kg soil dw | Extrapolation method: Equilibrium partition coefficient, using a PNEC water of 2.34 µg/L |
| Air | Hazard assessment conclusion: No hazard identified | Bis(α,α-dimethylbenzyl) peroxide has a low vapour pressure, and the substance is thus not expected to partition to air |

| | | |
|---|---|---|
| Secondary poisoning | No potential for bioaccumulation | Not expected to present a toxic hazard through accumulation in the food chain: Experimental data available in registration is below threshold value for bioaccumulation. |

The eMSCA agree with the derived PNEC's.

### 13.5. Conclusions of the environmental hazard assessment and related classification and labelling

Dicumyl peroxide has a harmonised classification as aquatic chronic 2. There are currently no available data that show effects in the acute or chronic aquatic toxicity tests that justify further classification for the environment. However, long term toxicity test on fish and sediment organisms have been requested by ECHA through dossier evaluation. These new data may justify further classification.

## 14. Human health hazard assessment

### 14.1. Toxicokinetic

In the registration it is stated that organic peroxides are metabolised by glutathione peroxidases. This fact is then used to imply that bis(α,α-dimethylbenzyl) peroxide is metabolised to 2-phenyl-2-propanol (CAS RN 617-94-7). However, in scientific literature the substrates for glutathione peroxidases are found to be hydroperoxides and no studies show that dialkylated peroxides are likely to be metabolised by these enzymes (pers. comm. from Professor Kristian Prydz, University of Oslo, 2016). We therefore have little knowledge of how this substance is metabolised, but there is no concern that would justify requiring more data on this endpoint.

### 14.2. Acute toxicity and Corrosion/Irritation

Not part of the assessment.

### 14.3. Sensitisation

Not part of the assessment.

### 14.4. Repeated dose toxicity

Two oral repeated dose toxicity studies have been performed: One 28-day (Unnamed, 2000) and one 90-day (Unnamed, 2014a). In addition, there is an inhalation study from 1986, non-guideline and only used as supporting information (Hansson AH, Petruson B, 1986).

**Table 14-1 Repeated dose toxicity studies**

| Study | Results | Remark |
|---|---|---|
| 90-day oral toxicity study (OECD TG 408)<br><br>Rat (Hsd.Brl.Han: Wistar)<br><br>0, 20, 80, 320 mg/kg bw/day (sunflower oil vehicle) | NOAEL: 80 mg/kg bw/day (findings ↑GGT, ↑ inorganic phosphorus, ↑ of urea and blood urea nitrogen (also at 20 mg/kg bw/day), organ weight change in thymus and adrenals).<br><br>LOAEL: 320 mg/kg bw/day based on ↓ body weight, and body weight gain. ↓ feed efficiency. (Both body weight | 1, reliable without restriction<br><br>Key study |

| | | |
|---|---|---|
| Reference: Unnamed (2014a) | gain and feed efficiency were equal to or exceeded the weight gain and feeding in the control group during the recovery period.) Changes in clinical chemistry (↑ALT, ↑GGT, ↑total bilirubin, ↑blood urea nitrogen, ↑ inorganic phosphorus, ↓ creatinine, ↓ cholesterol, ↓ Cl-, ↑ bile acids and calcium) and changes in organ weights (liver and kidney, reversible; thyroids and adrenals, heart, testes ↓ epididymis weight).<br><br>The registrant writes that the changes in the kidney and liver weights in male and female animals administered 320 mg/kg bw/day together with the elevated serum levels of some biochemical parameters were indicative of test item influence on the hepatic and renal functions.<br><br>Salivation was seen at all dose levels, in a dose related manner. | |
| 28-day oral toxicity study (OECD TG 407)<br><br>Rat (Crj: CD(SD))<br><br>0, 60, 200, 600 mg/kg bw/day (corn oil vehicle)<br><br>Reference: Unnamed (2000) | NOAEL: 60 mg/kg bw/day<br><br>LOAEL: 200 mg/kg bw/day, based on: ↑ relative liver weight in females, hypertrophy of hepatocytes, salivation was seen but was reversible.<br><br>At 600 mg/kg bw/day: salivation (reversible), ↓ body weight gain (reversible), ↑ serum gamma-GTP, ↑ ALT, ↑ absolute and relative liver weight. ↓ absolute and relative thymus weight. Enlarged livers. Hypertrophy of hepatocytes and degeneration of hepatocytes. Reversible mobilisation of Kupffer cells in males. | 1, reliable without restriction<br><br>Key study |
| 28-day inhalation toxicity study, 8- week recovery. 2-6 animals per dose (non-guideline)<br><br>Rabbit, Swedish landrace<br><br>50 µl of a 10 or 25 ppm concentration was placed three times daily, 5 days a week, in the right nostril. Vehicle phosphate buffered saline.<br><br>Reference: Hansson AH, | Signs of local irritation or damage were observed.<br><br>Dose-related increase in visible blood vessels and increasing crusting and mucus in the nasal cavity. Rapid damage of cilia was seen. Changes in mucosa was also seen and these were worse after 1 month exposure. Only partial recovery was apparent at 2 months after exposure terminated. | 4, non-guideline, supporting information. |

| | | |
|---|---|---|
| Petruson B, 1986, Acta Otolaryngol (Stockh) 101, 102-113. Nasal mucosa changes after acute and long-term exposure to bis(α,α-dimethylbenzyl) peroxide | | |

In summary, the repeated dose toxicity studies show that the substance induces liver injuries at high doses, shown by hypertrophy of hepatocytes (600 and 200 mg/kg, 28-day study) and Kupffer cell mobilisation (600 mg/kg, 28-day study). These findings were not quite consistent since a high dose in the 90-day study (320 mg/kg) did not reveal any hepatocyte hypertrophy. Other signs of liver and kidney effects were increased liver and kidney weight and changes in clinical biochemistry. Some changes were seen already at 80 mg/kg in the 90-day study, which is the NOAEL according to the registrant.

The eMSCA agrees that the NOAEL for the 90-day study should be set at 80 mg/kg bw/day since the effects seen at 80 mg/kg cannot be characterised as adverse, and since the effects seen at 320 mg/kg bw/day seem to be reversible. The 90-day study is considered a correct starting point for calculating the DNELs.

## 14.5. Mutagenicity

Not part of the assessment.

## 14.6. Carcinogenicity

Not part of the assessment.

## 14.7. Toxicity to reproduction (effects on fertility and developmental toxicity)

Following the adopted CLH of bis(α,α-dimethylbenzyl) peroxide as Repr.1B (H360D) based on an earlier rat study with findings of developmental toxicity (CLP ATP 15), a new OECD TG 414 prenatal development toxicity study (PNDT) was performed in a second species, rabbits.

*OECD TG 414 in rabbits (Unnamed, 2020)*

The study design was based on a dose range finding PNDT study (DRF) in groups of 6 pregnant New Zealand White rabbits per group with doses of 0, 100, 200 and 300 mg/kg bw/day administered via gavage on gestation day (GD 6-27). Body weight and body weight gain were slightly lower in the medium and high dose group from GD 9. Some maternal developmental toxicity was observed, justifying the doses in the main study. The high maternal toxicity observed in the main study was not seen in the DRF study. An explanation for the discrepancy is not immediately clear from the recently received study reports for both studies. In the DRF study limited investigation was performed, as no fetal visceral, skeletal, and craniofacial evaluations were included. Some signs of abortion were seen in treated groups in both the DRF and main studies. In the main study, groups of 20 pregnant New Zealand White rabbits per group (only 16 in the high dose group) received doses of 0, 20, 50, 150, 250/325 mg/kg bw/day in sunflower oil by gavage on gestation day 6-27 (Unnamed, 2020). The highest dose was reduced from 325 to 250 mg/kg/d from GD 22 due to severe effects that were not seen in the DRF study with comparable doses. All but one dam in the high dose group were sacrificed before the scheduled termination due to these effects, considered to be due to the severe local disturbance of the functioning of the gastro-intestinal tract due to the highly reactive substance (organic peroxide). These effects were assumed to be caused by irritation, osmosis, regurgitation, unabsorbed material from caecotrophy (rabbits eating the soft faecal pellets), leading to malnutrition, reduced spontaneous activity, loss of body weight and abortion. Due to high toxicity, the

dose of 20 mg/kg bw/d was chosen instead of additional high dose in the main study to increase the likelihood of generating dose-related data that includes a dose at the NOAEL using three dose level in the main study (no additional explanation is given by the registrant for the choice of the low dose of 20 mg/kg bw/day). No test item related changes in prenatal parameters or gross pathological findings were observed. NOAEL for maternal toxicity was set to 50 mg/kg bw/day based on effects due to severe local disturbance of the functioning of the gastro-intestinal tract at the high dose. The NOAEL for embryo/foetal developmental toxicity was 150 mg/kg bw/day based on terminally sacrificed females. As in the rat study, there were findings of some unossifications at higher incidence in the treated groups.

**Table 14-2 Summary prenatal data/litter data. Excerpt from ECHA dissemination site of Table 4 of OECD TG 414 study in rabbits (Unnamed, 2020)**

| | | Control (C) | Low dose (LD) | Medium dose (MD) | High dose (HD) | Low intermediate dose (LID) |
|---|---|---|---|---|---|---|
| Number of pregnant dams (used for calculation) | N | 20 | 17 (16) | 17 | 1 | 19 (18) |
| Corpora Lutea | No, per animal<br>Mean | 9.7u | 10.9 | 8.2 | 10.0X | 9.7 |
| Implantation sites | No, per animal<br>Mean | 8.9u | 10.1 | 7.1 | 10.0X | 8.9 |
| Preimplantation loss | %, per animal Mean | 5.2k | 7.4 | 15.1 | -X | 8.7 |
| Fetuses | No, per animal Mean | 8.5k | 7.9 | 6.2 | 9.0X | 6.7 |
| Live fetuses | No, per animal Mean | 8.4k | 7.9 | 5.7 | 9.0X | 6.7 |
| Early resorption | %, per animal Mean | 2.5k | 4.5 | 5.6 | 10.0X | 5 |
| Late resorption | %, per animal Mean | 1.8k | 4.7 | 0.7 | -X | 3.8 |
| Post implantation loss | %, per animal Mean | 5.2k | 22.1 | 17.4 | 10.0X | 26.1 |
| Fetus weight | Mean (g) | 32.8 | 28.3 | 32.3 | 30.7X | 32.4 |

u = KRUSKALL-WALLIS-DUNN; X = Group excluded from statistics; k = KRUSKALL-WALLIS; NA = No Test Applicable; a=ANOVA
Preimplantation Loss = Corpora Lutea - Implantation Sites
Post implantation Loss = Early/Late resorptions + Aborted Fetuses + Dead Fetuses

Affected Implants = Early/Late resorptions + Aborted Fetuses + Dead Fetuses + Malformed Fetuses

**Table 14-3 Summary mortality in dams. Excerpt from ECHA dissemination site of Table 5 of OECD TG 414 study in rabbits (Unnamed, 2020)**

| | | Number/ mg/kg bw/d | Control 0 | Low intermediate dose 20 | Low dose 50 | Medium dose 150 | High dose 325/250 |
|---|---|---|---|---|---|---|---|
| Day 0-27 | Animals examined | N | 20 | 20 | 20 | 20 | 16 |
| | Animals with signs | N | 0 | 1 | 1 | 0 | 15 |
| | Dead | N | 0 | 1 | 1 | 0 | 15 |
| | Found dead | N | 0 | 0 | 0 | 0 | 2 |
| | Euthanized | N | 0 | 1 | 1 | 0 | 13 |

**Table 14-4 Summary of Fetal malformations and variations (presented as no. of fetuses). Excerpt from ECHA dissemination site of Table 6 of OECD TG 414 study in rabbits (Unnamed, 2020)**

| | | Doses (mg/kg bw/d) | Control 0 | Low intermediate dose 20 | Low dose 50 | Medium dose 150 | High dose 325/250 |
|---|---|---|---|---|---|---|---|
| External malformations (no. of fetuses) | | | 3 | 1 | 0 | 0 | 1 |
| External variations | | | 0 | 0 | 0 | 0 | 0 |
| Skeletal malformations | | | 0 | 0 | 0 | 0 | 0 |
| Visceral malformations and variations | Incidences of a few malformations and variations were observed for various organs. However, these were not statistically significant from control or followed a dose-response. | | | | | | |
| Total craniofacial observations | | N | 0 | 0 | 0 | 0 | 0 |
| Skeletal variations: | | | | | | | |
| Vertebral sacral arches supernumerar | | % per litter, | 13.9u | 0*** | 0*** | 0*** | 0 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| y ossification | | mean | | | | | |
| Unossified 5th sternebra | | % per litter, mean | 5.99u | 12.22 | 40.99*** | 15.21 | 11.11 |
| Unossified hindlimb talus | | % per litter, mean | 1.06u | 8.36 | 13.39 | 5.77 | |

R= Region: Lower-Extremity (Bone), RLB = Region: Lower-Extremity (Bone), c = CHI-SQUARE, k = KRUSKAL-WALLIS, R = Region: Head-Neck Bone), RHB = Region: Head-Neck (Bone), u = KRUSKAL-WALLIS-DUNN, *** = $p < 0.001$, * = $p < 0.05$. R = Region: Trunk (Bone), RTB = Region: Trunk (Bone), i = CHI-SQUARE-FISHER

*OECD TG 414 in rats (Unnamed, 2014b)*

The adopted CLH Repr. 1B of EC 201-279-3 is founded on the results from an earlier OECD TG 414 study performed in rats (Unnamed, 2014b). Groups of pregnant Wistar rats received doses of 0, 50, 150, 450 mg/kg/day in sunflower oil by gavage on gestation day 5-19. Maternal and developmental NOAEL was 150 mg/kg/day. Maternal and developmental LOAEL was 450 mg/kg/day. In dams in the high dose group, clinical signs occurred and reductions in body weight, body weight gain, and food intake were observed when compared to the control group, as well as some necropsy findings.

In this rat study, there were clear test item related effects in the foetuses in the high dose group. This was manifested as increased intrauterine mortality, lower foetal weight and an increased incidence of skeletal malformations and variations in the pups in the high dose group, when compared to the control group. Post-implantation loss, late embryonic death, and foetal death were statistically increased in the high dose group. There was a statistically significant reduction in number of viable foetuses in the high dose group. When assessed on an individual basis, it was clear that there was no clear correlation between the dams with clinical signs of toxicity and/or necropsy findings and the intrauterine mortality. In conclusion, the findings of implantation losses and the total intrauterine mortality was considered by RAC to be related to the substance administration. See the tables below for details about maternal and developmental toxicity.

**Table 14-5 Maternal toxicity findings in OECD TG 414 in rats (Unnamed, 2014). Table copied from the RAC opinion adopted 8 June 2018**

| Effects | Control | 50 mg/kg bw/d | 150 mg/kg bw/d | 450 mg/kg bw/d |
|---|---|---|---|---|
| **Mortality** | 0 | 0 | 0 | 1 |
| **Salivation** | 0 | 0 | 4/21 | 8/17 |
| **Piloerection** | 0 | 0 | 0 | 3/17 |
| **Alopecia** | 0 | 0 | 0 | 3/17 |
| **Clinical signs**: (Reduced activity, vaginal bleeding, pale, cold, hypotonicity, red coloration around eye) | 0 | 0 | 0 | 10/17 |
| **Necropsy finding** | 0 | 0 | 0 | 6/17 |
| Enlarged adrenals | 0 | 0 | 0 | 4/17 |
| Blood in uterus | 0 | 0 | 0 | 3/17 |
| Enlarged spleen | 0 | 0 | 0 | 2/17 |
| Uterus filled with blood | 0 | 0 | 0 | 1/17 |
| Stomach distended fill up | 0 | 0 | 0 | 1/17 |
| Pale liver | 0 | 0 | 0 | 1/17 |
| Pale kidney | | | | |
| **Food consumption** | None | A statistically sign. temporary decrease was recorded. | Statistically sign. decrease was recorded | Statistically sign. decrease was recorded |
| **Body weight** | | | | |
| Start weight (g) | 236 ± 20.7 | 236.8 ± 14.9 | 233.1 ± 10.7 | 234.1 ± 11.0 |
| Weight day 11 (g) | 267.3 ± 21.5 | 265.3 ± 16.3 | **254. 8 ± 13.1*** | **246.3 ± 15.2**** |
| Weight day 20 (g) | 338.7 ± 27.6 | 335.8 ± 20.7 | **321.2 ± 14.5**** | **283.6 ± 24.5**** |
| Body weight gain (g) | 102.7 ± 14.7 | 99 ± 13.1 | **88 ± 12.8**** | **49.5 ± 20**** |

**Table 14-6 Observations relevant for the assessment of the developmental toxicity/teratogenicity classification in OECD TG 414 in rats (Unnamed, 2014). Table copied from the RAC opinion adopted 8 June 2018**

| Effects | Control | 50 mg/kg bw/d | 150 mg/kg bw/d | 450 mg/kg bw/d |
|---|---|---|---|---|
| **Pre implantation loss** | 7% | 12% | 9% | **14%**** |
| **Post implantation loss** | 7% (14/23 litters) | 4% | 5% | **17%** (15/17 litters)** |
| **Late embryonic death** | 1% | 1% | 1% | **12%**** |
| **Dead foetuses** | 0% | 0% | 0% | **3%**** |
| **Total intrauterine mortality** | 14% | 16% | 13% | **29%**** |
| **External examination** | | | | |
| **Foetuses with abnormalities** | 2.5% | 2.3% | 3.5% | **26.2%**** |
| **Variations** | 2.5% | 2.3% | 3.5% | **21.5%**** |
| **Malformations** | 0% | 0% | 0% | **4.7%**** |
| **Visceral examination** | | | | |
| **Foetuses with abnormalities** | 1.3% | 2% | 1% | 2% |
| **Skeletal examination** | | | | |
| **Foetuses with abnormalities** | 19.4% | 15% | 22.7% | **61.4%**** |
| **Variations** | 17.8% | 15% | 19.9% | **39.8%**** |
| **Malformations** | 1.6% | 0% | 2.9% | **21.6%**** |
| **Type of skeletal abnormalities, variations** | | | | |
| **Skull** | | | | |
| Incomplete ossification, marked (> three bones) | 1% | 0% | 0% | 1% |
| Incomplete ossification, marked (1 bone or more) | 2% | 2% | 4% | **13%**** |
| Supraoccipital not ossified | 0% | 1% | 1% | 1% |
| Hyoid not ossified | 1% | 0% | 0% | 1% |
| **Sternebrae** | | | | |
| Three or less ossified | 4% | 2% | 7% | **13%**** |
| Misaligned | 1% | 0% | 0% | 0% |

| | | | | |
|---|---|---|---|---|
| Bipartite | 0% | 0% | 0% | 1% |
| **Ribs** | | | | |
| Wavy | 6% | 6% | **14%*** | **32%**** |
| Wavy, marked | 0% | 1% | 1% | **8%**** |
| **Type of skeletal abnormalities, malformations** | | | | |
| **Sternebrae** | | | | |
| Xiphoid split | 1% | 0% | 1% | 3% |
| **Vertebrae, thoracic centra** | | | | |
| thoracic bipartite cartilage dumbbell shaped | 2% | 0% | 0% | 0% |
| **Pectoral girdle** | | | | |
| Scapula bent and/or short | 0% | 0% | 3% | **16%**** |
| Clavicula bent and/or short | 0% | 0% | 0% | 2% |
| **Forelimbs** | | | | |
| - Humerus bent and/or short | 0% | 0% | 0% | **12%**** |
| Ulna bent and/or short | 0% | 0% | 0% | **8%**** |
| Radius bent and/or short | 0% | 0% | 0% | **11%**** |
| **Hind limbs** | | | | |
| Femur short, bent | 0% | 0% | 0% | **5%**** |
| Tibia bent and/or short | 0% | 0% | 0% | 3% |
| Fibula bent and/or short | 0% | 0% | 0% | **4%*** |

Conclusion

Bis(α,α-dimethylbenzyl) peroxide has a harmonised classification as Repr.1B (H360D) based on the rat study with clear findings of developmental toxicity (CLP ATP 15). There is no information that the findings in rat are not relevant to humans, nor that rabbit is a more suitable species. The results from one positive, well performed study is sufficient to classify. Thus, the eMSCA considers that the new study in rabbits is not sufficient to change the conclusion on the harmonised classification Repro 1B. A testing proposal decision for an EOGRTS study (OECD TG 443) on dicumyl peroxide has been sent to the registrants in February 2022. The requested information shall be provided by 9 May 2024.

## 14.8. Hazard assessment of physicochemical properties

Not part of the assessment.

## 14.9. Selection of the critical DNEL(s)/DMEL(s) and/or qualitative/semi-quantitative descriptors for critical health effects

In a sub-chronic (90 d) oral toxicity study in rats a NOAEL of 80 mg/kg was identified for dicumyl peroxide. The eMSCA supports this NOAEL for derivation of DNELs for systemic long-term effects.

In the registration dossier, the registrants set the following DNELs for systemic long-term effects based on repeated dose toxicity studies (oral):

| | |
|---|---|
| Workers: | Inhalation, long-term: 5.6 mg/m$^3$ |
| | Dermal, long-term: 0.8 mg/kg bw/d |
| General population: | Oral, long-term: 0.4 mg/kg bw/d |
| | Inhalation, long-term: 1.4 mg/m$^3$ |
| | Dermal, long-term: 0.4 mg/kg bw/d |

The registrants have declared that there is no consumer exposure to the substance as such or in mixtures. In the following, only the DNELs for workers are considered further by the eMSCA.

The DNELs are set by the registrants based on the following assumptions:

The substance is not acutely toxic and a DNEL for acute toxicity is not derived by the registrants. The most relevant starting point is the NOAEL from the 90-day study (80 mg/kg bw/day) although the NOAEL for the 28-day study is lower. Although the 28-day study has a lower NOAEL, it is acceptable to use the 90-day study as a starting point since the 90-day study is closer to the exposure that is considered as relevant (long-term) and since the two NOAELs are relatively close (60 as opposed to 80 mg/kg bw/day).

Absorption is estimated to 100% via all routes (dermal absorption was estimated to 10% earlier but has been increased to 100% after dialogue between the eMSCA and the registrants). The eMSCA agree with the derived DNELs.

The assessment factors used by the registrants were default both for interspecies (4x2.5=10) and intraspecies (5), as well as for extrapolation from sub-chronic to chronic (2) and correction for dose-response and quality of dataset (1). The overall assessment factor is therefore set at 100.

Worker DNEL, dermal, long-term, systemic = 80 mg/kg bw/day/100 = 0.8 mg/kg bw/day

Worker DNEL, inhalation, long-term, systemic:
The starting point for this DNEL is the NOAEL of the 90 day-repeat dose toxicity study, 80 mg/kg bw/day.

The registrant has converted the oral dose in rat into the corresponding inhalative dose in humans following the ECHA guidance R8 in the following manner:

Corrected inhalatory NOAEC = oral NOAEL × 1/sRVrat x ABSoral-rat/ABSinh-human × sRVhuman/wRV:

$$80 \text{ mg/kg/day} \times 1/0{,}38 \text{m}^3\text{/kg/day} \times 6{,}7 \text{m}^3\text{(8h)}/10\text{m3(8h)} = 141 \text{ mg/m}^3$$

Correction for absorption ABSoral-rat/ABSinh-human: equal absorption based on physic-chemical properties = factor of 1

The assessment factors used by the registrants were default, Allometric scaling was not considered, which is in accordance with the ECHA guidance document R8 when the human exposure route is inhalation (See R.8 Table R.8-4 in ECHA, 2012). The assessment factor

for interspecies differences is therefore 2.5, for intraspecies 5, extrapolation from sub-chronic to chronic is 2 and correction for dose-response and quality of dataset is also the default factor of 1. The overall assessment factor is therefore set at 25.

Worker DNEL, inhalation, long-term, systemic = 141 mg/m$^3$/25 = 5.6 mg/m$^3$

**Table 14-7 Critical DNELS/DMELS**

| Endpoint of concern | Type of effect | Critical study(ies) | Corrected dose descriptor(s) (e.g., NOAEL, NOAEC) | DNEL/ DMEL | Justification/ Remarks |
|---|---|---|---|---|---|
| Systemic toxicity, repeat dose toxicity (oral) | Systemic effects, long-term | 90- day repeat dose toxicity study, kidney, and liver effects | 80 mg/kg bw/day (Original NOAEL 80 mg/kg bw/day) | Worker, **dermal**, long-term: 0.8 mg/kg bw/day | AF=100. |
| Systemic toxicity, repeat dose toxicity (oral) | Systemic effects, long-term | 90- day repeat dose toxicity study, kidney, and liver effects | Corrected starting point to inhalation to humans 141 mg/m$^3$<br><br>(Original NOAEL 80 mg/kg bw/day) | Worker, **inhalation**, long-term: 5.6 mg/m$^3$ | AF = 25 |

## 14.10. Conclusions of the human health hazard assessment and related classification and labelling

The need for CLH based on reproductive toxicity was a concern identified in the substance evaluation and established in ATP15 to CLP. The substance evaluation has not revealed any additional concerns regarding human health hazards of this substance. A new OECD TG 414 prenatal development toxicity study on a second species (rabbits) has been submitted. As explained above, the eMSCA suggests no change in the present harmonised classification and labelling (section 11) that was based on findings in the previous study in rats.

# 15. Endocrine disrupting (ED) properties assessment

Not assessed.

# 16. PBT/vPvB and PMT/vPvM assessment

## 16.1. Persistence

Bis(α,α-dimethylbenzyl) peroxide has a slow hydrolysis rate at environmentally relevant conditions and is demonstrated to be not readily biodegradable in OECD screening tests (OEC TG 301F, 301D and 301C). In a reliable test on aerobic mineralisation in surface water – OECD TG 309 Simulation Biodegradation Test – the substance is shown to have a half-life of 142 days at 12 °C. Bis(α,α-dimethylbenzyl) therefore fulfils the P and vP criteria of REACH Annex XIII.

## 16.2. Bioaccumulation

There are two studies of fish bioaccumulation on bis(α,α-dimethylbenzyl) peroxide in the registration dossier. The oldest study has a low reliability, but the newest study must be regarded as reliable. Although dicumyl peroxide has been seen to accumulate in fish to some degree, the B-criteria is not fulfilled. The bioaccumulation study in rainbow trout, indicates a lipid and growth corrected kinetic BCF of 747, well below the criteria for bioaccumulative substances of 2000 (B) or very bioaccumulative substances of 5000 (vB) of REACH Annex XIII.

## 16.3. Mobility

Bis(α,α-dimethylbenzyl) peroxide has a high Log $K_{OW}$ (5,6) and Log $K_{OC}$ (3,98) indicating a low potential for mobility in the environment.

## 16.4. Toxicity

Bis(α,α-dimethylbenzyl) peroxide has a harmonized classification as Repr. 1B which fulfills the T criteria of REACH Annex XIII. The classification was based on findings of implantation loss and intrauterine mortality in Wistar rats in a prenatal developmental toxicity study.

The substance has a harmonised classification as aquatic chronic 2. Based on the available ecotoxicity data bis(α,α-dimethylbenzyl) peroxide does not fulfil the T-criterion (EC10 /NOEC less than 0,01 mg/) of REACH Annex XIII.

## 16.5. Conclusions of the PBT/vPvB/PMT/vPvM assessment and related classification and labelling

Bis(α,α-dimethylbenzyl) peroxide fulfils the criterion for persistent and very persistent substances (P/vP) with an aqueous half-life of 142 days at 12 °°C. The bioaccumulation study in rainbow trout, indicates a lipid and growth corrected kinetic BCF of 747, well below the criteria for bioaccumulation of (B) or (vB). The toxicity criteria (T) are fulfilled based on the harmonized classification as Repr 1B.

Based on available experimental data the substance cannot be regarded as a a PBT/vPvB substance because the B/vB-criteria of REACH Annex XIII is not fulfilled.

Based on available experimental data the substance cannot be regarded as a PMT/vPvM substance because the M/vM-criteria is not fulfilled.

# 17. Exposure assessment

## 17.1. Human health

### 17.1.1. Worker

Occupational exposure can occur during manufacture and formulation of preparations and polymers and during uses at industrial sites. Further, professional uses of bis(α,α-dimethylbenzyl) peroxide have been reported in the past (ECHA (2023), see 10.2). Even though these uses are not registered currently, it cannot be excluded that such uses might take place again in the future. According to the database on substances in preparations in Nordic countries (SPIN) bis(α,α-dimethylbenzyl) peroxide has been used in considerable amounts (1->2000 t/a) in recent years (2015-2021) and exposure of workers is cannot be ruled out.

Worker exposure data was available from one published study. This was an investigation of bis(α,α-dimethylbenzyl) peroxide in workplace air, where the substance was used as a

cross-linking agent in a polymer producing plant (Spetz et al., 2002). Both personal and stationary samples were gathered using air sampling pumps in different parts of the plant. The concentrations of bis(α,α-dimethylbenzyl) peroxide were measurable along the polymer production line and were higher in the peroxide melting room, especially when work was done on the melting tank. In the polymer packaging room, the concentrations of bis(α,α-dimethylbenzyl) peroxide were 11 and 31 µg/m$^3$ in two personal samples. In the peroxide blender room the concentrations were 41, 22, and 278 µg/m$^3$ in three stationary samples, the highest was caused by spillage on the floor. In the peroxide melting room stationary measurements were between 298 and 565 µg/m$^3$, with 6 measurements at 310 +/-19 µg/m$^3$ in one spot.

The registrants have performed extensive exposure estimations by applying Ecetoc TRA modelling tool (version 3.0, included in Chesar). The eMSCA has not recalculated or cross-checked these estimations which all result in RCRs below 1.

### 17.1.2. Consumer

The registrants consider that exposure of consumers can generally be assumed to be negligible. In the assessment of regulatory needs for organic hydroperoxides and aliphatic/cumyl peroxides, exposure of consumers from articles have been reported in the past (ECHA (2023), see 10.2). Even though these uses are not registered currently, it cannot be excluded that such uses might take place again in the future. Further in the database on substances in preparations in Nordic countries (SPIN) bis(α,α-dimethylbenzyl) peroxide has been used in considerable amounts (1->2000 t/a) in recent years (2015-2021) and exposure of consumers cannot be excluded. However, no exposure data is available for assessment and the eMSCA does not consider the need for such data as critical in this substance evaluation.

## 17.2. Environment

Exposure of the environment can occur during manufacture and formulation of preparations and polymers and during uses at industrial sites. Due to the function of the substance as flame retardant synergist exposure can also occur during the article service life of articles. According to the database on substances in preparations in Nordic countries (SPIN) bis(α,α-dimethylbenzyl) peroxide has been used in considerable amounts (1->2000 t/a) in recent years (2015-2021) and exposure of the environment cannot be ruled out.

Data from Norwegian EPA monitoring program showed the substance in sewage treatment plant effluent at concentrations of between < 5 and 11 ng/L at two sites (Miljødirektoratet M-176, 2014).

The registrants have performed extensive exposure estimations by applying EUSES 2.1.2. All RCRs were below 1, although some were close. The eMSCA has previously reviewed estimations for the environment and found them to be reasonable and protective but has not reviewed them since the last update.

However, long term toxicity test on fish and sediment organisms have been requested by ECHA through dossier evaluation. These new data may justify future review of the estimates.

# 18. Risk characterisation

## 18.1. Human health

Consumer exposure is anticipated to be limited. Only a single publication is available with exposure data for workers. The registrants have calculated the worker exposure extensively and consider that this results in RCRs below 1. The eMSCA has not recalculated the estimations but has no reason to assume a concern. The exposure assessments for

workers submitted by the registrants cover formulation or repackaging, service life (professional worker), use at industrial sites in the polymer industry.

## 18.2. Environment

The eMSCA concludes that bis(α, α-dimethylbenzyl) peroxide meets the P/vP criterion and T criterion (Rep 1 B classification) of REACH Annex XIII. Therefore, the Registrant(s) should review their exposure scenarios and risk reduction measures to ensure the minimisation of emissions and subsequent exposure of humans and the environment, throughout the lifecycle of the substance.

Long term toxicity test on fish and sediment organisms have been requested by ECHA through dossier evaluation. These new data may justify future revision of the emission estimates and risk characterisation.

# 19. References

Environment Canada, Health Canada (2009). Screening Assessment for the Challenge Peroxide, [1,3(or 1,4)-phenylenebis(1-methylethylidene)]bis[(1,1-dimethylethyl) (PBMBDP, CAS 25155-25-3)

Donkers R, Maran F, Wayner D. D. M, Workentin M.(1999). Kinetics of the Reduction of Dialkyl Peroxides. New Insights into the Dynamics of Dissociative Electron Transfer. Journal of the American Chemical Society 1999 121 (31), 7239-7248 DOI: 10.1021/ja9906148

ECHA (2012). Guidance on information requirements and chemical safety assessment Chapter R.8: Characterisation of dose [concentration]-response for human health

ECHA (2017). Guidance on Information Requirements and Chemical Safety Assessment Chapter R.11: PBT/vPvB assessment.

ECHA (2023). Assessment of regulatory needs, Group Name: Organic hydroperoxides and aliphatic/cumyl peroxides, ARN/GMT 206.

Hansson AH, Petruson B, (1986). Acta Otolaryngol (Stockh) 101, 102-113. Nasal mucosa changes after acute and long-term exposure to bis(α,α-dimethylbenzyl) peroxide

Miljødirektoratet report M-176 (2014). Screening program 2013 - New bisphenols, organic peroxides, fluorinated siloxanes, organic UV filters and selected PBT substances. Published 2014

Miljødirektoratet report M-446 (2015)., Screening program 2014 - Organic phosphites, selected PBT substances and non-target screening, published December 2015

RAC Opinion (2018) proposing harmonised classification and labelling at EU level of bis(α,α-dimethylbenzyl) peroxide, EC Number: 201-279-3, CAS Number: 80-43-3, CLH-O-0000001412-86-217/F, Adopted 8 June 2018

Spetz, A., Svanström, M., & Ramnäs, O. (2002). Determination of dicumyl peroxide in workplace air. Annals of occupational hygiene, 46(7), 637-641.

Spin database: SPIN Substances in preparations in nordic countries (spin2000.net)

Unnamed (2000). Repeated dose toxicity study: 28-day oral toxicity study in rats. Unpublished study report (OECD TG 407).

Unnamed (2014a). Repeated dose toxicity study: 90-day oral toxicity study in rats. Unpublished study report (OECD TG 408).

Unnamed (2014b). Prenatal developmental Toxicity Study of Dicumyl Peroxide in rats by oral administration. Unpublished study report (OECD TG 414).

Unnamed (2020). Prenatal developmental Toxicity Study of Dicumyl Peroxide in rabbits by oral administration. Unpublished study report (OECD TG 414).

# 20. Abbreviations

| | |
|---|---|
| AR | applied radioactivity |
| BCF | Bioconcentration factor |
| BOD/ThOD | Biological oxygen demand/ Theoretical oxygen demand |
| BPR | Biocidal products regulation (EU) 528/2012 |
| CAS RN | CAS registry number |
| CCH | Compliance check |
| CLP | Classification, labelling and packaging |
| CLH | Harmonised classification and labelling (CLH). |
| CoRAP | Community rolling action plan |
| DMEL | Derived minimal effect level |
| DNEL | Derived no-effect level |
| DT 50 | Half-life |
| EC | European community |
| EC50 | Half maximal effective concentration |
| ECHA | European chemicals agency |
| ED | Endocrine disruption |
| EU | European union |
| EUSES | European union system for the evaluation of substances |
| GC | Gas chromatography |
| GLP | Good laboratory practice |
| HS | Hockey Stick model |
| LC50 | Lethal concentration 50 |
| LC-MS/MS | Liquid chromatography/ Mass spectrometry |
| LSC | Liquid scintillation counting |
| LOAEL | Lowest Observed Adverse Effect Level |
| LOEC | Lowest observed effect concentration |
| LOD | Limit of detection |
| LOQ | Limit of quantification |
| HS | Hockey-stick model |
| MSCA | Member state competent authority |
| NOAEC | No observed adverse effect concentration |
| NOAEL | No observed adverse effect level |
| NONs | Notification of new substances |
| NOEC | No observed effect concentration |
| OECD | Organisation for economic co-operation and development |
| PBT | Persistent, bioaccumulative and toxic |
| PMT | Persistent, mobile, and toxic |
| PNEC | Predicted no-effect concentration |
| POP | Persistent organic pollutants |
| PPP | Plant protection products regulation EC 1107/2009 |
| QSAR | Quantitative structure-activity relationship |
| RAR | Risk assessment report |
| RAC | Risk assessment committee |
| REACH | Regulation No 1907/2006 concerning registration, evaluation, authorisation, and restriction of chemicals |
| SFO | Single First order |
| SPE | Solid phase extraction |
| SPIN | substances in preparations in Nordic countries |
| STOT RE | Specific target organ toxicity – repeated exposure |
| STOT SE | Specific target organ toxicity – single exposure |
| STP | Sewage treatment plant |
| SVHC | Substances of very high concern |
| TG | Test guideline |
| TGD | Technical guidance document |
| TPE | Testing proposal examination |

| | |
|---|---|
| UNEP | United nations environment program |
| UVCB | Unknown or variable composition, complex reaction products or of biological materials. |
| vPvB | Very persistent and very bioaccumulative |
| vPvM | Very persistent and very mobile |
| WAF | Water accommodated fraction |