Committee for Risk Assessment

RAC

Annex 1

Background document

to the Opinion proposing harmonised classification and labelling at EU level of

Phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide

EC Number: 423-340-5
CAS Number: 162881-26-7

CLH-O-0000001412-86-152/F

The background document is a compilation of information considered relevant by the dossier submitter or by RAC for the proposed classification. It includes the proposal of the dossier submitter and the conclusion of RAC. It is based on the official CLH report submitted to public consultation. RAC has not changed the text of this CLH report but inserted text which is specifically marked as 'RAC evaluation'. Only the RAC text reflects the view of RAC.

Adopted

9 June 2017

CLH report

Proposal for Harmonised Classification and Labelling

Based on Regulation (EC) No 1272/2008 (CLP Regulation), Annex VI, Part 2

Substance Name:

Phenyl bis(2,4,6-trimethylbenzoyl) -phosphine oxide

EC Number: **423-340-5**

CAS Number: **162881-26-7**

Index Number: **015-189-00-5**

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Industry in accordance with Article 37(6) of CLP Regulation

Version number: 2.0 **Date: July 2016**

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Part A.

1 PROPOSAL FOR HARMONISED CLASSIFICATION AND LABELLING

1.1 Substance

Table 1: Substance identity

Substance name:	Phenyl bis(2,4,6-trimethylbenzoyl) - phosphine oxide
EC number:	423-340-5
CAS number:	162881-26-7
Annex VI Index number:	015-189-00-5
Degree of purity:	> 98.0 — < 99.9 % (w/w), typically ca. 99.8 % (w/w)
Impurities:	One impurity at > 0.1 — < 1.0 % (w/w), typically ca. 0.2 %

1.2 Harmonised classification and labelling proposal

Table 2: The current Annex VI entry and the proposed harmonised classification

	CLP Regulation
Current entry in Annex VI, CLP Regulation	Skin Sens. 1 – H317 Aquatic Chronic 4 – H413
Current proposal for consideration by RAC	Skin Sens. 1A – H317 Removal of Aquatic Chronic 4 – H413
Resulting harmonised classification (future entry in Annex VI, CLP Regulation)	Skin Sens. 1A – H317

1.3 Proposed harmonised classification and labelling based on CLP Regulation

Table 3: Proposed classification according to the CLP Regulation

CLP Annex I ref	Hazard class	Proposed classification	Proposed SCLs and/or M-factors	Current classification [1)]	Reason for no classification [2)]
2.1.	Explosives	None		None	Not assessed in this dossier.
2.2.	Flammable gases	None		None	Not assessed in this dossier.
2.3.	Flammable aerosols	None		None	Not assessed in this dossier.
2.4.	Oxidising gases	None		None	Not assessed in this dossier.
2.5.	Gases under pressure	None		None	Not assessed in this dossier.
2.6.	Flammable liquids	None		None	Not assessed in this dossier.
2.7.	Flammable solids	None		None	Not assessed in this dossier.
2.8.	Self-reactive substances and mixtures	None		None	Not assessed in this dossier.
2.9.	Pyrophoric liquids	None		None	Not assessed in this dossier.
2.10.	Pyrophoric solids	None		None	Not assessed in this dossier.
2.11.	Self-heating substances and mixtures	None		None	Not assessed in this dossier.
2.12.	Substances and mixtures which in contact with water emit flammable gases	None		None	Not assessed in this dossier.
2.13.	Oxidising liquids	None		None	Not assessed in this dossier.
2.14.	Oxidising solids	None		None	Not assessed in this dossier.
2.15.	Organic peroxides	None		None	Not assessed in this dossier.
2.16.	Substance and mixtures corrosive to metals				data lacking
3.1.	Acute toxicity - oral	None		None	Not assessed in this dossier.
	Acute toxicity - dermal	None		None	Not assessed in this dossier.
	Acute toxicity - inhalation				data lacking
3.2.	Skin corrosion / irritation	None		None	Not assessed in this dossier.
3.3.	Serious eye damage / eye irritation	None		None	Not assessed in this dossier.
3.4.	Respiratory sensitisation				data lacking
3.4.	Skin sensitisation	Skin Sens. 1A, H317		Skin Sens. 1, H317	

CLP Annex I ref	Hazard class	Proposed classification	Proposed SCLs and/or M-factors	Current classification [1)]	Reason for no classification [2)]
3.5.	Germ cell mutagenicity	None		None	Not assessed in this dossier.
3.6.	Carcinogenicity				data lacking
3.7.	Reproductive toxicity	None		None	Not assessed in this dossier.
3.8.	Specific target organ toxicity –single exposure	None		None	Not assessed in this dossier.
3.9.	Specific target organ toxicity – repeated exposure	None		None	Not assessed in this dossier.
3.10.	Aspiration hazard	None		None	Not assessed in this dossier.
4.1.	Hazardous to the aquatic environment	Not classified		Aquatic Chronic 4, H413	
5.1.	Hazardous to the ozone layer				conclusive but not sufficient for classification

[1)] Including specific concentration limits (SCLs) and M-factors
[2)] Data lacking, inconclusive, or conclusive but not sufficient for classification

Labelling: Signal word: Warning

Hazard statements: H317: May cause an allergic skin reaction

Precautionary statements: Not subject for Annex VI entry of CLP.

Hazard pictograms: GHS07: Exclamation mark

Proposed notes assigned to an entry: None

2 BACKGROUND TO THE CLH PROPOSAL

The dossier was prepared by industry according to Article 37(6) of the CLP Regulation.

For the purpose of this dossier the German CA has taken all nine registration dossiers available in December 2015 into account.

2.1 History of the previous classification and labelling

Phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide was previously discussed by the Technical Committee for Classification and Labelling (TC C&L) according to Directive 67/548/EEC. The Working Group on the Classification and Labelling of Dangerous Substances ECB agreed that phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide should be classified and labelled with Xi; R43 (May cause sensitization by skin contact), R53 (May cause long-term adverse effects in aquatic environment). Phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide was added to Annex I of Directive 67/548/EEC in 2004 by the 29th ATP.

Phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide is listed by Index number 015-189-00-5 in Annex VI, Part 3, and Table 3.1 (list of harmonised classification and labelling of hazardous substances) of the Regulation (EC) No 1272/2008 (CLP) as: Skin Sens.1, H317 (May cause an allergic skin reaction) and Aquatic Chronic 4, H413 (May cause long lasting harmful effects to aquatic life).

2.2 Short summary of the scientific justification for the CLH proposal

This proposal aims to update the existing harmonised classification and labelling of phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide.

Skin sensitization

Phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide has shown clear evidence of skin sensitisation according to OECD TG 406/EU B.6 (Guinea Pig Maximisation test, GPMT). Based on this animal model system strong potency of skin sensitization is determined for phenyl bis(2,4,6-trimethyl-benzoyl)-phosphine oxide. Based on the available data, phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide is classified as skin sensitizer category 1.

The existing experimental data on skin sensitization were evaluated for sub-categorizing of skin sensitization potency according to CLP and Commission Regulation (EU) No 487/2013 of 8 May 2013. In comparison to the given criteria for the hazard category and sub-category for skin sensitization according to CLP phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide fulfills the criteria for classification in the hazard class as skin sensitizer sub-category 1A, H317: May cause an allergic skin reaction, because skin sensitization responses of ≥ 60 % at > 0.1 % to ≤ 1 % intradermal induction doses were observed in the adjuvant type test method, GPMT.

Aquatic toxicity

The previous classification did not comprise an available bioaccumulation study which proves that the test item is not bioaccumulative (BCF < 5). This bioaccumulation study was discussed in the context of another ECHA-procedure (Compliance Check). Misgivings about the adequacy for (de-) classification were voiced. Referring to the prior compliance check, an ECHA dossier evaluation (compliance check) draft decision was sent to the lead REACH Registrant on 11 July 2011 requesting, among others, a new bioaccumulation study according to OECD 305 and via the dietary route of exposure. The requirement for this test was subsequently removed from the decision based

on proposals for amendment submitted by three Member States and agreement of the ECHA Member State Committee. The basis for the removal of the bioaccumulation test from the decision was the adequacy of the existing study in the technical dossier (despite some methodological shortcomings) for risk assessment and classification purposes (under REACH).

Regarding the hazard assessment for the environment, the classification criteria according to Table 4.1.0 ("Classification categories for hazardous to the aquatic environment") of Regulation (EC) No 1272/2008 for Aquatic Chronic 4 include

(1) poorly soluble substances for which no acute toxicity is recorded at levels up to the water solubility

(2) and which are not rapidly degradable

(3) and have an experimentally determined BCF ≥ 500 (or, if absent, a log Kow ≥ 4)

The current substance was tested in acute studies with fish, daphnids and algae as well as in a chronic toxicity study in daphnids. Neither of these studies showed toxic effects in the range of the water solubility. From the acute tests it is not apparent that daphnia is the most sensitive species as no effects occurred. No chronic study for fish is available. Nevertheless, a BCF study did not show any potential of the compound to significantly accumulate in organisms. The BCF was determined as < 5. Therefore, according to Regulation (EC) No 1272/2008 the substance should not be classified for the environment.

2.3 Current harmonised classification and labelling

Table 4: Current entry in Annex VI, Table 3.1 of CLP

Index-No	International Chemical Identification	EC-No	CAS-No	Classification		Labelling	
				Hazard Class and Category Code(s)	Hazard Statement Code(s)	Pictogram, Signal Word Code(s)	Hazard statement Code(s)
015-189-00-5	phenyl bis(2,4,6-trimethylbenzoyl) - phosphine oxide	423-340-5	162881-26-7	Skin Sens. 1 Aquatic Chronic 4	H317 H413	GHS07 Wng	H317 H413

2.4 Current self-classification and labelling

The CLP inventory contains two tables. One table lists classifications apparently submitted using the EC number as identifier (Table 5); the other lists classifications submitted using only the CAS number as identifier (Table 6).

Table 5: Entries in the C & L inventory for EC 423-340-5 (accessed July 17th 2015)

Classification		Labelling		Number of Notifiers
Hazard Class and Category Code(s)	Hazard Statement Code(s)	Hazard Statement Code(s)	Pictograms, Signal Word Code(s)	
Skin Sens. 1	H317	H317	Wng	1
Aquatic Chronic 4	H413	H413		
Skin Sens. 1	H317	H317	Wng	1

Classification		Labelling		Number of Notifiers
Hazard Class and Category Code(s)	**Hazard Statement Code(s)**	**Hazard Statement Code(s)**	**Pictograms, Signal Word Code(s)**	
Skin Sens. 1	H317	H317	GHS07 Wng	136
Aquatic Chronic 4	H413	H413		
Skin Sens. 1	H317	H317	GHS07 Wng	23
Aquatic Chronic 4	H413	H413		
Not Classified				1
Skin Sens. 1	H317	H317	GHS07 Wng	1
Aquatic Chronic 4	H413	H413		
Skin Sens. 1	H317	H317	GHS07 Wng	1
Aquatic Chronic 4	H413	H413		

Table 6: Entries in the C & L inventory for CAS 162881-26-7 (accessed July 17th 2015)

Classification		Labelling		Number of Notifiers
Hazard Class and Category Code(s)	**Hazard Statement Code(s)**	**Hazard Statement Code(s)**	**Pictograms, Signal Word Code(s)**	
Skin Sens. 1	H317	H317	GHS07 Wng	111
Aquatic Chronic 4	H413	H413		
Skin Sens. 1	H317	H317	GHS07 Wng	73
Aquatic Chronic 2	H413	H413		
Acute tox 4	H317	H317	Wng	1
Aquatic Chronic 2	H413	H413		
Skin Irrit. 2	H315	H315	GHS07 Wng	1
Skin Sens. 1	H317	H317		
Eye Irrit. 2	H319	H319		

3 JUSTIFICATION THAT ACTION IS NEEDED AT COMMUNITY LEVEL

According to Article 36(3) of CLP for a substance that fulfills the criteria for other hazard classes or differentiations than those of CMR or respiratory sensitization (Category 1) and the substance is not an active substance regulated under the Plant Protection Product Directive (PPPD) and Biocidal Product Directive (BPD), a harmonised classification and labelling proposal can be submitted if a justification is provided demonstrating the need for such action at community level. For phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide a harmonised classification had been developed under 67/548/EEC with the 29th ATP. Currently, phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide has a harmonised classification for aquatic toxicity and skin sensitization (CLP Annex VI Index number 015-189-00-5) that is the result of the translation from the previous legislation (Directive 67/548/EEC). Based on the in depth evaluation of the existing *in vivo* toxicity data a change of the existing entry is needed for the classification for the human health hazard class 'skin sensitization'. The available data reflect the criteria for classification in the hazard class as skin sensitizer sub-category 1A, H317. This will ascertain adequate handling and use of risk minimization measurements. Furthermore, the new evaluation of the existing environment data showed the need to revise the current classification for 'hazardous to the aquatic environment'. Phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide no longer reflects the criteria for classification and labelling as

Aquatic Chronic 4, H413 in Annex I of CLP. Action is needed to revise the CLP Regulation entry in Annex VI Table 3.1.

Part B.

SCIENTIFIC EVALUATION OF THE DATA

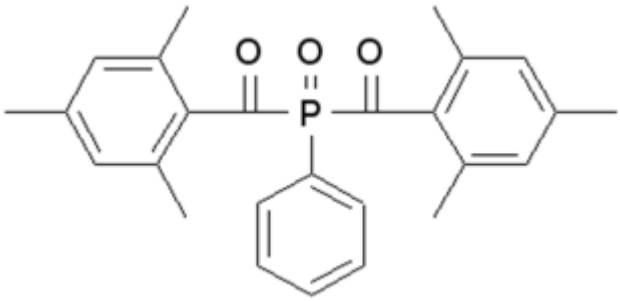
1 IDENTITY OF THE SUBSTANCE

1.1 Name and other identifiers of the substance

Table 7: Substance identity

EC number:	423-340-5
EC name:	Phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide
CAS number:	162881-26-7
CAS name:	Phosphine oxide, phenylbis(2,4,6-trimethylbenzoyl)-
IUPAC name:	phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide
CLP Annex VI Index number:	015-189-00-5
Molecular formula:	C26 H27 O3 P
Molecular weight:	418.47

Structural formula:



1.2 Composition of the substance

The substance is of high purity (ca. 99.8 % (w/w)).

1.2.1 Composition of test material

The test material purity was greater than 95 %.

1.3 Physico-chemical properties

The physicochemical properties of the compound are listed in Table 8.

Table 8: Summary of physico-chemical properties

Property	Value	Reference	Comment (e.g. measured or estimated)
Water solubility	< 0.1 mg/L at 20°C at pH 7.5	CIBA-GEIGY (1996)	The determination was carried out by flask method in high-purity water. The water solubility was below the detection limit of our analytical method. The flask method was used instead of the column elution method, because a change in crystal structure might occur, when the test material is deposited on the support material.
Partition coefficient n-octanol/water	logPow= 5.8 at 22°C at pH 8.3	CIBA-GEIGY (1996a)	The measurement was performed by HPLC
Solubility in organic solvents / fat solubility	13.9 g/kg of fat at 37°C	CIBA-GEIGY (2000)	
Surface tension	71 mN/m at 20°C (Filtrate of 0.1g/L suspension)	CIBA-GEIGY (1996d)	Based on the criteria as outlined in the OECD Guideline it is concluded that the test substance should not be regarded as being surface-active material
Physical state	yellow fine crystalline powder		solid at 20°C and 101.3 kPa
Melting / freezing point	131.4°C	CIBA-GEIGY (1997g)	
Boiling point	not applicable (decomposed at >=168°C)	CIBA-GEIGY (1996e)	
Relative density	1190 kg/m³ at 21°C	CIBA-GEIGY (1996f)	
Vapour pressure	<0.0000002 Pa at 20 °C (extrapolated)	CIBA-GEIGY (1996g)	

2 MANUFACTURE AND USES

Phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide is a photoinitiator. Upon irradiation, the phosphorus - acyl carbon bond of the molecule is homolytically cleaved into radicals which initiate the polymerization of monomeric or oligomeric polymer precursors for various applications.

3 CLASSIFICATION FOR PHYSICO-CHEMICAL PROPERTIES

Not classified for physicochemical properties.

4 HUMAN HEALTH HAZARD ASSESSMENT

4.1 Toxicokinetics (absorption, metabolism, distribution and elimination)

Not evaluated in the scope of this dossier.

4.2 Acute toxicity

Not evaluated in the scope of this dossier

4.3 Specific target organ toxicity – single exposure (STOT SE)

Not evaluated in the scope of this dossier.

4.4 Irritation

Not evaluated in the scope of this dossier.

4.5 Corrosivity

Not evaluated in the scope of this dossier.

4.6 Sensitization

4.6.1 Skin sensititsation

4.6.1.1 Non-human information

The results of experimental studies on skin sensitisation are summarised in the following table:

Table 9: Overview of experimental studies on skin sensitisation

Method	Results	Remarks	Reference
Guinea pig maximisation test (GPMT) According to OECD TG 406 (Skin Sensitisation, 1992)/ EU B.6, GLP-compliant guinea pig (Pirbright White Strain) male/female; TG: 10/sex; Negative control: 10/sex; Vehicle control: 10/sex Induction: 0.5 % in peanut oil intradermal; 50 % in vaseline topical application	**Skin sensitising** **Number with positive reactions after** **Challenge with 10 % in vaseline:** TG: 24h: 18/20 (90 %), (m: 9/10; f: 9/10); 48h: 16/20 (80 %), (m: 8/10, additionally 8/10 scaling; f: 8/10, additionally 7/10 scaling) Vehicle control: 24h: 1/20 (m: 0/10; f: 1/10); 48h: 0/20 (m: 0/10, f: 0/10)	1 (reliable without restriction) key study **Test material (EC name): phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide**	CIBA-GEIGY (1996c)

Method	Results	Remarks	Reference
Challenge: 10 % in vaseline topical application Study was performed under normal light	Negative control: 24h/48h: 0/20 (m: 0/10, f: 0/10) <u>Reliability check (1995):</u> 2-Mercaptothiacole (2-MBT): TG: 10/sex; vehicle control: 10 (sex not given); Induction: 5.0 % in peanut oil intradermal; 50 % in vaseline topical application; challenge: 10 % in vaseline topical application: 24h: 17/20 (85 %), (m: 9/10; f: 8/10), 48h: 14/20 (70 %), (m: 7/10; f: 7/10), no irritation vehicle control: 24h/48h: 0/10 According to CLP phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide fulfils the criteria for classification as: **Skin Sens.1A, H317: May cause an allergic skin reaction**	Purity: > 95 %	
Guinea pig maximisation test (GPMT) According to OECD TG 406 (Skin Sensitisation, 1992)/EU B.6, GLP-compliant guinea pig (Dunkin-Hartley) male; TG: 10; Negative control: 5 Induction :1.0 % in 5.0 % acetone in Alembicol D (product of coconut oil) intradermal ; 70 % in acetone topical application (pretreated with 10 % sodium lauryl sulfate in petrolatum) Challenge: 70 % and 35 % in acetone topical application Test formulations were prepared under safelight; formulation containers wrapped in aluminium foil; aluminium foil was incorporated in the dressings	**Skin sensitising** **Number with positive reactions after** **Challenge with 70 % in acetone:** TG: 24h: 0/10 (0 %); 48h: 5/10 (50 %); 72h: 5/10 (50 %); additionally 1/10 assessed as positive (60 %) Conclusion (24h & 48h & 72h): **5+1/10 (60 %)** **Challenge with 35 % in acetone:** TG: 24h: 2/10; 48h: 3/10; 72h: 2/10; additionally 2/10 assessed as positive Conclusion (24h & 48h & 72h): **4+2/10 (60 %)** Negative Control: 24h/48h: 0/5 <u>Reliability check (1996):</u> 2-MBT: TG/Control: 10 males; Induction: 10 % intradermal (vehicle not given), 83.33 % topical application (vehicle not given); challenge: 83.33 % and 40 % (vehicle not given): 24h/48h: always 10/10 (100 %); control: always 0/10 (0 %) According to CLP phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide fulfils the criteria for classification as: **Skin Sens.1A, H317: May cause an allergic skin reaction**	1 (reliable without restriction) key study **Test material (EC name): phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide** Purity: 98.4 %	Huntingdon Life Sciences Ltd. (1997)

4.6.1.2 Human information

No human data on the sensitising potential of phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide are available.

4.6.1.3 Summary and discussion of skin sensitisation

Data on skin sensitization of phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide were obtained from animal testing according to the existing testing guidelines. No information is available on phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide induced sensitization by skin contact in humans.

Two guideline conform GPMTs according to the testing protocol of OECD TG 406/EU B.6 are available for the assessment of the skin sensitization potential of phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide. In both studies guinea pigs exhibited positive results.

One study was performed under normal light condition (CIBA-GEIGY 1996c). However, storage of the test substance was in the dark at room temperature. Phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide with a purity of > 95 % was prepared as a 0.5 % solution in peanut oil for intradermal induction. The epidermal induction was performed with 50 % using vaseline as vehicle. For the topical challenge application, a 10 % formulation in vaseline was used. Eighteen of 20 animals (90 %) treated with the test substance showed a clear skin sensitization response after challenge at the 24 h reading. At the 48 h reading there were still 16/20 animals with positive skin reactions corresponding to a sensitization rate of 80 %. In addition scaling skin reactions were recorded for eight males and seven females at the 48 h reading. No irritant skin reactions were recorded for control animals. No information if and to what extent the substance had undergone light-induced degradation prior to application is reported in the study protocol. However, the treatment of the skin was performed with occlusive wrapping so that light protection during treatment should have been provided. In conclusion, the maximal skin sensitization rate after intradermal induction with a concentration of 0.5 % phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide was 90 %.

In the other study performed by Huntingdon Life Sciences Ltd. (1997), the test formulations were prepared under safelight and the formulation containers were wrapped in aluminum foil because solutions of the substance are sensitive to light of the UV-range and the near visible violet light range. Aluminum foil was also incorporated in the dressings to minimize photoinduced degradation of the test material. Compared to the GPMT performed by CIBA-GEIGY (1996c) higher concentrations for induction and challenge treatment, different vehicles and another strain of guinea pig were used. Phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide with a purity of 98.4 % was prepared as a 1.0 % solution in 5.0 % acetone in Alembicol D for intradermal induction. The application area was pretreated with 10 % sodium lauryl sulfate (SLS) in petrolatum 24 hours before topical induction with 70 % in acetone occurred because the test substance was non-irritating. Test substance concentrations of 70 % and 35 % in acetone were used for the challenge topical application. Readings were performed 24, 48 and 72 hours after challenge. After 24 h with a challenge concentration of 70 % in acetone none of the test substance treated animals (0/10) showed positive reactions. Reading of the challenge reaction after 48 h and 72 h revealed a clear positive skin sensitization response in 5/10 (50 %) animals. A further animal treated with the test substance showed an inconclusive response. For this animal in question the skin of the challenge site showed thickening, dryness and sloughing of the epidermis at the 72 h reading which were assessed as signs of skin sensitization (delayed contract hypersensitivity). Taken all data together, 6/10 (60 %) animals showed a positive skin sensitization reaction and 4/10 (40 %) animals a clear negative skin sensitization response after challenging with 70 % of the test substance. After challenge with a concentration of 35 % in acetone a clear positive skin sensitization response was noted in 2/10 animals at the 24 h reading, 3/10 animals

at 48 h and 2/10 animals at 72 h. In addition an inconclusive response was seen in two further test substance treated animals at the reading after 72 h. The skin of the challenge application site showed the same findings, i.e. thickening, dryness and sloughing of the epidermis, which were noted in one animal after challenge with 70 % in acetone. Accordingly, these skin reactions were also assessed as signs of skin sensitization. Taken all measurement time points together, 6/10 (60 %) animals were found with positive reactions and 4/10 (40 %) animals showed a negative skin reaction at a challenge concentration of 35 %. In conclusion, the skin sensitization rate after intradermal induction with a concentration of 1.0 % phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide was 60 %.

Phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide is currently classified as skin sensitizer Category 1 and is listed in Annex VI of CLP as Skin Sens. 1, H317.

4.6.1.4 Comparison with criteria

Skin sensitisers shall be classified in Category 1 where data are not sufficient for sub-categorisation. Where data are sufficient a refined evaluation according to section 3.4.2.2.1.3 allows the allocation of skin sensitisers into sub-category 1A, strong sensitisers, or sub-category 1B for other skin sensitisers.

Hazard category and sub-categories for skin sensitisers:

'Category 1: Substances shall be classified as skin sensitisers (Category 1) where data are not sufficient for sub-categorisation in accordance with the following criteria:

(a) if there is evidence in humans that the substance can lead to sensitisation by skin contact in a substantial number of persons; or

(b) if there are positive results from an appropriate animal test (see specific criteria).'

Based on the available data, phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide is classified as skin sensitizer category 1 and is listed in Annex VI of CLP. The classification is based on positive results from two animal tests, GPMT according to OECD TG 406/EU B.6.

A substance should be classified as a skin sensitizer of high potency if a high potency observed in animal studies can be presumed to result in a significant skin sensitization hazard in humans. For the GPMT, criteria for inclusion in either sub-category 1A or 1B are based on the incidence and the concentration used for induction.

'Sub-category 1A: Substances showing a high frequency of occurrence in humans and/or a high potency in animals can be presumed to have the potential to produce significant sensitisation in humans. Severity of reaction may also be considered.'

'Sub-category 1B: Substances showing a low to moderate frequency of occurrence in humans and/or a low to moderate potency in animals can be presumed to have the potential to produce sensitisation in humans. Severity of reaction may also be considered.'

Comparing with criteria for hazard category and sub-categories for skin sensitizers according to CLP a substance shall be classified for:

Skin sensitisation: Animal test results for Sub-category 1A:

GPMT of ≥ 30 % responding at ≤ 0.1 % intradermal induction dose or

≥ 60 % responding at > 0.1 % to ≤ 1.0 % intradermal induction dose

The available results from animal testing with phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide are sufficient for a refined evaluation allowing the sub-categorisation.

In comparison to the given criteria for the hazard category and sub-categories for skin sensitisation according to CLP, phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide fulfils the criteria for classification in the hazard class as skin sensitizer sub-category 1A, H317, because the GPMT (adjuvant type test method) performed under normal light showed a skin sensitization rate of 90 % which is higher than 60 % at an intradermal induction concentration of 0.5 % in peanut oil (CIBA-GEIGY, 1996c) which is lower than 1.0 %.

The other study (Huntingdon Life Sciences Ltd., 1997) conducted under safelight resulted in a skin sensitization rate of 60 % with an intradermal induction concentration of 1.0 % in 5.0 % acetone in Alembicol D. The range of the latter study arises from the fact that five of ten animals showed a clear skin sensitization response after challenge with 70 % in acetone. One further animal gave an inconclusive response (seen as thickening, dryness and sloughing of the epidermis) and the remaining four animals gave negative responses. After challenge with 35 % in acetone 4/10 (40 %) animals were considered as positive and additionally two animals showed the same inconclusive skin reactions as observed after challenge with 70 % in acetone. As a worst case assumption, the skin reactions assessed as inconclusive results from both challenge concentrations (70 % and 35 %) are considered as positive skin sensitization responses which yields a worst-case sensitization rate of 60 %. Since the induction concentration of 1.0 % is in the range of 0.1-1.0 % and the worst-case sensitization rate of 60 % does comply with the limit value of 60 %, the results of the skin sensitization response from this study fall also under sub-category 1A.

Skin sensitisation: Animal test results for Sub-category 1B:

GPMT of ≥ 30 % to < 60 % responding at > 0.1 % to ≤ 1.0 % intradermal induction dose or

≥ 30 % responding at > 1.0 % intradermal induction dose.

Since the worst-case challenge response rates of both studies are equal or higher than 60 %, the criteria for CLP sub-category 1B of a response rate of < 60 % with intradermal induction concentrations of > 0.1 % and ≤ 1.0 % are not fulfilled.

In conclusion, the CLP criteria for Sub-category 1A are met and a classification of phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide as Skin Sens. 1A, H317 is warranted.

Consideration of setting a specific concentration limit (SCL):

According to section 3.4.2.2.5 (Guidance on the Application of the CLP Criteria) a SCL can be set based on potency of a certain substance in animal tests for extreme sensitisers. Based on Table 3.4.2-g of said guidance document (Potency on basis of the Guinea Pig Maximisation Test in the Guidance on the Application of the CLP Criteria) substances leading to ≥ 60 % incidence of sensitised guinea pigs at an intradermal induction concentration of > 0.1 % and ≤ 1.0 % (w/v) in a Guinea Pig Maximisation Test are considered to be sensitisers of strong potency. Thus phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide can be considered as a strong but not extreme sensitising substance.

For sensitizing substances with strong potency the general concentration limit (GCL) of 0.1 % w/v applies. Thus, for phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide the GCL of 0.1 % w/v is set and a SCL is not proposed.

4.6.1.5 Conclusions on classification and labelling

According to CLP criteria, phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide should be classified and labelled as Skin Sens. 1A, H317 (May cause an allergic skin reaction).

RAC evaluation of skin sensitisation

Summary of the Dossier Submitter's proposal

The Dossier Submitter (DS) proposed to classify phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide as a skin sensitiser in category 1A (Skin Sens. 1A; H317) based on results of two Guinea Pig Maximisation Tests (GPMT) performed according to OECD TG 406 and GLP.

The GPMT sensitisation study (CIBA-GEIGY 1996c) was performed under normal light condition as required by OECD TG 406. However, it was noted by the DS that phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide is a photoinitiator. Upon irradiation, the phosphorus - acyl carbon bond of the molecule is homolytically cleaved into radicals which initiate the polymerisation of monomeric or oligomeric polymer precursors for various applications.

The intradermal induction (CIBA-GEIGY 1996c) was performed using a 0.5% solution of phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide (purity > 95%) in peanut oil. The epidermal topical induction was performed with 50% using vaseline as vehicle. For the topical challenge application, a 10% formulation in vaseline was used. Eighteen out of 20 animals (90%) treated with the test substance showed a clear skin sensitisation response after challenge at the 24 h reading. At the 48 h reading there were still 16/20 animals with positive skin reactions corresponding to a sensitisation rate of 80%. In addition, scaling skin reactions were recorded for eight males and seven females at the 48 h reading. No skin reactions were recorded for control animals. No information was reported in the study protocol whether and to what extent the substance had undergone a light-induced degradation prior to or during application on skin. However, the treatment of the skin was performed with occlusive wrapping so at least partial light protection during treatment was provided. In conclusion, the maximal skin sensitisation rate after intradermal induction with a concentration of 0.5% phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide was 90%.

In the second study (Huntingdon Life Sciences Ltd., 1997), the test formulations were prepared under safelight and the formulation containers were wrapped in aluminium foil because solutions of the substance are sensitive to light of the UV-range and the near visible violet light range. Aluminium foil was also incorporated in the dressings to minimise photo-induced degradation of the test material. Compared to the GPMT study performed by CIBA-GEIGY (1996c) the higher concentrations for induction and challenge, different vehicles and another strain of guinea pig were used.

Phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide (purity of 98.4%) was used for intradermal induction as a 1.0% solution in 5.0% acetone in Alembicol D. 24 h before topical induction with 70% solution of phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide in acetone the skin area for topical application was pre-treated with 10% sodium lauryl sulfate (SLS) in petrolatum. The 70% solution of test substance was taken as non-irritating,

although the extent and results of skin irritation were not provided in the study description. Test substance concentrations of 70% and 35% in acetone were used for the challenge topical application using occlusive dressing for 48 h, instead of 24 h as required in technical guidance OECD TG 406. Readings were performed 24, 48 and 72 h after challenge.

Results: After 24 h of skin contact with a challenge concentration of 70% in acetone none of the test substance treated animals (0/10) showed positive reactions. Reading of the challenge reaction after 48 and 72 h revealed a clear positive skin sensitisation response in 5/10 (50%) animals. Additionally, one animal treated with the test substance showed an inconclusive response. For this animal, the skin of the challenge site showed thickening, dryness and sloughing of the epidermis at the 72 h reading, which were assessed as signs of skin sensitisation (delayed contract hypersensitivity). Taken all data together, 6/10 (60%) animals showed a positive skin sensitisation reaction and 4/10 (40%) animals showed a clear negative skin sensitisation response after challenging with 70% of the test substance. After challenge with a concentration of 35% in acetone a clear positive skin sensitisation response was noted in 2/10 animals at the 24 h reading, 3/10 animals at 48 h and 2/10 animals at 72 h. In addition, an inconclusive response was seen in two further treated animals at the reading after 72 h. The skin of the challenge application site showed the same findings, i.e. thickening, dryness and sloughing of the epidermis, which were noted in one animal after challenge with 70% in acetone. Accordingly, these skin reactions were also assessed as signs of skin sensitisation. Taken all measurement time points together, 6/10 (60%) animals were found with positive reactions. In conclusion, the skin sensitisation rate after intradermal induction with a concentration of 1.0% phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide was 60%.

Table 1: Individual animal results from study Huntingdon Life Sciences Ltd. (1997)

Animal No.	E (Erythema) O (Oedema)	70% challenge 24 h	70% challenge 48 h	70% challenge 72 h	35% challenge 24 h	35% challenge 48 h	35% challenge 72 h
1	E O	0 0	1 1	1 0	1 0	1 1	1 0
2	E O	0 0	0 0	0 0	1 0	0 0	0 0
3	E O	0 0	0 0	0 0	0 0	0 0	0 0
4	E O	0 0	1 1*	1 0	0 0	0 0	0 0
5	E O	0 0	0 0	0 0	0 0	0 0	0 0
6	E O	0 0	0 0	1* 0	0 0	1 1	1 1*
7	E O	0 0	1 0	1 0	0 0	1 1*	1* 0
8	E O	0 0	1 1	1 0	0 0	0 0	1* 0
9	E O	0 0	1 1*	1 1	0 0	0 0	1* 0

10	E O	0 0	0 0	0 0	0 0	0 0	0 0
no. of animals with positive reaction		0/10	5/10	6/10*	2/10	3/10	5/10*

*Dryness and sloughing of the epidermis or dryness and sloughing and thickening of the epidermis; interpreted as positive results according to Schlede and Eppler (1995).

The Generic Concentration Limit (GCL) for Skin Sens. 1A is 0.1% w/w. As the results of two GPMT tests (≥ 60% responding at intradermal induction concentrations > 0.1% to ≤ 1.0%) indicated a strong potency class according to criteria (section 3.4.2.2.5. of the Guidance on the Application of the CLP Criteria, Version 4.1 June 2015), no SCL was proposed by the DS.

Comments received during public consultation

Three Member State Competent Authorities (MSCA) commented during the public consultation. One of them supported the proposed classification (Skin Sens. 1A; H317), but two supported the current harmonised classification Skin Sens. 1; H317 without sub-categorisation.

As noted by one MSCA supporting sub-categorisation, it cannot be excluded that workers are exposed to the light-activated form of phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide, therefore the assessment of sensitising properties in the CIBA-GEIGY study (1996c) is appropriate. Therefore, the MSCA agreed with the proposal to sub-categorise phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide in category 1A.

Another MSCA questioned the validity and reliability of the study conducted under normal light conditions (CIBA-GEIGY, 1996) due to lack of information on the possible light-induced degradation of the substance.

Industry did not provide any comments.

Assessment and comparison with the classification criteria

Currently, phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide is classified as skin sensitiser category 1 and is listed in Annex VI to CLP. The results of two studies submitted by the DS demonstrate that it is a potent skin sensitizer.

Taking into account that in practise people might be exposed to phenyl bis(2,4,6-trimethylbenzoyl)-phosphine also under normal light conditions, RAC considers that the results of the study CIBA-GEIGY (1996c), performed under normal daylight and showing strong skin sensitising properties of the substance or its potential metabolites formed by daylight irradiation, should be considered for classification. In this study, phenyl bis(2,4,6-trimethylbenzoyl)-phosphine sensitised 90% of animals in the GPMT at intradermal induction concentration of 0.5% that meets the criteria of subcategory Skin Sens. 1A: ≥ 60% responding at > 0.1% to ≤ 1% intradermal induction dose. In principle the criteria for subcategory Skin Sens. 1A are also met in a second study (Huntingdon Life Sciences Ltd., 1997) (where the samples of the test substance were protected against daylight with aluminium foil), in which 60% of animals showed positive skin reaction in the GMPT after

intradermal induction with the test substance at a concentration of 1.0%. RAC considers that an atypical skin response under a form of thickening, dryness and sloughing of the epidermis at the 72 h in one guinea pig, not seen in any control animals challenged and assessed the same way, can be treated as a skin reaction due to skin sensitisation taking into account clear typical skin sensitisation responses in so many quinea pigs in two studies.

The available results from animal testing with phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide are considered sufficient for a refined evaluation allowing the sub-categorisation. Having in mind the results of both studies RAC is of the opinion that phenyl bis(2,4,6-trimethylbenzoyl)–phosphine warrants sub-categorisation of its sensitising properties to sub-category **Skin Sens. 1A with H317: May cause an allergic skin reaction**.

4.6.2 Respiratory sensitisation

Not evaluated in the scope of this dossier.

4.7 Repeated dose toxicity

Not evaluated in the scope of this dossier.

4.8 Specific target organ toxicity (CLP Regulation) – repeated exposure (STOT RE)

Not evaluated in the scope of this dossier.

4.9 Germ cell mutagenicity (Mutagenicity)

Not evaluated in the scope of this dossier.

4.10 Carcinogenicity

Not evaluated in the scope of this dossier.

4.11 Toxicity for reproduction

Not evaluated in the scope of this dossier.

4.12 Other effects

Not evaluated in the scope of this dossier.

5 ENVIRONMENTAL HAZARD ASSESSMENT

5.1 Degradation

Table 10: Summary of relevant information on degradation

Method	Results	Remarks	Reference
Test type: ready biodegradability activated sludge, domestic, non-adapted OECD Guideline 301 B (Ready Biodegradability: CO2 Evolution Test)	under test conditions no biodegradation observed % Degradation of test substance: 1 after 29 d (CO_2 evolution)	1 (reliable without restriction) key study experimental result **Test material (EC name): phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide**	CIBA-GEIGY (1997)
Test type: ready biodegradability mixture of sewage, soil and natural water OECD Guideline 301 C (Ready Biodegradability: Modified MITI Test (I))	under test conditions no biodegradation observed % Degradation of test substance: -2 after 28 d (O2 consumption) (Bottle No. 1) -2 after 28 d (O2 consumption) (Bottle No. 2) -3 after 28 d (O2 consumption) (Bottle No. 3) -1 after 28 d (Test mat. analysis) (Bottles No. 1, 2 and 3)	2 (reliable with restrictions) supporting study experimental result **Test material (EC name): phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide**	CIBA-GEIGY (1997a)

5.1.1 Stability

A hydrolysis study was technically not feasible due to the low water solubility of the compound. The compound is generally resistant to hydrolysis because it does not contain any labile functional groups.

5.1.2 Summary and discussion of degradation

A hydrolysis study was technically not feasible due to the low water solubility of the compound. The compound is generally resistant to hydrolysis because it does not contain any labile functional groups.

The biotic degradation was assessed in a guideline study conducted according to OECD guideline 301 B which determined the CO_2 evolution within a 28 day test period. Non-adapted bacteria collected from the activated sludge of the sewage treatment plant of Oakley, England were used as test system. The biodegradability of the test substance was determined by measurements of the CO_2 formation. Five test vessels (five-liter brown glass carboys) each containing mineral salts medium and the bacterial inoculum at a concentration of 1 % were used for the test. In each case the volume prepared was three liters. The test material was added as ultrasound-treated suspensions. The cumulative CO_2 production in the controls was within the acceptable range for this assay system. The degradation of the reference compound was rapid. These results confirm that the inoculum was viable and that the test was valid. Cumulative CO_2 production by the mixtures containing the test substance

at 10 mgC/L was negligible (1 % of the TCO_2, 106.4 mg CO_2). The substance is poorly biodegradable.

Additionally, a supporting study was conducted according to OECD guideline 301 C which determined the O_2 consumption and included specific test material analysis. The sludge was collected from different places in Japan, combined and cultivated for one month and then used for testing. The test substance was incubated with the sludge for 4 weeks at 25 ºC and the compound analyzed by HPLC. Furthermore, the oxygen consumption was measured and the biodegradability determined. According to O_2 consumption the degradation was -2 and -3 %, respectively. Test material analysis by HPLC revealed a degradation of -1 %. The supporting study clearly supports the results of the OECD 301 B study. The compound is not readily biodegradable.

5.2 Environmental distribution

Table 11: Summary of relevant information on the environmental distribution

Method	Results	Remarks	Reference
Study type: adsorption (soil) HPLC estimation method equivalent or similar to OECD Guideline 121 (Estimation of the Adsorption Coefficient (Koc) on Soil and on Sewage Sludge using High Performance Liquid Chromatography (HPLC))	Adsorption coefficient: log Koc: 3.85	1 (reliable without restriction) key study experimental result **Test material (EC name): phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide**	CIBA-GEIGY (1996b)
Calculation using SRC HENRYWIN v3.20	Henry's Law constant H: 0 Pa m³/mol at 25 °C	2 (reliable with restrictions) key study estimated by calculation **Test material (EC name): phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide**	BASF SE (2010)

5.2.1 Adsorption/Desorption

The adsorption/desorption potential of the substance was assessed in a study conducted according to OECD guideline 121. A suitable set of reference substances with adsorption coefficients (log Koc), which had been determined using the OECD guideline 106, and the test substance were chromatographed under standard chromatographic conditions and their retention times were determined. Using the retention times and the column dead time, which was determined by means of formamide, the corresponding capacity factors were calculated. The log k' of the reference substances and their log Koc-values were used to construct a calibration plot of log k' versus log Koc. The adsorption-coefficient (log Koc) of the test substance was calculated using the log k' of the test substance and the fitted regression line. The compound was determined to have a log Koc of 3.85. Therefore adsorption to the solid soil phase is expected.

5.2.2 Volatilisation

The Henry's Law Constant of the compound was estimated with HENRYWIN v3.20 which is integrated in the US EPA's EPISuite. HENRYWIN estimates the Henry's Law Constant of organic compounds at 25 ºC using the methodology originally described by Hine and Mookerjee (1975). The original methodology was updated and expanded at Syracuse Research Corporation as described in Meylan and Howard (1991). A subsequent update (HENRYWIN version 2) included additional fragment and correction factors. The current HENRYWIN program (version 3) extends the methodology to allow estimation of Henry's law constant over a temperature range (0 to 50ºC). In addition, version 3 includes an experimental Henry's law constant database of 1829 compounds. For the present compound the Henry's Law Constant was determined as 0 Pa m^3/mol. Due to this result, it is not expected that the compound will evaporate into the atmosphere from the water surface.

5.3 Aquatic Bioaccumulation

Table 12: Summary of relevant information on aquatic bioaccumulation

Method	Results	Remarks	Reference
Cyprinus carpio aqueous (freshwater) flow-through Total uptake duration: 4 wk Study Methods Concerning New Chemical Substances: The Test on the Degree of Bioconcentration in Fish and Shellfish (Kanpogyo No.5, Yakuhatsu No.615, 49-Kikyoku No.392, 1974) equivalent or similar to OECD Guideline 305 (Bioconcentration: Flow-through Fish Test)	BCF: < 5 Lipid content: 4 % (± 0.3 %)	2 (reliable with restrictions) key study experimental result **Test material (EC name): phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide**	CIBA-GEIGY (1997b) CIBA-GEIGY (1997c)

5.3.1 Aquatic bioaccumulation

In a Japanese study according to "Study Methods Concerning New Chemical Substances: The Test on the Degree of Bioconcentration in Fish and Shellfish (Kanpogyo No.5, Yakuhatsu No.615, 49-Kikyoku No.392, 1974)" equivalent to OECD Guideline 305 C the test fish (*Cyprinus carpio*) were continuously exposed to a concentration of 1 µg/L test material. The solubility of the test substance in water described in the same test protocol (Acute Toxicity Test in Ricefish) was 2 µg/L. The mean recovery rate of the test substance was 94.8 ± 0.2 %. The concentration of the test substance was maintained at a nominal concentration using a continuous flow through system. To prepare the final concentration a stock solution in hydrogenated castor oil (HCO-80) was prepared for further dilution. The mean bodyweight of the carps was 20.8 ± 1.2 g, and the mean length 9.0 ± 0.3 cm. The volume of the glass aquarium was 100 L and the flow rate amounted to 300 mL per minute. The pH value was 7.0 to 7.5, and the dissolved oxygen (DO) amounted to 7.0 to 7.4 ppm. 18 fishes belonged to the treated group (2 groups), and 6 fishes to the control group. The test temperature was 24.3 ± 0.5 °C. A group of 3 fishes were sampled using a hand net from the treated and the control groups. The fish was weighed and the entire body length was measured. Two fishes (in OECD 305: a minimum of four) were analyzed via HPLC for each group. The remaining one fish was frozen for storage. The analyses

of fish were performed on day 7, 14, 21, and 28 (OECD 305: at least five occasions during uptake phase and on at least four occasions during depuration phase of the substance). After an exposure period of 4 weeks a BCF below 5 was determined and it was concluded that the compound does not bioaccumulate in aquatic organisms.

5.3.2 Summary and discussion of aquatic bioaccumulation

According to the results of a Japanese bioaccumulation study the compound does not significantly accumulate in aquatic organisms. The BCF was well below the CLP criteria of 500.

5.4 Aquatic toxicity

Data on the acute aquatic toxicity are available for three trophic levels (fish, aquatic invertebrates and aquatic algae). Furthermore, data on the long-term toxicity towards *Daphnia magna* are available.

Neither the acute toxicity studies in fish, daphnids and algae (OECD 203, 202, 201) nor the chronic toxicity study in daphnids showed effects in the range of the water solubility of the compound. The acute studies were exclusively conducted with filtrations of supersaturated suspensions of the compound in test medium. Due to the very low water solubility the test solutions for the chronic study in daphnids were prepared with DMF whereupon the solubility was determined in advance to ensure that the study is conducted up to the solubility limit in the test medium. Furthermore, within the scope of the acute daphnid study the water solubility of the compound was determined in the test medium to be 0.8 µg/L (1.1 µg/L corrected for the recovery). This test medium was used in both the acute studies in fish and daphnids and in the chronic study in daphnids. Therefore, it can be clearly stated that these studies were conducted up to the saturation limit of the compound. In the algae study a different test medium was used but a supersaturated solution was prepared as well to ensure testing up to the solubility limit of the compound.

The substance did not have any acute effect on *Danio rerio* in the range of solubility in a study conducted according to OECD guideline 203. The LC_{50} was determined to be > 90 µg/L (measured). A second study investigating the acute toxicity to fish was conducted within the scope of the bioaccumulation study and was regarded as invalid. This study determined a 48 h LC_{50} of 84 µg/L which clearly exceeds the solubility of the compound in the test medium. The solubility in the test medium was additionally determined in the scope of the acute toxicity test to *Daphnia magna* (see Table 14). The acute toxicity towards *Daphnia magna* was investigated in a study according to OECD guideline 202. The EC_{50} was determined to be > 1175 µg/L. This result clearly exceeds the solubility of the compound in the test medium which was determined to be 0.8 µg/L (1.1 µg/L corrected for the recovery). The toxicity towards aquatic algae was investigated in a study conducted according to OECD guideline 201. No effects in the range of the water solubility could be detected. The EC_{50} was determined to be > 260 µg/L and the NOEC ≥ 260 µg/L.

Furthermore, a long-term study towards *Daphnia magna* according to OECD guideline 211 revealed a NOEC of ≥ 8.1 µg/L which clearly exceeds the solubility of the compound in the test medium.

Table 13: Summary of relevant information on aquatic toxicity

Method	Results	Remarks	Reference
OECD 203	LC_{50} (96 h) > 90 µg/L	Clearly exceeding the limit of water solubility in the test medium.	CIBA-GEIGY (1997d)
OECD 202	EC_{50} (48 h) > 1175 µg/L	Clearly exceeding the limit of water solubility in the test medium.	CIBA-GEIGY (1997e)
OECD 201	EC_{50} (72 h) > 260 µg/L NOEC (72 h) ≥ 260 µg/L	Clearly exceeding the limit of water solubility in the test medium.	CIBA-GEIGY (1997f)
OECD 211	NOEC (21 d) ≥ 8.1 µg/L	Clearly exceeding the limit of water solubility in the test medium.	CIBA-GEIGY (2003a,b)

Table 14: Further relevant information to assess the toxicity of the compound

Method	Results	Remarks	Reference
EU Method A.6	WS < 0.1 mg/L	Solubility measured in high-purity water.	CIBA-GEIGY (1996)
Within the scope of the acute daphnid study	0.8 µg/L (1.1 µg/L corrected for the recovery)	Actual water solubility measured in the test medium used for the acute studies in fish and daphnids and the long-term study in daphnids	CIBA-GEIGY (1997f)

5.4.1 Fish

5.4.1.1 Short-term toxicity to fish

In a GLP-guideline study (OECD 203) using *Danio rerio*, a LC_{50} > 90 µg/L based on measured test concentrations was detected (CIBA-GEIGY 1997). No acute toxicity could be recorded within the range of solubility in the test medium.

The test was conducted as semi-static test with a daily test medium renewal. Both the preparation of the stock solutions and the test media and the test itself were conducted under light protection due to the photosensitivity of the test compound. Due to the very low water solubility of the test substance a supersaturated stock suspension with a nominal concentration of 100 mg/L was continuously stirred at room temperature in the dark over 2 hours. This stock suspension was filtered. The undiluted filtrate with the maximum concentration of dissolved respectively very fine dispersed test substance was used as the highest test medium. Additionally, several dilutions of this filtrate and a control were tested in parallel. The concentrations found in the freshly prepared filtrate of the supersaturated sock suspension on sampling days 0 and 3 were 170, respectively 67 µg test substance/L. During a period of 24 hours the test substance concentration in the test medium decreased to a value of 29 µg/L. The water solubility of the test substance in the test medium was determined within the scope of the acute study on *Daphnia magna* (see below) which used exactly the same test medium as the fish study. The solubility of the compound in the medium was determined with 0.8 µg/L (1.1 µg/L corrected for the recovery). The 96 h fish NOEC was determined to be at least 90 µg test substance/L and the LC_{50} is clearly higher than 90 µg/L. This value could not be quantified because the test substance has no toxic effect up to the concentration of 90 µg/L and thus far above the solubility limit of the test substance in the used test water. Therefore, there is a high probability that the compound is not acutely harmful to fish.

A second study was conducted within the scope of the bioaccumulation study. *Oryzias latipes* were exposed to the test substance which was brought into solution with hydrogenated castor oil. The fish were exposed for 48 hours. The LC_{50} was determined to be 84 µg/L. Due to the limited exposure time and the use of the vehicle the study is regarded as invalid. Nevertheless, the LC_{50} value is above the water solubility.

Table 15: Overview of the valid short-term effects on fish

Method	Results	Remarks	Reference
Danio rerio (reported as Brachydanio rerio) freshwater semi-static OECD Guideline 203 (Fish, Acute Toxicity Test)freshwater static	LC_{50} (96 h): > 90 µg/L test mat. (meas. (arithm. mean)) based on: mortality	1 (reliable without restriction) key study experimental result **Test material (EC name): phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide**	CIBA-GEIGY (1997d)

5.4.1.2 Long-term toxicity to fish

No data available.

5.4.2 Aquatic invertebrates

5.4.2.1 Short-term toxicity to aquatic invertebrates

In a GLP-guideline study (OECD 202) using *Daphnia magna*, an EC_{50} > 1175 µg/L based on measured test concentrations was detected (CIBA-GEIGY 1997). No acute toxicity could be recorded within the range of solubility in the test medium.

The test was conducted as static test. Both the preparation of the stock solutions and the test media and the test itself were conducted under light protection due to the photosensitivity of the test compound. Due to the very low water solubility of the test substance a supersaturated stock suspension with a nominal concentration of 100 mg/L was continuously stirred at room temperature in the dark over 2 hours. The stock suspension was filtered just before the start of the test and the undiluted filtrate of the supersaturated stock suspension with the maximum concentration of dissolved respectively very fine dispersed test substance was used as the highest test concentration. Additionally, several dilutions and a control were tested in parallel. The mean measured test concentrations found in the undiluted filtrate of the supersaturated stock suspension and in the test dilutions up to the dilution 1:100 were determined to be 1175, respectively 99, 15, 4.4 and 3.1 µg/L. During the test period of 48 hours a decrease of test substance concentration in the test medium was determined. This decrease might be due to a precipitation of test substance due to the low water solubility. The water solubility of the compound in the test medium (which is identical to the test media in the acute fish and the chronic daphnid study) was determined to be 0.8 µg/L (1.1 µg/L corrected for the recovery). The 48h EC_{50} was higher than 1175 µg/L (undiluted filtrate) and the 48 h NOEC was 3.1 µg/L. All test substance concentrations showing an effect on the mobility of the

daphnids were clearly above the solubility limit of the test substance in the test medium. Therefore, there is a high probability that the compound is not acutely harmful to aquatic invertebrates.

Table 16: Overview of short-term effects on aquatic invertebrates

Method	Results	Remarks	Reference
Daphnia magna freshwater static OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test)	EC50 (48 h): > 1175 µg/L test mat. (meas. (arithm. mean)) based on: mobility	2 (reliable with restrictions) key study experimental result **Test material (EC name): phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide**	CIBA-GEIGY (1997e)

5.4.2.2 Long-term toxicity to aquatic invertebrates

In a GLP-guideline study (OECD 211) using *Daphnia magna*, a NOEC ≥ 8.1 µg/L based on mean measured concentrations was detected (CIBA-GEIGY 2003a, b). No toxic effects on the survival rates and reproduction rates of the daphnids up to the solubility limit of the test item in the test medium could be recorded.

The test was conducted as semi-static test with a total number of 8 test medium renewals. Both the preparation steps of the test media and the test itself were performed under reduced light conditions due to the photosensitivity of the test substance. For the determination of the solubility limit of the test item in test water six individual dispersion of the test item in test water were prepared at a concentration of 100 mg/L. This concentration is clearly above the water solubility limit of the test item. The dispersions were treated ultrasonically for 15 minutes and were stirred on a magnetic stirrer. After stirring for 48, 72, and 96 hours, two of the dispersions each were filtered. The actual concentrations of the test item in the test media were analytically determined. Due to the low solubility and the instability of the test item in test water, the solubility limit of the test item could not be quantified in the filtrates, however, all test item concentrations measured were below 5 µg/L. Additionally, the water solubility of the compound in the test medium was assessed within the scope of the acute study on daphnids. This study uses exactly the same test medium as the chronic study. Here a water solubility of the test compound of 0.8 µg/L (1.1 µg/L corrected for the recovery) was determined. Due to the low water solubility in the test medium the test item was dosed into test water by use of an organic solvent (N,N-dimethylformamide = DMF). The following concentrations were tested: 0.20, 0.63, 2.0, 6.3, and 20 µg/L. To prepare the different test solutions a concentrated stock solution of the test item in DMF with a concentration of nominal 400 mg/L was prepared. This stock solution was used as application solution for the preparation of the test medium with the highest test concentration. In a series of subsequent dilutions the stock solution was diluted with DMF to obtain the application solutions of the dosage of the test media with the lower test concentrations. Then, at each test medium preparation date the test media with the different test concentrations were prepared by mixing equal volumes of each of the application solutions into an equal volume of test water. These test media were intensively mixed for 5 minutes. In addition, a solvent control and a control with test medium were run in parallel. The measured test item concentrations in the analysed test medium of nominally 20 µg/L varied in the range of 68 to 79 % of the nominal value at the start of the test medium renewal periods. The variation could be due to inhomogeneous distribution of the

test item, since the concentration of nominally 20 µg/L was above the solubility limit of the test item in test water. The test substance concentration was below the limit of quantification of the analytical method at the end of the test medium renewal periods of 48 and 72 hours. In the control, the solvent control and at all test concentrations the survival rate of the test animals at the end of the test was at least 90 % or higher. Thus, the survival rate of *Daphnia magna* after 21 days was not reduced up to and including the highest test concentration of nominally 20 µg/L (8.1 µg/L mean measured). No significant toxic effect of the test item on the mean reproduction rate was determined up to and including the highest test concentration of 20 µg/L (8.1 µg/L mean measured). No visible abnormalities were observed at the test animals. Taking into account the survival rates and the reproduction rates of the test animals, the 21-day NOEC was at least 8.1 µg/L (mean measured). This value might even be higher but concentrations above 20 µg/L have not been tested, since this concentration is already clearly exceeding the water solubility limit of the compound in the test medium. In conclusion, based on long-term (chronic) toxicity study data, the compound is very likely not harmful to aquatic organisms.

Table 17: Long-term effects on aquatic invertebrates

Method	Results	Remarks	Reference
Daphnia magna freshwater semi-static OECD Guideline 211 (Daphnia magna Reproduction Test)	NOEC (21 d): >= 8.1 µg/L test mat. (meas. (arithm. mean)) based on: reproduction (revised data (amendment)) LOEC (21 d): >= 8.1 µg/L test mat. (meas. (arithm. mean)) based on: immobilisation (revised data (amendment))	1 (reliable without restriction) key study experimental result **Test material (EC name): phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide**	CIBA-GEIGY (2003a) CIBA-GEIGY (2003b)

5.4.3 Algae and aquatic plants

In a GLP-guideline study (OECD 201) using *Scenedesmus subspicatus*, an EC_{50} > 260 µg/L and a NOEC ≥ 260 µg/L based on measured test concentrations were detected (CIBA-GEIGY 1997). No inhibitory effect on the growth of *Scenedesmus subspicatus* could be detected within the range of solubility in the test medium.

The test was conducted as limit test. Due to the very low water solubility of the test substance, a supersaturated stock suspension of the test substance with a nominal concentration of 100 mg/L was continuously stirred at room temperature in the dark over 2 hours. Then, the stock suspension was filtered. Only the undiluted filtrate with the maximum concentration of dissolved respectively very fine dispersed test substance was used as the test medium. Additionally, a control was tested in parallel. Due to the photosensitivity of the test compound and the fact that an algae study cannot be performed under light protection, the test included two experimental parts. In the first part of the test the filtrate of the stock suspension was incubated before the start of the test for 24 hours and illuminated at about 9200 Lux as in the definitive test. Due to the photosensitivity of the compound the parent compound reacts to degradation products. This filtrate was used as one test concentration. In the second part of the test the filtrate of the stock suspension was freshly prepared just before the start of the test. The analytically determined test substance concentration in the freshly prepared test medium (the undiluted filtrate of the supersaturated stock suspension) amounted to 260 µg/L at the start of the test. In this test medium, incubated under the test conditions during the test period (but

without algae), the measured concentrations of the compound decreased continuously during the performance of the test to 12 µg/L at the end of the test. In the filtrate illuminated for 24 hours before the start of the test 18 µg/L parent compound were found. This decrease could be due to degradation of the compound as a consequence of the intense irradiation of the samples. Neither the parent compound nor its degradation products had any inhibitory effect on the growth of *Scenedesmus subspicatus* during the exposure period of 72 hours up to the concentration of 260 µg/L. Based on these results the compound is very likely neither acutely nor chronically harmful to aquatic algae.

Table 18: Effects on algae and aquatic plants

Method	Results	Remarks	Reference
Desmodesmus subspicatus (reported as Scenedesmus subspicatus) (algae) freshwater static OECD Guideline 201 (Alga, Growth Inhibition Test)	EC_{50} (72 h): > 260 µg/L test mat. (meas. (initial)) based on: growth rate EC_{50} (72 h): > 260 µg/L test mat. (meas. (initial)) based on: biomass NOEC (72 h): >= 260 µg/L test mat. (meas. (initial)) based on: Growth rate; biomass yield	1 (reliable without restriction) key study experimental result **Test material (EC name): phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide**	CIBA-GEIGY (1997f)

5.4.4 Other aquatic organisms (including sediment)

No data available.

5.5 Comparison with criteria for environmental hazards (sections 5.1 – 5.4)

Table 19: Comparison with criteria for environmental hazards

Endpoint	Criteria for environmental hazards	Phenyl bis(2,4,6-trimethylbenzoyl) -phosphine oxide	Conclusion
Rapid Degradation	Readily biodegradable in a 28-day test for ready biodegradability	1 % after 29 days (CO_2 evolution)	Not rapidly degradable
Bioaccumulation	BCF ≥ 500	BCF < 5	Not bioaccumulative
Aquatic Toxicity	Acute toxicity data: $LC_{50}/EC_{50}/ErC_{50}$ ≤ 1 mg/L Chronic toxicity data: NOEC ≤ 1 mg/L	<u>Fish:</u> LC_{50} (96 h) > 90 µg/L NOEC not available <u>Invertebrates:</u> EC_{50} (48 h) > 1175 µg/L NOEC (21 d) ≥ 8.1 µg/L <u>Algae:</u> ErC_{50} (72 h) > 260 µg/L NOEC (72 h) ≥ 260 µg/L	No acute and chronic toxic up to the water solubility

Criteria for the classification with "Aquatic Chronic 4"

- Poorly soluble substance for which no acute toxicity is recorded up to the water solubility

  AND

- which are not rapidly degradable

  AND

- have an experimentally determined BCF ≥ 500 (or, if absent, a Log Kow ≥ 4)

The compound has an experimentally derived BCF of < 5 which is evidence that the classification with Aquatic Chronic 4 is unnecessary.

5.6 Conclusions on classification and labelling for environmental hazards (sections 5.1 – 5.4)

The available data do not justify a classification with Aquatic Chronic 4. The substance has an experimentally derived BCF < 5. Therefore, the substance should not be classified for the environment.

RAC evaluation of aquatic hazards (acute and chronic)

Summary of the Dossier Submitter's proposal

Phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide is a photoinitiator and is currently listed in Annex VI to CLP with Aquatic Chronic 4 - H413 classification. The DS proposed to remove this aquatic hazard classification based on a bioaccumulation study in which the results show that the bioconcentration factor for this substance is less than 5. According to the DS, this test had previously been considered by the ECHA Member State Committee to be adequate for REACH purposes despite some methodological shortcomings. According to the DS, the substance is not rapidly degradable and there is no acute or chronic toxicity in the water solubility range.

<u>Degradation</u>

A hydrolysis study was not technically feasible due to the low water solubility of the substance. The substance does not contain any labile functional groups and it can be assumed to be resistant to hydrolysis.

No information is available on photolysis although the substance is mentioned to be photosensitive in relation to the aquatic toxicity studies.

There are two ready biodegradation studies available. The OECD TG 301B test (CO2 Evolution Test) showed 1% degradation after 29 days. The test material was added as ultrasound-treated suspensions. In the OECD TG 301C test (Modified MITI Test (I)), no biodegradation was observed after 28 days. The DS concluded that the substance is not readily biodegradable.

<u>Bioaccumulation</u>

The Log Pow of 5.8 at 22°C and pH of 8.3 would suggest that the substance has a high potential to bioaccumulate. In a non-GLP study equivalent to the OECD TG 305C Guideline, the test fish *Cyprinus carpio* were continuously exposed to a concentration of 1 µg/L test material. The solubility of the test substance in water was 2 µg/L. The mean recovery rate of the test substance was 94.8 ± 0.2%. The concentration of the test substance was maintained at a nominal test concentration using a continuous flow through system. To prepare the final concentration, a stock solution in hydrogenated castor oil (HCO-80) was prepared for further dilution. The mean bodyweight of the carp was 20.8 ± 1.2 g and the mean length 9.0 ± 0.3 cm. The volume of the glass aquarium was 100 L and the flow rate amounted to 300 mL per minute. The pH value was 7.0 to 7.5, and the dissolved oxygen amounted to 7.0 to 7.4. 18 fish belonged to a treated group (2 groups), and 6 fish to the control group. The test temperature was 24.3 ± 0.5°C. A group of 3 fish were sampled using a hand net from the treated and the control groups. The fish was weighed and the entire body length was measured. Two fish were analysed via HPLC for each group. The single remaining fish was frozen for storage. The analyses of fish were performed on day 7, 14, 21, and 28. After an exposure period of 4 weeks a BCF below 5 was determined and it was concluded that the compound has a low potential for bioaccumulation.

Aquatic toxicity

Data on acute aquatic toxicity are available for three trophic levels (fish, invertebrates and algae). Furthermore, data on long-term toxicity towards *Daphnia magna* and algae are available although long-term toxicity data for fish are not available. The water solubility of the substance is < 100 µg/L in the water solubility test (EU Method A.6). During the acute daphnia study, the water solubility is 0.8 µg/L (1.1 µg/L corrected for the recovery). The same test medium is used for acute studies in fish, daphnids and the long-term study on daphnids.

Table 2. Aquatic toxicity studies available for bis(2,4,6-trimethylbenzoyl)-phosphine oxide

Method	Species		Results	Remarks
OECD TG 203, GLP, semistatic, daily renewal	*Danio rerio*	light protection	96 h LC_{50} > 90 µg/L (mean measured)	No toxicity within the range of solubility (1.1 µg/L)
unknown guideline within the scope of the BCF test, static	*Oryzias latipes*	no light adjustment, hydrogenated castor oil used as dispersant and dichloromethane as solvent[1]	48 h, LC_{50} 84µg/L (measured)	Effect concentration clearly exceeds solubility
OECD TG 202, GLP, static	*Daphnia magna*	light protection	48 h EC_{50} > 1175 µg/L (mean measured)	No toxicity within the range of solubility (1.1 µg/L)

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OECD TG 201, GLP, static, limit test	*Scenedesmus subsbicatus*	test arrangement to take into account photodegradation	72 h EC_{50} > 260 µg/L NOEC ≥ 72h 260 µg/L (initial measured)	No toxicity within the range of solubility
OECD TG 211, GLP, semistatic	*Daphnia magna*	light protection, DMF solvent	21 d NOEC (reproduction): ≥ 8.1 µg/L (mean measured	No toxicity within the range of solubility (1.1 µg/L)

The acute toxicity test with *Danio rerio* was conducted as a semi-static test with a daily test medium renewal. Both the preparation of the stock solutions and the test media as well as the test itself were conducted under light protection conditions due to the photosensitivity of the test compound. Also, due to the very low water solubility of the test substance, a supersaturated stock suspension with a nominal concentration of 100 mg/L was stirred and filtered. The undiluted filtrate with the maximum concentration of dissolved respectively very fine dispersed test substance was used as the highest test medium. Additionally, several dilutions of this filtrate and a control were tested in parallel. The concentrations found in the freshly prepared filtrate of the supersaturated stock suspension on sampling days 0 and 3 was 170 and 67 µg test substance/L, respectively. During a period of 24 h the test substance concentration in the test medium decreased to a value of 29 µg/L. The water solubility of the test substance in the test medium namely 0.8 µg/L (1.1 µg/L corrected for the recovery) was determined in the acute *Daphnia magna* study, which used exactly the same test medium as the fish study. The 96 h fish NOEC was determined to be at least 90 µg test substance/L and the LC_{50} is clearly higher than 90 µg/L (arithmetic mean). This value could not be quantified because the test substance has no toxic effect up to the concentration of 90 µg/L and thus far above the solubility limit of the test substance in the test water used.

An additional fish study was conducted with *Oryzias latipes* being exposed to the test substance which was brought into solution with hydrogenated castor oil. The fish were exposed for 48 h. The LC_{50} was determined to be 84 µg/L. Due to the limited exposure time and the use of the vehicle, the study is regarded as invalid. Nevertheless, the LC_{50} value is above the water solubility.

In a study using *Daphnia magna*, no acute toxicity could be recorded within the range of solubility in the test medium. The test was conducted as a static test. Both the preparation of the stock solutions and the test media and the test itself were conducted under light protection. Due to the very low water solubility of the test substance, a supersaturated stock suspension with a nominal concentration of 100 mg/L was made and handled accordingly to the *Danio rerio* test above. The mean measured test concentrations found in the undiluted filtrate of the supersaturated stock suspension and in the test dilutions up to the dilution of 1:100 were determined to be 1175 µg/L and 99, 15, 4.4 and 3.1 µg/L, respectively. During the test period of 48 h, a decrease of test substance concentration in the test medium was determined. This decrease might be due to precipitation of the test substance resulting from the low water solubility. The water solubility of the compound in the test medium was determined to be 0.8 µg/L (1.1 µg/L corrected for the recovery). The 48h EC_{50} was higher than 1175 µg/L (arithmetic mean, undiluted filtrate) and the 48 h NOEC was 3.1 µg/L. All test substance concentrations showing an effect on the mobility of the daphnids were clearly above the solubility limit of the test substance in the test medium.

In a long-term study using *Daphnia magna*, no toxic effects on the survival rates and reproduction rates of the daphnids up to the solubility limit of the test item in the test medium were recorded. The test was conducted as semi-static test with a total number of 8 test medium renewals. Both the preparation steps of the test media and the test itself were performed under reduced light conditions. Due to the low solubility and the instability of the test item in water, the solubility limit of the test item could not be quantified in the filtrates, however, all test item concentrations measured were below 5 µg/L. The water solubility of the test compound of 0.8 µg/L (1.1 µg/L corrected for the recovery) was determined in the acute Daphnia study (same test medium). The test item was dosed into test water by use of an organic solvent (N,N-dimethylformamide = DMF). The following concentrations were tested: 0.20, 0.63, 2.0, 6.3, and 20 µg/L. A solvent control and a control with test medium were run in parallel. The measured test item concentrations in the analysed test medium of nominally 20 µg/L varied in the range of 68 to 79% of the nominal value at the start of the test medium renewal periods. The variation could be due to inhomogeneous distribution of the test item, since the nominal concentration of 20 µg/L was above the solubility limit of the test item in test water. The test substance concentration was below the limit of quantification of the analytical method at the end of the test medium renewal periods of 48 and 72 h. In the control, the solvent control, and at all test concentrations, the survival rate of the test animals at the end of the test was at least 90 % or higher. Thus, the survival rate of *Daphnia magna* after 21 days was not reduced up to and including the highest nominal test concentration of 20 µg/L (8.1 µg/L mean measured). No significant toxic effect of the test item on the mean reproduction rate was determined up to and including the highest test concentration of 20 µg/L (8.1 µg/L arithmetic mean measured). No visible abnormalities were observed in the test animals. Taking into account the survival rates and the reproduction rates of the test animals, the 21-day NOEC was at least 8.1 µg/L (arithmetic mean measured). This value might even be higher but concentrations above 20 µg/L have not been tested, since this concentration is already clearly exceeding the water solubility limit of the compound in the test medium.

In a study using *Scenedesmus subspicatus*, no inhibitory effect on the growth of *Scenedesmus subspicatus* could be detected within the range of solubility in the test medium. The test was conducted as a limit test. A supersaturated stock suspension of the test substance with a nominal concentration of 100 mg/L was continuously stirred at room temperature in the dark over 2 h. The stock suspension was filtered. Only the undiluted filtrate with the maximum concentration of dissolved respectively very fine dispersed test substance was used as the test medium. Additionally, a control was tested in parallel. Due to the photosensitivity of the test compound and the fact that an algae study cannot be performed under light protection, the test included two experimental parts. In the first part of the test, the filtrate of the stock suspension was incubated before the start of the test for 24 h and illuminated at about 9200 Lux as in the definitive test. Due to the photosensitivity of the compound the parent compound reacts to degradation products. This filtrate was used as one test concentration. In the second part of the test, the filtrate of the stock suspension was freshly prepared just before the start of the test. The analytically determined test substance concentration in the freshly prepared test medium (the undiluted filtrate of the supersaturated stock suspension) amounted to 260 µg/L at the start of the test. In this test medium, incubated under the test conditions during the test period (but without algae), the measured concentrations of the compound decreased continuously to 12 µg/L at the end of the test. In the filtrate illuminated for 24 h before

the start of the test, 18 µg/L parent compound were found. This decrease could be due to degradation of the compound as a consequence of the intense irradiation of the samples. Neither the parent compound nor its degradation products had any inhibitory effect on the growth of *Scenedesmus subspicatus* during the exposure period of 72 h up to the concentration of 260 µg/L.

Neither the acute toxicity studies in fish, daphnids and algae nor the chronic toxicity study in daphnids showed effects in the range of the water solubility of the compound. The acute studies were exclusively conducted with filtrates from supersaturated suspensions of the compound in the test medium. Due to the very low water solubility, the test solutions for the chronic study in daphnids were prepared with DMF whereupon the solubility was determined in advance to ensure that the study is conducted up to the solubility limit in the test medium. Furthermore, in the acute daphnia study, the water solubility of the compound was determined in the test medium to be 0.8 µg/L (1.1 µg/L corrected for the recovery). This test medium was used in both the acute studies in fish and daphnids and in the chronic study in daphnids. Therefore, it can be clearly stated that these studies were conducted up to the saturation limit of the compound. In the algae study, a different test medium was used but a supersaturated solution was prepared to ensure testing up to the solubility limit of the compound.

Comments received during public consultation

There were comments received from four MS and one Industry organisation concerning the environmental hazards during the public consultation (PC). Industry supported removing the Aquatic Chronic 4 - H413 classification. Two MS did not support the removal of classification. One MS felt that the available experimental bioaccumulation data is not adequate for declassification based on the study deficiencies (e.g. not according to GLP, non-standard guideline, only 1 test concentration, use of castor oil as vehicle and less fish than standard test guideline). They also noted that a chronic toxicity to fish study is not available and the most sensitive species is not known.

The other MS wanted more information on the BCF test. In their opinion, it was not clear if steady state was reached after 28 days. It was also unclear whether the concentrations were measured during the study. It was not clear whether the mean concentrations were high enough during the uptake phase. They also wondered about the use of castor oil. It was also recognised that a substance with low water solubility and high Log K_{OW} is difficult to assess.

One MS supported the removal of classification.

The DS referred to the Member State Committee (MSC) agreement on "*no need to request for repeating the bioaccumulation test in fish*". No long-term fish toxicity test was requested by the MSC. Regarding the BCF study, the DS explained that as no substance was analytically detectable, steady-state could not be reached. The mean recovery rate of 94.8% is in their view the recovery of the analytical method. They are not aware of any disadvantages of the castor oil as dispersant.

Assessment and comparison with the classification criteria

The substance is not rapidly degradable based on the results of two ready biodegradability tests (OECD TG 301B, OECD TG 301C) where 1% or 0% degradation was observed after 29 and 28 days, respectively.

The Log Pow of 5.8 would suggest that the substance has a high potential to bioaccumulate. The DS presented study results showing the BCF value below 5. The BCF study is from 1974 and it is not known which version of the OECD TG 305 Guideline is referred to when stating that the test is equivalent and similar to the OECD Guideline. The substance has a high solubility in lipids (13 900 mg/kg at 37°C). Despite the difference in temperatures used in the studies, if it is assumed that the water solubility is around 0.001 mg/L, the lipid-water partition coefficient is about 1.4×10^7, which implies a high capacity for transfer from the dissolved phase into fatty tissues. So, unless uptake is hindered (no evidence on this point is provided) or metabolism is rapid (which is not suggested by the degradation information), it seems possible for fish to accumulate significant amounts, especially over long time periods.
RAC is also of the opinion that the BCF study provided does not contain enough information to assess its reliability for classification purposes. Only two fish were analysed via HPLC for each group as opposed to four fish required in OECD TG 305 (1996). Also, the analyses of fish did not follow the guidelines; they were performed on day 7, 14, 21, and 28 even though the guideline requires at least five occasions during the uptake phase and at least four occasions during the depuration phase. There is no information available on the analytical detection limit of the test substance in either water or fish tissues. There is no information on the growth rate of the fish during the test period. Only one nominal concentration of 0.001 mg/L was tested. The measured values after week 1 and week 2 are 0.001 mg/L and after weeks 3 and 4 they are 0.00101 mg/L.[2] It is mentioned in relation to aquatic toxicity tests that the substance is photosensitive. The BCF study is presumably performed without light adjustment.

There are acute toxicity test results for all three trophic levels; two tests for fish, one for algae and one for Daphnia. There are long-term data available on algae and Daphnia. The substance is photosensitive. All toxicity tests were performed under light protection except for the one fish test in the bioaccumulation test. This study is, however, poorly described.

The algae test was performed in two phases. In part one of the test, filtrate of the stock suspension with dissolved and very finely dispersed test substance was incubated for 24 h with an illumination of about 9200 Lux to let the photoreaction happen (aged filtrate). This filtrate was used as one test concentration in the second part of the test along with the freshly prepared filtrate (fresh filtrate). The concentration of the test substance in fresh filtrate was 260 µg/L at the start of the test and 12 µg/L at the end of the test. In the aged filtrate only 18 µg/L of the parent compound was found. This decrease could be due to degradation of the compound as a consequence of the intense irradiation. No inhibitory effects on the growth of *Scenedesmus subsbicatus* were seen when using aged filtrate up to the concentration of 260 µg/L. Unfortunately there is no information available on the degradation products or the rate of the photoreaction in water. Consequently, there is no

[2] REACH Registration file

information on the toxicity of the substance to fish and Daphnia in the medium exposed to normal light conditions.

RAC is of the opinion that in the aquatic toxicity tests performed with fish, Daphnia and algae under light protection there is no toxicity within the range of solubility. This is also the case for algae in test medium exposed to light. Chronic test data for fish is lacking. The information on photodegradation should be available to reach a conclusion on the aquatic toxicity of the substance.

Comparison to the CLP criteria

According to Table 4.1.0 of the CLP Regulation, the criteria for Aquatic Chronic 4 are applicable, e.g. for substances that:

- are poorly soluble and no acute toxicity is recorded up to the water solubility and

- are not rapidly degradable and

- have an experimentally derived BCF ≥ 500 (or, if absent, a Log K_{ow} ≥ 4),

which will be classified in this category unless other scientific evidence exists showing classification to be unnecessary. Such evidence includes chronic toxicity NOECs > water solubility or > 1 mg/L, or other evidence of rapid degradation in the environment than the ones provided by any of the methods listed in section 4.1.2.9.5.

RAC agrees that phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide has no acute toxicity at concentrations up to the water solubility, when tested with light protection, to fish and Daphnia, and no acute toxicity to algae with or without light protection. No chronic toxicity is seen in Daphnia in the dark, and to algae with or without light protection. There is no information on chronic toxicity to fish. The substance is not rapidly degradable. RAC is of the opinion that the BCF study provided does not contain enough information to assess its reliability for classification purposes and the light conditions in the test are unknown. The Log Kow for the substance is 5.8 thus exceeding the classification criteria Log Kow ≥ 4.

Consequently, RAC does not support the DS proposal to remove the aquatic classification Aquatic Chronic 4 - H413.

6 OTHER INFORMATION

No applicable.

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8 ANNEXES

Not applicable.