

# **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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# Part A.

## 1 PROPOSAL FOR HARMONISED CLASSIFICATION AND LABELLING

### 1.1 Substance

Table 1: Substance identity

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

	<b>CLP Regulation</b>
<b>Current entry in Annex VI, CLP Regulation</b>	Skin Sens. 1 – H317 Aquatic Chronic 4 – H413
<b>Current proposal for consideration by RAC</b>	Skin Sens. 1A – H317  Removal of Aquatic Chronic 4 – H413
<b>Resulting harmonised classification (future entry in Annex VI, CLP Regulation)</b>	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 <sup>1)</sup>	Reason for no classification <sup>2)</sup>
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.

CLP Annex I ref	Hazard class	Proposed classification	Proposed SCLs and/or M-factors	Current classification <sup>1)</sup>	Reason for no classification <sup>2)</sup>
3.4.	Respiratory sensitisation				data lacking
3.4.	Skin sensitisation	Skin Sens. 1A, H317		Skin Sens. 1, H317	
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

<sup>1)</sup> Including specific concentration limits (SCLs) and M-factors

<sup>2)</sup> 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 29<sup>th</sup> 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-trimethylbenzoyl)-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  $\geq 60\%$  at  $> 0.1\%$  to  $\leq 1\%$  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  $\geq 500$  (or, if absent, a log Kow  $\geq 4$ )

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	1628-81-26-7	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 &amp; 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 29<sup>th</sup> 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

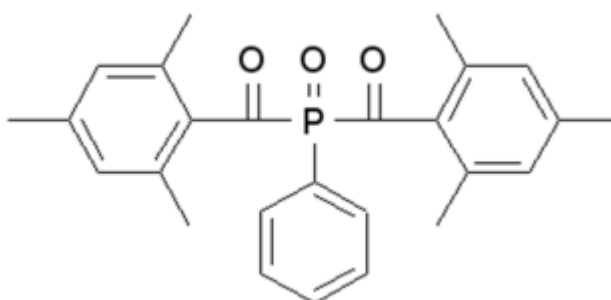
#### 1 IDENTITY OF THE SUBSTANCE

##### 1.1 Name and other identifiers of the substance

Table 7: Substance identity

<b>EC number:</b>	423-340-5
<b>EC name:</b>	Phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide
<b>CAS number:</b>	162881-26-7
<b>CAS name:</b>	Phosphine oxide, phenylbis(2,4,6-trimethylbenzoyl)-
<b>IUPAC name:</b>	phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide
<b>CLP Annex VI Index number:</b>	015-189-00-5
<b>Molecular formula:</b>	C <sub>26</sub> H <sub>27</sub> O <sub>3</sub> P
<b>Molecular weight:</b>	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/m <sup>3</sup> 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 sensitisation

##### 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
<b>Guinea pig maximisation test (GPMT)</b>  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	<b>Skin sensitising</b>  <b>Number with positive reactions after</b>  <b>Challenge with 10 % in vaseline:</b>  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)  Negative control: 24h/48h: 0/20 (m: 0/10,	1 (reliable without restriction)  key study  <b>Test material (EC name):</b> <b>phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide</b>	CIBA-GEIGY (1996c)

Method	Results	Remarks	Reference
<p>Challenge: 10 % in vaseline topical application</p> <p>Study was performed under normal light</p>	<p>f: 0/10)</p> <p><u>Reliability check (1995):</u></p> <p>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</p> <p>According to CLP phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide fulfils the criteria for classification as:</p> <p><b>Skin Sens.1A, H317: May cause an allergic skin reaction</b></p>	<p>Purity: &gt; 95 %</p>	
<p><b>Guinea pig maximisation test (GPMT)</b></p> <p>According to OECD TG 406 (Skin Sensitisation, 1992)/EU B.6, GLP-compliant</p> <p>guinea pig (Dunkin-Hartley) male; TG: 10; Negative control: 5</p> <p>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)</p> <p>Challenge: 70 % and 35 % in acetone topical application</p> <p>Test formulations were prepared under safelight; formulation containers wrapped in aluminium foil; aluminium foil was incorporated in the dressings</p>	<p><b>Skin sensitising</b></p> <p><b>Number with positive reactions after</b></p> <p><b>Challenge with 70 % in acetone:</b></p> <p>TG: 24h: 0/10 (0 %); 48h: 5/10 (50 %); 72h: 5/10 (50 %); additionally 1/10 assessed as positive (60 %)</p> <p>Conclusion (24h &amp; 48h &amp; 72h): <b>5+1/10 (60 %)</b></p> <p><b>Challenge with 35 % in acetone:</b></p> <p>TG: 24h: 2/10; 48h: 3/10; 72h: 2/10; additionally 2/10 assessed as positive</p> <p>Conclusion (24h &amp; 48h &amp; 72h): <b>4+2/10 (60 %)</b></p> <p>Negative Control: 24h/48h: 0/5</p> <p><u>Reliability check (1996):</u></p> <p>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 %)</p> <p>According to CLP phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide fulfils the criteria for classification as:</p> <p><b>Skin Sens.1A, H317: May cause an allergic skin reaction</b></p>	<p>1 (reliable without restriction)</p> <p>key study</p> <p><b>Test material (EC name): phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide</b></p> <p>Purity: 98.4 %</p>	<p>Huntingdon Life Sciences Ltd. (1997)</p>

#### 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 contact 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 sensitizers 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 sensitizers into sub-category 1A, strong sensitizers, or sub-category 1B for other skin sensitizers.

Hazard category and sub-categories for skin sensitizers:

*'Category 1:* Substances shall be classified as skin sensitizers (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  $\geq 30\%$  responding at  $\leq 0.1\%$  intradermal induction dose or  
 $\geq 60\%$  responding at  $> 0.1\%$  to  $\leq 1.0\%$  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  $\geq 30\%$  to  $< 60\%$  responding at  $> 0.1\%$  to  $\leq 1.0\%$  intradermal induction dose or  
 $\geq 30\%$  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  $\leq 1.0\%$  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 sensitizers. 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  $\geq 60\%$  incidence of sensitised guinea pigs at an intradermal induction concentration of  $> 0.1\%$  and  $\leq 1.0\%$  (w/v) in a Guinea Pig Maximisation Test are considered to be sensitizers 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).

#### **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 (CO2 evolution)	1 (reliable without restriction)  key study  experimental result  <b>Test material (EC name): phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide</b>	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  <b>Test material (EC name): phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide</b>	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<sub>2</sub> 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<sub>2</sub> 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<sub>2</sub> 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<sub>2</sub> production by the mixtures containing the test substance at 10 mgC/L was negligible (1 % of the TCO<sub>2</sub>, 106.4 mg CO<sub>2</sub>). The substance is poorly biodegradable.

Additionally, a supporting study was conducted according to OECD guideline 301 C which determined the O<sub>2</sub> 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 °C and the compound analyzed by HPLC. Furthermore, the oxygen consumption was measured and the biodegradability determined. According to O<sub>2</sub> 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  <b>Test material (EC name): phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide</b>	CIBA-GEIGY (1996b)
Calculation using SRC HENRYWIN v3.20	Henry's Law constant H:  0 Pa m <sup>3</sup> /mol at 25 °C	2 (reliable with restrictions)  key study  estimated by calculation  <b>Test material (EC name): phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide</b>	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 K<sub>oc</sub> 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 °C 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 50°C). 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<sup>3</sup>/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
<i>Cyprinus carpio</i> 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  <b>Test material (EC name): phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide</b>	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  $24.3 \pm 0.5$  °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  $NOEC \geq 260$  µg/L.

Furthermore, a long-term study towards *Daphnia magna* according to OECD guideline 211 revealed a  $NOEC$  of  $\geq 8.1$  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 <sub>50</sub> (96 h) > 90 µg/L	Clearly exceeding the limit of water solubility in the test medium.	CIBA-GEIGY (1997d)
OECD 202	EC <sub>50</sub> (48 h) > 1175 µg/L	Clearly exceeding the limit of water solubility in the test medium.	CIBA-GEIGY (1997e)
OECD 201	EC <sub>50</sub> (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<sub>50</sub> > 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 stock 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<sub>50</sub> 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<sub>50</sub> 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<sub>50</sub> value is above the water solubility.

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

Method	Results	Remarks	Reference
<i>Danio rerio</i> (reported as <i>Brachydanio rerio</i> ) freshwater semi-static OECD Guideline 203 (Fish, Acute Toxicity Test) freshwater static	LC <sub>50</sub> (96 h): > 90 µg/L test mat. (meas. (arithm. mean)) based on: mortality	1 (reliable without restriction) key study experimental result <b>Test material (EC name): phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide</b>	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<sub>50</sub> > 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<sub>50</sub> 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
<i>Daphnia magna</i> 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  <b>Test material (EC name): phenyl bis(2,4,6- trimethylbenzoyl)- phosphine oxide</b>	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  $\geq$  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
<i>Daphnia magna</i> freshwater semi-static OECD Guideline 211 ( <i>Daphnia magna</i> Reproduction Test)	NOEC (21 d): $\geq 8.1$ µg/L test mat. (meas. (arithm. mean)) based on: reproduction (revised data (amendment))  LOEC (21 d): $\geq 8.1$ µg/L test mat. (meas. (arithm. mean)) based on: immobilisation (revised data (amendment))	1 (reliable without restriction)  key study  experimental result  <b>Test material (EC name): phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide</b>	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  $NOEC \geq 260$  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
<i>Desmodesmus subspicatus</i> (reported as <i>Scenedesmus subspicatus</i> ) (algae) freshwater static OECD Guideline 201 (Alga, Growth Inhibition Test)	EC <sub>50</sub> (72 h): > 260 µg/L test mat. (meas. (initial)) based on: growth rate  EC <sub>50</sub> (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  <b>Test material (EC name): phenyl bis(2,4,6-trimethylbenzoyl)-phosphine oxide</b>	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 <sub>2</sub> evolution)	Not rapidly degradable
Bioaccumulation	BCF ≥ 500	BCF < 5	Not bioaccumulative
Aquatic Toxicity	Acute toxicity data: LC <sub>50</sub> /EC <sub>50</sub> /ErC <sub>50</sub> ≤ 1 mg/L Chronic toxicity data: NOEC ≤ 1 mg/L	<u>Fish:</u> LC <sub>50</sub> (96 h) > 90 µg/L NOEC not available <u>Invertebrates:</u> EC <sub>50</sub> (48 h) > 1175 µg/L NOEC (21 d) ≥ 8.1 µg/L <u>Algae:</u> ErC <sub>50</sub> (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  $\geq 500$  (or, if absent, a Log Kow  $\geq 4$ )

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.

## 6 OTHER INFORMATION

No applicable.

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## **8 ANNEXES**

Not applicable.