CLH report

Proposal for Harmonised Classification and Labelling

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

Substance Name: (1-methylethylidene)di-4,1-phenylene tetraphenyl diphosphate; aka Bisphenol A Diphosphate; aka Bisphenol A Polyphosphate

EC Number: 425-220-8

CAS Number: 5945-33-5

Index Number: 015-188-00-X

Contact details for dossier submitter: UK CA (HSE)
Dossier prepared by: Chemtura Corporation in accordance with Article 37(6) of CLP.

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Part A.

1 PROPOSAL FOR HARMONISED CLASSIFICATION AND LABELLING

1.1 Substance

Table 1: Substance identity

Substance name:	**(1-methylethylidene)di-4,1-phenylene tetraphenyl diphosphate; BDP;BAPP**
EC number:	**425-220-8**
CAS number:	**5945-33-5**
Annex VI Index number:	**015-188-00-X**
Degree of purity:	**>80%**
Impurities:	**The impurities are claimed as confidential and further information can be found in the IUCLID technical dossier. The confidential information on does not effect the classification proposal.**

1.2 Harmonised classification and labelling proposal

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

	CLP Regulation	**Directive 67/548/EEC (Dangerous Substances Directive; DSD)**
Current entry in Annex VI, CLP Regulation	Hazard class: Aquatic Chronic 4 Hazard statement code: H413	R53: May cause long-term adverse effects in the aquatic environment
Current proposal for consideration by RAC	Removal of Aquatic Chronic 4 classification.	Removal of R53 classification.

Resulting harmonised classification (future entry in Annex VI, CLP Regulation)		

1.3 Proposed harmonised classification and labelling based on CLP Regulation and/or DSD criteria

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				
2.2.	Flammable gases				
2.3.	Flammable aerosols				
2.4.	Oxidising gases				
2.5.	Gases under pressure				
2.6.	Flammable liquids				
2.7.	Flammable solids				
2.8.	Self-reactive substances and mixtures				
2.9.	Pyrophoric liquids				
2.10.	Pyrophoric solids				
2.11.	Self-heating substances and mixtures				
2.12.	Substances and mixtures which in contact with water emit flammable gases				
2.13.	Oxidising liquids				
2.14.	Oxidising solids				
2.15.	Organic peroxides				
2.16.	Substance and mixtures corrosive to metals				
3.1.	Acute toxicity - oral				
	Acute toxicity - dermal				
	Acute toxicity - inhalation				
3.2.	Skin corrosion / irritation				
3.3.	Serious eye damage / eye irritation				
3.4.	Respiratory sensitisation				
3.4.	Skin sensitisation				
3.5.	Germ cell mutagenicity				
3.6.	Carcinogenicity				
3.7.	Reproductive toxicity				
3.8.	Specific target organ toxicity –single exposure				
3.9.	Specific target organ toxicity – repeated exposure				
3.10.	Aspiration hazard				

4.1.	Hazardous to the aquatic environment	Not classified	-	Aq. Chronic 4	Conclusive but not sufficient for classification
5.1.	Hazardous to the ozone layer				

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

Labelling: Signal word: Not applicable
Hazard statements: Not applicable
Precautionary statements: Not applicable

Proposed notes assigned to an entry:

Table 4: Proposed classification according to DSD

Hazardous property	Proposed classification	Proposed SCLs	Current classification [1)]	Reason for no classification [2)]
Explosiveness				
Oxidising properties				
Flammability				
Other physico-chemical properties *[Add rows when relevant]*				
Thermal stability				
Acute toxicity				
Acute toxicity – irreversible damage after single exposure				
Repeated dose toxicity				
Irritation / Corrosion				
Sensitisation				
Carcinogenicity				
Mutagenicity – Genetic toxicity				
Toxicity to reproduction – fertility				
Toxicity to reproduction – development				
Toxicity to reproduction – breastfed babies. Effects on or via lactation				
Environment	Not classified	-	R53	Conclusive but not sufficient for classification

[1)] Including SCLs
[2)] Data lacking, inconclusive, or conclusive but not sufficient for classification

Labelling: Indication of danger: Not applicable
R-phrases: Not applicable
S-phrases: Not applicable

2 BACKGROUND TO THE CLH PROPOSAL

2.1 History of the previous classification and labelling

The substance (1-methylethylidene)di-4,1-phenylene tetraphenyl diphosphate (bisphenol A diphosphate) (EC. No 425-220-8) is currently classified and labelled as R53 (Annex VI, Table 3.2 in the CLP regulation) and Aquatic Chronic 4 (Annex VI, Table 3.1 in the CLP regulation).

Based on the properties of the substance and the study data available on the substance a CLH proposal has been made for the removal of the R53 (Aquatic Chronic 4) classification.

This substance has previously been notified under the NONS scheme (Dir. 67/548/EEC) by a number of different registrants, some of whom have shared study data relating to the classification previously.

The classification of the substance has been reviewed by Member State Competent Authorities (UK and NL) under NONS. Additional study information has been provided to update registrations and agreements reached that the removal of the R53 (Aquatic Chronic 4) classification is valid.

For example, Great Lakes Chemical Corporation, the predecessor company to Chemtura had notified Reofos BAPP to the UK in 1998 (Notification Number 98-06-1163). On the basis of bioaccumulation data on an analogous product (AFR-1) provided to the UK in the course of their assessment of the substance, the UK sent a communication in 1999 indicating that they agreed with the removal of the R53 classification from the product (called CN-1985) at the time. This communication also states that a bioaccumulation study on CN-1985 (Noguchi S (1999)) was to be submitted and if the study indicated R53 should apply then the UK CA would revert their decision to remove R53. This study was subsequently submitted and the decision to remove the R53 was allowed to stand by the UK CA. This study has been evaluated as the key bioaccumulation study in this dossier.

More recently the Dutch CA (RIVM) has agreed that the R53 classification is not required (for Israel Chemicals Ltd-Industrial products (ICL-IP) notification based on the data available, such as results from further Daphnia Reproduction studies (Desjardin, D. et al (2002b)).

All the relevant study data for the removal of R53 (Aquatic Chronic 4) classification is evaluated in this dossier and a formal proposal to remove the classification put forward.

In addition, as stipulated in Part 2 of Annex VI to the CLP regulation, submitted REACH registration dossiers on this substance (dossiers registered for EC No. 425-220-8) were evaluated and taken into consideration in the preparation of this proposal.

Four records for EC No. 425-220-8 are publically available on the ECHA website. These dossiers were evaluated to ensure the data provided in this proposal is consistent with other submitted data for this substance.

The data in the available registration dossiers is consistent with the information supplied in this report for substance identity, current harmonised classification and key study data.

The substance identity information is consistent with this report. All the dossiers are submitted for EC No. 425-220-8, two of the dossiers indicate the same IUPAC name as in this report (with the other two having slight variations) and the molecular formula and molecular weight given in the dossiers are consistent with those given in this report for the substance.

The classifications in the available registration dossiers are also consistent with this proposal. Three dossiers classify the substance according to the current harmonised classification (Aquatic chronic 4 / R53). One dossier states no classification, based on similar arguments and data as provided in this proposal, and references correspondence from RIVM to support this classification.

The study data in the available registration dossiers are also consistent to the key study data provided in this proposal. The water solubility and partition coefficient results are in line with those presented in this proposal. The results from the ecotoxicological studies (acute fish, Daphnia, algae) are consistent with the acute results in this proposal i.e. no toxicity at the limit of solubility. The available chronic results (in Daphnia) in the available registration dossiers are also consistent with those in this proposal.

Therefore, it is considered that the relevant information in the available REACH registration dossiers on this substance are consistent with the information in this proposal and are also in line with the proposal for the removal of the current classification.

2.2 Short summary of the scientific justification for the CLH proposal

This proposal has been prepared by Chemtura Corporation in accordance with Article 37(6) of CLP, and submitted by the UKCA.

The justification for the CLH proposal to remove the environmental classification of R53 (under DSD) and Chronic Category 4 (under CLP) is based upon relevant bioaccumulation study data (Noguchi S (1999) and Hori K (1996)), chronic toxicity in fish (Knight B (2003)) and Daphnia (Hargreaves TL & Clayton MA (2003) and Desjardin, D. et al (2002 a/b)) study data on the substance.

The experimental results show the BCF values are below the qualifying criteria for BCFs (>100 for DSD and >500 for CLP) and therefore that the substance does not show the potential to bioaccumulate in the aquatic environment. One result of <159 is not relevant to classification as 159 was the limit of detection in the study.

A chronic fish study (Early-Life Stage Test) and three chronic daphnia studies (Daphnia Reproduction studies) showed an absence of chronic toxicity effects at the solubility limits determined in the studies.

For full details on the justification for the removal of the classification please see the results section of this dossier and Section 5.6: Conclusions on classification and labelling for environmental hazards.

2.3 Current harmonised classification and labelling

2.3.1 Current classification and labelling in Annex VI, Table 3.1 in the CLP Regulation

Hazard Class and Category Code: Aquatic Chronic 4

Hazard Statement Code: H413

2.3.2 Current classification and labelling in Annex VI, Table 3.2 in the CLP Regulation

Classification: R53

Risk phrase: R53

Safety phrase: S61

2.4 Current self-classification and labelling

2.4.1 Current self-classification and labelling based on the CLP Regulation criteria

The harmonised classification is applied. However Chemtura and ICL-IP, consider that the substance should not be classified.

2.4.2 Current self-classification and labelling based on DSD criteria

The harmonised classification is applied. However Chemtura and ICL-IP, consider that the substance should not be classified.

3 JUSTIFICATION THAT ACTION IS NEEDED AT COMMUNITY LEVEL

There are data to indicate that the existing classification in Annex VI of CLP (i.e. R53 or Aquatic Chronic 4) is incorrect. As there are a number of suppliers of this substance in the EU, action is required at the Community level to amend the harmonised classification to ensure accurate communication of the (non) hazardous properties of the substance and therefore ensure adequate risk management throughout the Community. Failure to amend the classification could impact on the use of this substance in certain applications within the EU. A number of Member State Competent Authorities (Dutch CA and UK CA) have reviewed data on this substance and agreed in principle to the removal of the R53 (Aquatic Chronic 4) classification.

This proposal has been prepared by Chemtura Corporation in accordance with Article 37(6) of CLP, and submitted by the UKCA.

Part B.

SCIENTIFIC EVALUATION OF THE DATA

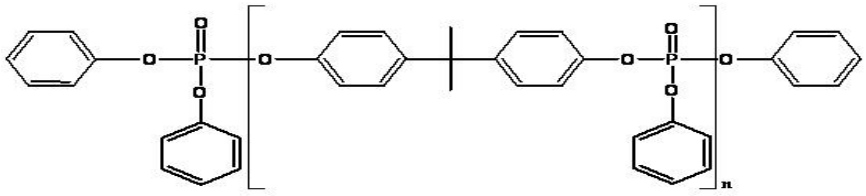
1 IDENTITY OF THE SUBSTANCE

1.1 Name and other identifiers of the substance

Table 5: Substance identity

EC number:	425-220-8
EC name:	(1-methylethylidene)di-4,1-phenylenetetraphenyl diphosphate.
CAS number (EC inventory):	
CAS number:	5945-33-5
CAS name:	Phosphoric acid, P,P'-[(1-methylethylidene)di-4,1-phenylene] P,P,P',P'-tetraphenyl ester
IUPAC name:	(1-methylethylidene)di-4,1-phenylenetetraphenyl diphosphate.
CLP Annex VI Index number:	015-188-00-X
Molecular formula:	C39 H34 O8 P2
Molecular weight range:	692

Structural formula:



where n~1

1.2 Composition of the substance

Table 6: Constituents (non-confidential information)

Constituent	Typical concentration	Concentration range	Remarks
(1-methylethylidene)di-4,1-phenylene tetraphenyl diphosphate	>80%	Confidential	Concentration range is claimed as confidential and is not provided in this public document. The value is provided in the accompanying IUCLID dossier. The confidential information does not effect the classification proposal.

Current Annex VI entry:

DSD: R53

CLP: Aquatic Chronic 4

Table 7: Impurities (non-confidential information)

Impurity	Typical concentration	Concentration range	Remarks
Confidential			

Current Annex VI entry: None.

The impurities are confidential and further information can be found in the technical dossier. These impurities have been taken into account in the proposal and are not considered to be of additional concern.

Table 8: Additives (non-confidential information)

Additive	Function	Typical concentration	Concentration range	Remarks
None				

Current Annex VI entry: Not applicable.

1.2.1 Composition of test material

The purity of the substance used in the physico-chemical and eco-toxicological studies relevant to this proposal, are as follows:

Water solubility:

Study reference: Sydney P (1998); CN-1985 Physico-Chemical Properties

Purity: 98.5%

Study reference: Hogg, AS & Bartlett, AJ (1997); Determination of general physico-chemical properties

Purity: Not stated in test report.

Partition coefficient n-octanol/water:

Study reference: Sydney P (1998); CN-1985 Physico-Chemical Properties

Purity: 98.5%

Study reference: Kenneth W (2002); Determination of the n-Octanol/Water partition coefficient of Fyroflex BDP by the shake flask method.

Purity: Not stated in test report.

Hydrolysis:

Study reference: Hogg, AS & Bartlett, AJ (1997); Determination of general physico-chemical properties

Purity: Not stated in test report.

Biodegradation:

Study reference: Tsujimura (1998); Biodegradation test of CN-1985 by microorganisms

Purity: 97.4%

Study reference: Mitsubishi-kasei Institute (1994); Ready biodegradation test.

Purity: 95.8%

Bioaccumulation:

Study reference: Noguchi S (1999); Bioaccumulation of CN-1985 in carp

Purity: 97.4%

Study reference: Hori K (1996); Bioaccumulation test of AFR-1 in carp

Purity: 95.0%

Short-term toxicity to fish:

Study reference: Jenkins CA (1998a); CN-1985: ACUTE TOXICITY TO RAINBOW TROUT (Oncorhynchus mykiss)

Purity: 98.5%

Long-term toxicity to fish:

Study reference: Knight B (2003); DVP 506 Fathead Minnow, Early-Life Stage Test (Continuous Flow).

Purity: >95%

Short-term toxicity to aquatic invertebrates:

Study reference: Jenkins CA (1998b); CN-1985: ACUTE TOXICITY TO DAPNIA MAGNA

Purity: 98.5%

Long-term toxicity to aquatic invertebrates:

Study reference: Hargreaves TL & Clayton MA (2003); DVP 506 Daphnia Reproduction Test

Purity: Not stated in test report

Study reference: Desjardin, D. et al (2002a) ; A life cycle test with the cladoceran (Daphnia magna).

Purity: Not stated in test report

Study reference: Desjardin, D. et al (2002b); A flow through life cycle test with the cladoceran (Daphnia magna)

Purity: Not stated in test report.

Algae and aquatic plants:

Study reference: Jenkins C (1998); CN-1985: ALGAL GROWTH INHIBITION

Purity: 98.5%

1.3 Physico-chemical properties

Table 9: Summary of physico - chemical properties

Property	Value	Reference	Comment (e.g. measured or estimated)
State of the substance at 20°C and 101,3 kPa	Liquid.	Observed from all referenced studies.	Observation Not evaluated further for the purposes of this dossier.
Melting/freezing point	Pour point: 7°C	Sydney P (1998)	Measured (EEC method No A1, OECD guideline No 102) Not evaluated further for the purposes of this dossier. Purity of test substance: 98.5%
Boiling point	Not determined – decomposes above 350°C without boiling	Sydney P (1998)	Measured (EEC method No A2, OECD guideline No 103) Not evaluated further for the purposes of this dossier. Purity of test substance: 98.5%
Relative density	1.26	Sydney P (1998)	Measured (EEC method No A3, OECD guideline No 109) Not evaluated further for the purposes of this dossier. Purity of test substance: 98.5%
Vapour pressure	1.3×10^{-12} Pa at 25°C	Sydney P (1998)	Measured (EEC method No A4, OECD guideline No 104) Not evaluated further for the purposes of this dossier. Purity of test substance: 98.5%
Surface tension	71.0 mN/m (90% saturated aqueous solution) at 21°C	Sydney P (1998)	Measured (EEC method No A5, OECD guideline No 115) Not evaluated further for the purposes of this dossier. Purity of test substance: 98.5%
Water solubility	i) 1.88 mg/L (at 20°C, pH 7.13 – 7.61); ii) 0.415 mg/L (at 20°C, pH 5.5 – 6.1)	i) Sydney P (1998); ii) Hogg, AS & Bartlett, AJ (1997)	Measured values for substance from two different suppliers. EEC method No A6 (Flask), OECD guideline No 105

			i) Purity of test substance: 98.5%
Partition coefficient n-octanol/water	i) Log_{10} Pow >4.9 (at 20°C, pH 7.29 – 7.37) ; ii) Log_{10} Pow 4.5 (at 25°C, pH 5.65)	i) Sydney P (1998) ; ii) Kenneth W (2002)	Measured value for substance from two different suppliers. EEC method No A8 (Shake Flask), OECD guideline No 107 i) Purity of test substance: 98.5%
Flash point	281°C	Sydney P (1998)	Measured (EEC method No A9) Not evaluated further for the purposes of this dossier. Purity of test substance: 98.5%
Flammability	Non-flammable	Sydney P (1998)	(EEC method No A12/13) Not evaluated further for the purposes of this dossier. Purity of test substance: 98.5%
Explosive properties	Not explosive	Sydney P (1998)	Measured (EEC method No A14) Not evaluated further for the purposes of this dossier. Purity of test substance: 98.5%
Self-ignition temperature	None below 400°C	Sydney P (1998)	Measured (EEC method No A15) Not evaluated further for the purposes of this dossier. Purity of test substance: 98.5%
Oxidising properties	Non-oxidising.		Observation due to experience in handling and use. Not evaluated further for the purposes of this dossier.
Granulometry	Not applicable.		Not evaluated for the purposes of this dossier.
Stability in organic solvents and identity of relevant degradation products	No data available.		Not evaluated for the purposes of this dossier.
Dissociation constant	Not found to dissociate	Sidney, P (1999)	OECD Test Guideline 112

	below pH 11.		Not evaluated for the purposes of this dossier.
Viscosity	>210 - <220 mPa.s (dynamic) at 70ºC	Registration dossier on EC No. 425-220-8 available on ECHA website.	Measured (OECD Test Guideline 114) Not evaluated for the purposes of this dossier. Data on viscosity is available from the published registration dossiers on substance EC No. 425-220-8 that are available on the ECHA website. This data on viscosity is anticipated to be consistent with the viscosity of the substance addressed in this proposal.

2 MANUFACTURE AND USES

2.1 Manufacture

The substance is manufactured in several member states.

2.2 Identified uses

The substance is used as a flame retardant additive in thermoplastic resins for production of components used in electrical and electronic goods (e.g. housings for PCs, Televisions, etc).

3 CLASSIFICATION FOR PHYSICO-CHEMICAL PROPERTIES

Table 10: Summary table for relevant physico-chemical studies

Method	Results	Remarks	Reference
Water solubility (OECD method No. 105 / EEC method No. A6) – Flask method	1.88 mg/l at 20°C (pH 7.13 – 7.61)	Experimental value – purity of test substance: 98.5%	Sydney P (1998)
Water solubility (Method A6 of Commission Direction 92/69/EEC) – Flask method	0.415 mg/l at 20°C (pH 5.5 – 6.1)	Experimental value – purity of test substance: not stated	Hogg, AS & Bartlett, AJ (1997)
Partition coefficient (OECD method No. 107/117 / EEC method No. A8) – shake-flask method	Log_{10} Pow >4.9 at 20°C (pH 7.29 – 7.37)	Experimental value – purity of test substance: 98.5%	Sydney P (1998)
Partition coefficient (OECD method No. 117 / EEC method No. A8) – shake-flask method	Log_{10} Pow 4.5 at 25°C (pH 5.65)	Experimental value – purity of test substance: not stated	Kenneth W (2002)

3.1.1 Summary and discussion of relevant physico-chemical studies.

Water solubility:

Experimental water solubility results are available for the substance from two different suppliers (notifications: Chemtura: 98-06-1163 and ICL-IP: 97-03-0400).

The water solubility of the test substance was found to be 1.88 mg/l at 20°C (pH 7.13 – 7.61) and 0.415 mg/l at 20°C (pH 5.5 – 6.1) in the respective studies.

Both water solubility studies were conducted to the EEC Method A6 (flask method). It has been considered that the flask method may not be the most suitable method to test a poorly soluble substance. The water solubility study (Hogg AS & Bartlett AJ 1997) gives the following discussion on the method used:

The preliminary water solubility test indicated that the column elution method should have been performed as the solubility was less than 1×10^{-2} g/l. However, due to the physical nature of the test material, it was not possible to use this method without blocking the column. Liquid test materials coated onto glass beads cause these beads to adhere together forming a plug within the column and thus preventing water circulation.

The difference in solubility results is presumed to be due to slight differences between the substances composition between suppliers, interlaboratory differences and slight test method differences. However, both products are considered to be identical and the proposal in this report to be valid for both suppliers results.

Partition coefficient:

Experimental partition coefficient results are available for the substance from different suppliers (notifications: Chemtura: 98-06-1163 and ICL-IP: 97-03-0400).

The partition coefficient (log_{10} Pow) of the test substance was found to be >4.9 at 20°C (pH 7.29 – 7.37) and 4.5 at 25°C (pH 5.65) in the respective studies.

Both studies were conducted to EEC Method A8, OECD Method 107/117 (shake-flask method).

The difference in partition coefficient results is presumed to be due to slight differences between the substances composition between suppliers, interlaboratory differences and slight test method differences. However, both products are considered to be identical and the proposal in this report to be valid for both suppliers results.

3.1.2 Comparison with criteria

Not applicable.

3.1.3 Conclusions on classification and labelling

The substance is not classified for any physico-chemical properties.

For the purposes of this dossier (removal of R53 classification) the relevant physico-chemical results are the water solubility and the partition coefficient of the substance. No further physico-chemical results are evaluated in this dossier.

4 HUMAN HEALTH HAZARD ASSESSMENT

Not evaluated for the purposes of this dossier.

5 ENVIRONMENTAL HAZARD ASSESSMENT

5.1 Degradation

Table 11: Summary of relevant information on degradation

Method	Results	Remarks	Reference
equivalent or similar to OECD Guideline 301 C (Ready Biodegradability: Modified MITI Test (I))	Average 0% degradation after 28 days.	See biodegradation section below.	Tsujimura (1998)
Hydrolysis as a function of pH (Method C.7 of directive 92/69/EEC)	Half life: >1 year at 25°C	See stability section below.	Hogg, As & Bartlett, AJ (1997)

5.1.1 Stability

Abiotic degradation:

Hydrolysis:

The test results are summarised in the following table:

Table 12. Overview of studies on hydrolysis

Method	Results	Remarks	Reference
Method C.7 of directive 92/69/EEC - (Hydrolysis as a Function of pH)	Half-life (DT50): t1/2 (pH 4): > 8760 h at 25 °C t1/2 (pH 7): > 8760 h at 25 °C t1/2 (pH 9): > 8760 h at 25 °C Transformation products: no	1 (reliable without restriction) key study experimental result **Test material (IUPAC name): (1-methylethylidene)di-4,1-phenylene tetraphenyl diphosphate**	Hogg, AS & Bartlett, AJ (1997)

The hydrolysis of the substance was studied at test concentration of 0.25 mg/l at pH 4, 7 and 9. The tests were carried out in the dark at 50°C for a period of 5 days. The test solutions were analyzed using a HPLC technique.

Less than 10% hydrolysis was detected after 5-day period at 50°C, equivalent to a half life greater than 1 year at 25°C. Transformation products were not measured since no hydrolysis occurred.

As no hydrolysis occurred and the substance has a half life of greater than 1 year at 25°C, hence no degradants are rapidly formed, it is demonstrated that environmental classification should be based on the properties of the parent substance.

5.1.2 Biodegradation

5.1.2.1 Biodegradation estimation

No data available.

5.1.2.2 Screening tests

The test results are summarised in the following table:

Table 13. Overview of screening tests for biodegradation in water

Method	**Results**	**Remarks**	**Reference**
Test type: ready biodegradability activated sludge (adaptation not specified) equivalent or similar to OECD Guideline 301 C (Ready Biodegradability: Modified MITI Test (I))	not readily biodegradable % Degradation of test substance: 0 after 28 d (Percentage biodegradation by BOD) (Average from 3 vessels) 0 after 28 d (Test mat. analysis (: Percentage biodegradation by HPLC)) (Average from 3 vessels) Test temperature: 25 ± 1°C	1 (reliable without restriction) key study experimental result **Test material (IUPAC name): (1-methylethylidene)di-4,1-phenylene tetraphenyl diphosphate**	Tsujimura (1998)
Test type: readily biodegradability activated sludge (non-adapted). According to OECD Guideline 301 C (Ready Biodegradability: Modified	not readily biodegradable. % Degradation of test substance: 6% degradation after 28 d (based on O_2 depletion)	1 (reliable without restriction) Supporting study experimental result	Mitsubishi-kasei Institute (1994).

MITI Test (I))	Mean 2.5% degradation after 28 d (based on residual test substance). Test temperature: 25 ± 1°C	**Test material (IUPAC name): (1-methylethylidene)di-4,1-phenylene tetraphenyl diphosphate**	

5.1.2.3 Simulation tests

No data available.

5.1.3 Summary and discussion of degradation

Experimental biodegradation results are available for the substance from two different suppliers (notifications: Chemtura: 98-06-1163 and ICL-IP: 97-03-0400).

Study Reference: Tsujimura (1998)

Ready biodegradation of the substance was tested by:

1) Measurement of biochemical oxygen demand (BOD) by means of a closed system oxygen consumption measuring apparatus.

2) Determination of test substance by means of HPLC.

After 28 days the average percentage degradation observed was 0%.

The test substance was not biodegraded by microorganisms under the test conditions and is not considered to be readily biodegradable.

Study Reference: Mitsubishi-kasei Institute (1994).

The substance is not readily biodegradable. After 28 days the mean degradation level was 2.5%.

5.2 Environmental distribution

5.2.1 Adsorption/Desorption

Not evaluated for the purposes of this dossier.

5.2.2 Volatilisation

Not evaluated for the purposes of this dossier.

5.2.3 Distribution modelling

Not evaluated for the purposes of this dossier.

5.3 Aquatic Bioaccumulation

Table 14: Summary of relevant information on aquatic bioaccumulation

Method	Results	Remarks	Reference
equivalent or similar to OECD Guideline 305 C (Bioaccumulation: Test for the Degree of Bioconcentration in Fish)	Study 1: BCF range: <= 1.1 - <= 159 Study 2: BCF range: 6.8 – 62	See bioaccumulation section below.	Noguchi S (1999) and Hori K (1996)

5.3.1 Aquatic bioaccumulation

The studies on aquatic bioaccumulation are summarised in the following table:

Table 15. Overview of studies on aquatic bioaccumulation

Method	Results	Remarks	Reference
Cyprinus carpio aqueous (freshwater) flow-through Total uptake duration: 8 wk equivalent or similar to OECD Guideline 305 C (Bioaccumulation: Test for the Degree of Bioconcentration in Fish)	BCF: <= 1.1 (whole body d.w.) (Time of plateau: 8 wk)(steady state) BCF: <= 2.7 (whole body d.w.) (Time of plateau: 8 wk)(steady state) BCF: <= 16 (whole body d.w.) (Time of plateau: 8 wk)(steady state) BCF: <= 11 (whole body d.w.) (Time of plateau: 8 wk)(steady state) BCF: <= 27 (whole body d.w.) (Time of plateau: 8 wk)(steady state) BCF: <= 159 (whole body d.w.) (Time of plateau: 8 wk)(steady state) Lipid content: 4.1 % (start of exposure)	1 (reliable without restriction) key study experimental result **Test material (IUPAC name): (1-methylethylidene)di-4,1-phenylene tetraphenyl diphosphate**	Noguchi S (1999)

Cyprinus carpio aqueous (freshwater) flow-through Total uptake duration: 8 wk equivalent or similar to OECD Guideline 305 C (Bioaccumulation: Test for the Degree of Bioconcentration in Fish)	BCF: 6.8 — 40 (whole body d.w.) (Time of plateau: 8 wk)(steady state) BCF: 22 — 62 (whole body d.w.) (Time of plateau: 8 wk)(steady state) Lipid content: 3.9 % (start of exposure)	1 (reliable without restriction) supporting study experimental result **Test material (IUPAC name): (1-methylethylidene)di-4,1-phenylene tetraphenyl diphosphate**	Hori K (1996)

5.3.1.1 Bioaccumulation estimation

5.3.1.2 Measured bioaccumulation data

5.3.2 Summary and discussion of aquatic bioaccumulation

Study 1:

Bioaccumulation test of CN-1985 in carp (Noguchi S (1999))

Results:

Acute toxicity test:

48 -hour LC50 value: > 500 mg/L. No toxic effects were observed up to the water solubility limit.

Bioaccumulation factors:

The following factors have been taken into consideration for interpretation of the BCF results.

Preparation of test solution:

The test substance supplied and dispersant HCO-40 (Hydrogenated castor oil) (20 times amount of test substance) were dissolved with acetone. After the acetone was evaporated from the solution, ion-exchanged water was added to the mixture to prepare relevant stock solutions.

Analysis of test water and fish:

Three peaks were detected by HPLC analysis of the test substance. The peaks of the chromatogram were named peak 1, peak 2 and peak 3 in the elution order.

Determination limit of the test substance in test water:

The determination limits were calculated as:

Level 1:	Level 2:
Peak 1: 0.031 mg/l	Peak 1: 0.0031 mg/l
Peak 2: 0.18 mg/l	Peak 2: 0.018 mg/l
Peak 3: 1.1 mg/l	Peak 3: 0.11 mg/l

Determination limit of the test substance in test fish:

The determination limit of test substance in test fish was calculated as follows, assuming fish weight of 30g.

Peak 1: 1.9 µg/g

Peak 2: 4.9 µg/g

Peak 3: 29 µg/g

Calculation of bioconcentration factors (BCFs).

From the minimum determination limit of the test substance in fish, BCFs could be obtained for cases of a BCF exceeding the following values:

Level 1	Level 2
Peak 1: 1.1	Peak 1: 11
Peak 2: 2.7	Peak 2: 27
Peak 3: 16	Peak 3: 159

Results:

Concentrations of test substance in test water:

Each average concentration of the test substance in test water was maintained at 90% or more of the nominal concentration. It is therefore considered that it is acceptable to base the results on the nominal concentrations.

Bioconcentration Factors:

	Level 1 (2 mg/L)	**Level 2 (0.2 mg/L)**
Peak 1	≤ 1.1 -1.2	≤ 11
Peak 2	≤ 2.7	≤ 27
Peak 3	≤ 16	≤ 159

Discussion:

The BCF values obtained are less than or equal to values as these were the limits of detection for the BCK calculations i.e. no detectable test item was found in the fish so the BCF is lower than the limit of detection.

The wide range of BCF values is due to the different concentrations used for the two test levels, and are considered as valid.

The study results indicate that the test item does not bioaccumulate.

Study 2:

Bioaccumulation test of AFR-1 in carp (Hori K (1996))

Results:

Acute toxicity test:

48 -hrs LC50: 500 mg/L and over. No toxic effects were observed up to the water solubility limit.

Bioaccumulation test:

The following factors have been taken into consideration for interpretation of the BCF results.

Preparation of test solution:

The test substance supplied and dispersant HCO-40 (Hydrogenated castor oil) which was 20 times amount of test substance were dissolved with acetone and then the acetone was. The mixture was dissolved with deionised water.

Determination limit of the test substance in test water:

The minimum limit of determination was calculated as:

Level 1: 0.051 mg/l

Level 2: 0.0051 mg/l

Determination limit of the test substance in test fish:

The determination limit of test substance in test fish was calculated as 0.53 µg/g, assuming fish weight of 30g.

Calculation of bioconcentration factors (BCFs).

From the minimum determination limit of the test substance in fish, BCFs could be obtained for cases of a BCF exceeding the following values:

Level 1: 0.6

Level 2: 5.7

Results:

Concentrations of test substance in test water:

Each average exposure level was maintained at 90% and over of the nominated concentration levels.

Bioconcentration factors:

Level 1 (1.0 mg/L): 6.8 - 40

Level 2 (0.1 mg/L): 22 – 62

Discussion:

A different analytical method was used in this study to the Noguchi S (1999) study. The analytical method has not separated the test item into three test item peaks. This has resulted in some test item being seen in the fish (greater than the limit of detection) and so BCF values have been calculated.

The low and variable results are typical of a low bioaccumulating substance and suggest that the test item does not bioaccumulate.

Summary:

Two bioconcentration studies have been conducted on the test substance (from two sources). Different analytical methods were used in the studies and both are considered valid. In one study (Noguchi S (1999)) the BCF values are reported to be less than or equal to the limits of detection determined i.e. no detectable test item was found in the fish. In the other study (Hori K (1996)) BCF values have been calculated and the low, variable results are typical of a low BCF substance.

Based on the two study results it is considered that the substance does not bioaccumulate.

5.4 Aquatic toxicity

Table 16: Summary of relevant information on aquatic toxicity

Method	Results	Remarks	Reference

OECD Guideline 203 (Fish, Acute Toxicity Test), OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test) OECD Guideline 201 (Alga, Growth Inhibition Test)	No toxicity at limit of solubility.	LC50 and NOEC not identified.	Jenkins CA (1998a). Jenkins CA (1998b). Jenkins CA (1998).
OECD Guideline 210 (Fish, Early-Life Stage Toxicity Test)	NOELr: 5 mg/l	No observed effect loading result based on initial loading rate of 5 mg/l.	Knight B (2003).
OECD Guideline 211 (Daphnia magna Reproduction Test)	NOELr for reproduction: 5 mg/l (5 ppm).	No observed effect loading result based on initial loading rate of 5 mg/l.	Hargreaves TL & Clayton MA (2003).

5.4.1 Fish

5.4.1.1 Short-term toxicity to fish

The results are summarised in the following table:

Table 17. Overview of short-term effects on fish

Method	Results	Remarks	Reference
Oncorhynchus mykiss freshwater semi-static OECD Guideline 203 (Fish, Acute Toxicity Test) EU Method C.1 (Acute Toxicity for Fish)	LC50 (96 h): No toxicity at limit of solubility.	1 (reliable without restriction) key study experimental result **Test material (IUPAC name): (1-methylethylidene)di-4,1-**	Jenkins CA (1998a)

		phenylene tetraphenyl diphosphate	

Discussion

A study was performed to assess the acute toxicity of test substance to rainbow trout (Oncorhynchus mykiss) under semi-static conditions.

A group of ten juvenile fish were exposed to a single concentration of test substance, dispersed in water at nominally 10 mg/l; to aid dispersion acetone and ultrasound were employed. The test substance (1 g) was dissolved in acetone (10 ml) and an aliquot (1.1 ml) was added to warm diluent water (approximately 23°C) in a volumetric flask (2:l) to aid dissolution and/or dispersion. The contents of the flask were treated by ultrasound for fifteen minutes before being poured into a test vessel. The flask was refilled with cold diluent water (approximately 30°C) and the rinsings poured into the vessel; the volume was then adjusted to 11 litres by the further addition of cold water.

The selected exposure level intentionally exceeded the limit of aqueous solubility of test substance (stated value 1.9 mg/l) and was the highest concentration considered practical to prepare.

Measured concentrations of test substance ranged between 0.65l and 3.93 mg/l in unfiltered samples of medium, with an overall mean measured level of 1.44 mg/l. In filtered samples, the measured levels ranged from <0.1 to 0.141 mg/l. Although a stable concentration was not maintained, a condition of maximum attainable exposure is considered to have been employed.

No mortalities were noted during the test at a measured level of 1.44 mg/l; this value reflects the amount of test substance that remained suspended in the test medium during the test although, at most, only 0.141 mg/l was dissolved.

Sub-lethal effects were exhibited by some fish between 24 and 72 hours; these were attributed to the presence of aggressive fish in the test vessel and were not considered to be treatment-related.

Based on these findings, neither the 96-hour median lethal concentration (LC50) nor the no-observed effect concentration (NOEC) were identified.

In conclusion, the test substance was not found to be toxic to rainbow trout when dispersed in water at a concentration (1.44 mg/l) in excess of its limit of aqueous solubility under test conditions (at most, 0.141 mg/l).

5.4.1.2 Long-term toxicity to fish

The results are summarised in the following table:

Table 18. Overview of long-term effects on fish

Method	Results	Remarks	Reference
Pimephales promelas freshwater	NOELr (28 d): 5 mg/L (initial loading rate) based on: number	1 (reliable without	Knight B (2003)

early-life stage: reproduction, (sub)lethal effects flow-through OECD Guideline 210 (Fish, Early-Life Stage Toxicity Test)	hatched (hatching success), mortality (larval survival), length (larval growth), weight (larval growth). No toxicity at limit of solubility.	restriction) key study experimental result **Test material (IUPAC name): (1-methylethylidene)di-4,1-phenylene tetraphenyl diphosphate**	

Discussion

The effect of prolonged exposure to test substance on the early-life stages of the Fathead Minnow (Pimephales promelas) was assessed over embryo development, hatching and for 28 days post-hatch.

The test was conducted under continuous flow conditions, with embryos and larvae exposed to the following initial loading rates of test substance (prepared as water accommodated fraction (WAF)): 0.5 and 5 mg/l. A control (0 mg/l) was also included in the test. Duplicate tanks were tested at each loading rate, including control.

Individual WAF's were prepared by adding weighed amounts of test substance (24.9-25.3 and 249.7-250.4 mg respectively) to test water (50 litres) and stirring this for a period of ca 48 h. Following the period of stirring, the contents of the vessel were allowed to settle for 1 h after which ca 35-40 litres of solution (WAF) was removed via the tap at the base of the container, with the first ca 1 litre being discarded. This WAF was then connected to the flow-through system (via the stock tank) and delivered at the appropriate rate to the test and control tanks.

The hatching success of embryos in individual replicates ranged from 88 to 100%. Statistical analysis indicated no significant difference in hatching success at initial loading rates of 0.5 and 5 mg/l when compared to the control. The no observed effect loading (NOEL) would be regarded as 5 mg/l, based on initial loading rates.

Larval survival was found to be unaffected at initial loading rates of 0.5 and 5 mg/l when compared to the control. One larvae at 0.5 and one at 0 mg/l were dead by the end of the test period. The NOEL would be regarded as 5 mg/l, based on initial loading rates.

Larval growth (length measured at the end of the test) was found to be unaffected at initial loading rates of 0.5 and 5 mg/l when compared to the control. The NOEL would be regarded as 5 mg/l, based on initial loading rates.

Larval growth (weight measured at the end of the test) was found to be unaffected at initial loading rates of 0.5 and 5 mg/l when compared to the control. The NOEL would be regarded as 5 mg/l, based on initial loading rates.

Comments on Water Accommodated Fraction (WAF):

The test solutions used in the study were prepared as water accommodated fractions (WAFs) from specific loading rates of the test item, in view of the difficulties associated with the evaluation of aquatic toxicity of poorly water soluble test items. This modification to the standard method for the preparation of aqueous media was performed in line with the OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures (2000) No. 23.

Therefore, the results are considered to be highly reliable and suitable for the assessment of chronic effects and for the purposes of classification.

Summary of Fish Toxicity Studies and Methods

Two fish toxicity studies have been conducted on the test substance, an acute toxicity test (conducted to OECD test guideline 203) and a long-term toxicity test (early-life stage toxicity test conducted to OECD test guideline 210).

Both studies show no toxicity at the limit of solubility in the respective studies.

The test substance is considered as a ‘difficult substance’ due to its low water solubility and therefore testing was performed in line with the OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures (2000) No. 23.

The acute toxicity study (Jenkins CA (1998a)) was conducted exposing the test fish to a single concentration of test substance. To aid dispersion of the test material in the test solution, acetone and ultrasound were employed (see discussion section on short-term toxicity to fish for details of test solution preparation).

In comparison, the early-life stage toxicity test (Knight B (2003)) was conducted using test solutions prepared as water accommodated fractions (WAFs). WAFs are commonly used for complex mixtures and multi-component substances. The substance is considered as a mono-constituent substance but for the purposes of the study, the test substance was considered as a multi-component substance based on the analytical work in the study, described below:

The substance consists of four components. Components 1 and 2 account for ≥95% of the test item on a component peak (HPLC-UV) basis. The analytical method quantified components 1 and 2 of the test item, therefore analysis of the test samples measured these components.

The use of WAFs was therefore considered appropriate to this substance for the study. The other components (2, 3 and 4) detected are now regarded as impurities (all below <10% w/w concentration).

The use of WAF in the early-life stage toxicity study (Knight B (2003)) and not in the acute toxicity study (Jenkins CA (1998a)) can also be accounted for by the fact that the studies were conducted at different testing facilities and different study protocols being agreed by the study sponsor. The studies were also conducted at different times (1998 and 2003) which may also explain in differing approaches.

However, as both studies were conducted to GLP and in compliance with agreed protocols, with no or minor deviations from standard test guidelines, it is therefore considered that the results of both studies are of high reliability and suitable for the assessment of acute and chronic effects and for the purposes of classification.

5.4.2 Aquatic invertebrates

5.4.2.1 Short-term toxicity to aquatic invertebrates

The results are summarised in the following table:

Table 19. Overview of short-term effects on aquatic invertebrates

Method	Results	Remarks	Reference
Daphnia magna freshwater static OECD Guideline 202 (Daphnia sp. Acute Immobilisation Test) EU Method C.2 (Acute Toxicity for Daphnia) EPA OTS 797.1300 (Aquatic Invertebrate Acute Toxicity Test, Freshwater Daphnids)	LC50 (48 h): No toxicity at limit of solubility.	1 (reliable without restriction) key study experimental result **Test material (IUPAC name): (1-methylethylidene)di-4,1-phenylene tetraphenyl diphosphate**	Jenkins CA (1998b)

Discussion

The acute toxicity of test substance to Daphnia magna was assessed under static exposure conditions.

A group of twenty Daphnia, less than 24 hours old, was exposed for 48 hours to a single concentration of test substance, dispersed in Elendt M4 medium at a nominal concentration of 10 mg/l; to aid dispersion, acetone and ultrasound treatment were employed. The test substance (100 mg) was dissolved in acetone (10 ml) and an aliquot (100 µl) was added to dilution water in a volumetric flask (1 l); to aid dissolution and/or dispersion, the contents of the flask were treated by ultrasound for ten minutes before aliquots (100 ml) were poured into the test vessels.

The selected exposure level intentionally exceeded the limit of aqueous solubility of test substance (stated value 1.9 mg/l) and was the highest concentration considered practicable to prepare.

Measured concentrations of CN- 1 985 in unfiltered samples of medium ranged from 2.82 mg/l at the start to 0.195 mg/l after 48 hours; in calculation of the test results, the worst estimate of 0.195 mg/l has been used. In filtered samples, the measured levels were below the limit of accurate quantification (<0.1 mg/l). Although a stable concentration was not maintained, a condition of maximum attainable exposure is considered to have been employed.

Observations of the Daphnia in each control and test vessel were made after 3, 24 and 48 hours. No immobilisation or effects on the Daphnia were noted at a measured concentration of 0.195 mg/l; this value reflects the amount of test substance that remained in suspension at the end of the test although <0.1 mg/l was dissolved.

Based on these findings, neither the 48-hour median effect concentration (EC50) nor the no-observed effect concentration (NOEC) were identified.

In conclusion, the test substance was not found to be toxic to Daphnia magna when dispersed in water at a concentration (0.195 mg/l) in excess of its limit of solubility under the test conditions (<0.1 mg/l).

5.4.2.2 Long-term toxicity to aquatic invertebrates

The results are summarised in the following table:

Table 20. Overview of long-term effects on aquatic invertebrates

Method	Results	Remarks	Reference
Daphnia magna freshwater semi-static OECD Guideline 211 (Daphnia magna Reproduction Test)	EL50 (21 d): > 5 ppm Initial loading rate (nominal) based on: reproduction NOELR (21 d): 5 ppm Initial loading rate (nominal) based on: reproduction No toxicity at limit of solubility.	1 (reliable without restriction) key study experimental result **Test material (IUPAC name): (1-methylethylidene)di-4,1-phenylene tetraphenyl diphosphate**	Hargreaves TL & Clayton MA (2003)
Daphnia magna freshwater flow-through OECD Guideline 211 (Daphnia magna Reproduction Test)	NOEC (21 d): 1.8 mg/L test mat. (meas. (geom. mean)) based on: immobilisation/mortality, reproduction, growth No toxicity at limit of solubility.	1 (reliable without restriction) supporting study experimental result **Test material (IUPAC name): (1-methylethyliden**	Desjardin, D. et al (2002a)

		e)di-4,1-phenylene tetraphenyl diphosphate	
Daphnia magna freshwater flow-through OECD Guideline 211 (Daphnia magna Reproduction Test)	NOEC (21 d): 1.2 mg/L test mat. (meas. (geom. mean)) based on: immobilisation/mortality, reproduction, growth No toxicity at limit of solubility.	1 (reliable without restriction) supporting study experimental result **Test material (IUPAC name): (1-methylethylidene)di-4,1-phenylene tetraphenyl diphosphate**	Desjardin, D. et al (2002b)

Discussion

Key study (Hargreaves TL & Clayton MA (2003)):

This study was designed to determine the effects of the test substance on the reproductive capacity of the freshwater flea, *Daphnia magna* Straus.(Cladocera: Crustacea).

The method of preparation was selected to create conditions that maximised the solubility of the test item. Weighed amounts of test substance were added to known volumes of test medium (Elendt M4) and stirred for 48 h. After 48 h the solutions were allowed to settle for 1 h and a volume of the water was removed with a siphon. This mid water sample was considered to contain the water accommodated fraction of the test item (WAF), i.e. the soluble components of the test item at their highest achievable concentration under these conditions.

Following the results of a range finding test, a definitive test was conducted with WAF solutions at initial test substance loading rates of 5, 4, 3, 2 and 1 p.p.m., with an untreated control (Elendt M4). For each WAF or control solution 10 daphnia neonates (<24 h old) were individually placed into 100 ml glass beakers, i.e. one neonate per vessel, and their condition observed over a 21 day test period. Test solutions were renewed with freshly prepared WAF solutions ca. 3 times every 7 days. Neonates were fed daily with a green algae (Chlorella vulgaris) suspension, at a rate of 0.1 mg carbon/daphnid/day. The time taken for the daphnids to mature and produce their first brood of neonates was recorded, together with the number of neonates produced per day and cumulative production over the entire 21 day test period.

The concentrations of test substance found in solution were assessed by chemical analysis (using 2 indicator components), for freshly prepared (after stirring) and expired (72 h after renewal) WAF solutions. Test substance in solution was calculated to be many times less than the initial loading

rates. Concentrations in freshly prepared WAF solutions were between 0.4 and 1.9% of nominal loading rates and between 0.3 and 1.3% in expired solutions.

For all initial loading rates of test substance tested there was no significant decrease in reproduction compared to the control after 21 days. Therefore the EL50 (reproduction) was greater than 5 p.p.m. and the No Observed Effect Loading rate (NOELr) for reproduction was at least 5 p. p. m., under the conditions of the test.

Comments on Water Accommodated Fraction (WAF):

The test solutions used in the study were prepared as water accommodated fractions (WAFs) from specific loading rates of the test item, in view of the difficulties associated with the evaluation of aquatic toxicity of poorly water soluble test items. This modification to the standard method for the preparation of aqueous media was performed in line with the OECD Guidance Document on Aquatic Toxicity Testing of Difficult Substances and Mixtures (2000) No. 23.

Therefore, the results are considered to be highly reliable and suitable for the purposes of classification.

Additional studies:

Two further Daphnia Reproduction study results are available. The studies were conducted using two different batches of the test material form the same supplier.

Results:

1) Desjardin, D. et al (2002a)

The objective of this study was to determine the effects of the test substance on the survival, growth and reproduction of the cladoceran, Daphnia magna, during a 21-day exposure period under flow through conditions.

Nominal concentrations used in this study were 0.19, 0.38, 0.75, 1.5 and 3.0 mg/l. A primary stock was prepared in DMF at a concentration of 36.0 mg/ml. The stock solution was sonicated for approximately 2 minutes and mixed by inversion (at least 20 times), and appeared clear and colourless. Proportional dilutions of the 36.0 mg/ml stock were made to prepare 500 mL each of 2.3, 4.5, 9.0 and 18 mg/l stock solutions. The stock solutions were delivered to the mixing chambers (at a rate of 12.50 µl/minute) where they were mixed with dilution water (at a rate of 150 ml/minute) to achieve the desired test concentrations of 0.19, 0.38, 0.75 and 3.0 mg/L.

The highest test concentration for this test was based on two times the functional water solubility (given in report as 1.5 mg/l). When measured concentrations of samples collected during the test were averaged, the mean test concentrations were 0.14, 0.26, 0.52, 1.1 and 1.8 mg/l, which represented 75, 67, 69, 74 and 61% of the nominal concentrations respectively. Mean measured concentrations were used to express to NOEC, LOEC and MATC. Concentrations were determined by HPLC.

Daphnia magna exposed to the test substance up to a concentration of 1.8 mg/l for 21 days showed no significant reductions in survival, reproduction or growth. Consequently, the no mortality/immobility concentration and NOEC were 1.8 mg/l, and the LOEC was >1.8 mg/l. The

MATC (maximum acceptable toxicant concentration) was determined to be >1.8 mg/l. The 21-day EC50 was estimated to be >1.8 mg/l.

2) Desjardin, D. et al (2002b)

The objective of this study was to determine the effects of the test substance on the survival, growth and reproduction of the cladoceran, Daphnia magna, during a 21-day exposure period under flow through conditions.

Nominal concentrations used in this study were 0.19, 0.38, 0.75, 1.5 and 3.0 mg/l. A primary stock was prepared in DMF at a concentration of 36.0 mg/ml. The stock solution was sonicated for approximately 2 minutes and mixed by inversion (at least 20 times), and appeared clear and colourless. Proportional dilutions of the 36.0 mg/ml stock were made to prepare 500 mL each of 2.3, 4.5, 9.0 and 18 mg/l stock solutions. The stock solutions were delivered to the mixing chambers (at a rate of 12.50 µl/minute) where they were mixed with dilution water (at a rate of 150 ml/minute) to achieve the desired test concentrations of 0.19, 0.38, 0.75 and 3.0 mg/L.

The highest test concentration for this test was based on two times the functional water solubility (given in report as 1.5 mg/l). When measured concentrations of samples collected during the test were averaged, the mean test concentrations were 0.15, 0.32, 0.52, 1.2 and 1.4 mg/l, which represented 81, 85, 70, 83 and 45% of the nominal concentrations respectively. Mean measured concentrations were used to express to NOEC, LOEC and MATC. Concentrations were determined by HPLC.

Daphnia magna exposed to the test substance up to a concentration of 1.4 mg/l for 21 days showed no significant reductions in reproduction or survival. However, a treatment related reduction in growth was apparent in the highest treatment level (1.4 mg/l). Consequently, the no mortality/immobility concentration and NOEC were 1.2 mg/l, and the LOEC was 1.4 mg/l. The MATC (maximum acceptable toxicant concentration) was determined to be 1.3 mg/l. The 21-day EC50 was estimated to be >1.4 mg/l.

Summary of Daphnia Reproduction Studies:

Three studies have been conducted on the test substance from two suppliers. All three studies show no toxicity at the limit of solubility determined in the respective studies.

All studies were conducted to OECD Guideline 211, with one study (Hargreaves TL & Clayton MA (2003)) using test solutions prepared as water accommodated fractions (WAF), due to the difficulties associated with the evaluation of aquatic toxicity of poorly water soluble test items.

The use of WAF in one study ((Hargreaves TL & Clayton MA (2003)) and not in the remaining two studies (Desjardin, D. et al (2002a/b)) can be accounted for by the fact that the relevant studies were conducted at different testing facilities and sponsored by different companies who agreed different study protocols.

However, as all the studies were conducted to GLP and in compliance with agreed protocols, with no or minor deviations from standard test guidelines, it is therefore considered that the results are considered to be highly reliable and suitable for the assessment of chronic effects and for the purposes of classification.

5.4.3 Algae and aquatic plants

The results are summarised in the following table:

Table 21. Overview of effects on algae and aquatic plants

Method	Results	Remarks	Reference
Selenastrum capricornutum (new name: Pseudokirchnerella subcapitata) (algae) freshwater static OECD Guideline 201 (Alga, Growth Inhibition Test) EU Method C.3 (Algal Inhibition test)	EC50 (96 h): No toxicity at limit of solubility.	1 (reliable without restriction) key study experimental result **Test material (IUPAC name): (1-methylethylidene)di-4,1-phenylene tetraphenyl diphosphate**	Jenkins C (1998)

Discussion

Effects on algae / cyanobacteria

The effect of the test substance on the growth of the unicellular green alga Selenastrum capricornutum was assessed under non-axenic conditions.

Six replicate algal cultures, with an initial cell density of 1 x 10^4cells/ml, were exposed to the test substance dispersed in algal nutrient medium at a nominal concentration of 10 mg/l; to aid dispersion, acetone was employed. The test substance (1 g) was dissolved in acetone (10 ml) and an aliquot (10 µl) was added directly to nutrient algal medium in the test vessels.

The selected exposure level intentionally exceeded the limit of aqueous solubility of test substance (stated value 1.9 mg/l) and was the highest concentration considered practicable to prepare.

Cultures were incubated in an orbital incubator under continuous illumination at temperatures ranging from 20.7 to 23.5°C for 96 hours.

The measured concentrations of test substance in unfitered samples of the test culture, ranged between 1.61 and 2.93 mg/l, with an overall mean measured level of 2.17 mg/l. No test material was detected (<20 µg/l) in filtered samples of medium. These data were not unexpected in view of the low aqueous solubility of the test material. Although the concentration of dissolved test substance to which the algae were exposed was not identified, a condition of maximum attainable exposure is considered to have been employed.

Cell numbers were counted daily to monitor growth. The test results are expressed in terms of the area under the growth curve and growth rate. Compared to the solvent control cultures, neither the area under the growth curve nor the growth rate were significantly reduced at a mean measured level of 2.17 mg/l; this concentration reflects the amount of test substance that remained suspended during the test, although less than 20 µg/l was dissolved.

Neither the 96-hour median effect concentrations (EbC50 and ErC50) nor the no-observed effect concentration of test substance were identified for inhibition of growth.

In conclusion, the test substance was not found to be inhibitory to Selenastrum capricornutum when dispersed in algal nutrient medium at a concentration (2.17 mg/l) in excess of its limit of aqueous solubility under test conditions (<20 µg/l).

5.4.4 Other aquatic organisms (including sediment)

Not evaluated for the purposes of this dossier.

5.4.5 Overview of water solubility

There is a difference in the measured water solubility of the substance measured in the water solubility studies and the solubility levels obtained in the ecotoxicity studies. These differences in solubility levels are attributed to slight differences in the test material, slightly differing methodologies in the studies and between testing laboratories. It is also considered that other factors may have some influence on the varying solubility levels, such as differences in test media used e.g demin-water in water solubility tests versus deep well water in Daphnia studies (Desjardin, D. et al (2002a/b), and differences in laboratory water between testing laboratories.

It is considered that a condition of maximum attainable exposure has been employed in all the relevant studies and therefore that the all the results are suitable for assessing the toxicity of the test substance i.e. the slight differences in water solubility levels do not affect the assessment of the substance.

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

5.1 Degradation:

The test substance is not considered to be readily biodegradable.

5.2 Environmental distribution:

Not relevant for the purpose of this dossier.

5.3 Aquatic bioaccumulation:

Study 1
Bioaccumulation test of CN-1985 in carp (Noguchi S (1999))
BCF range: <= 1.1 - <= 159

The BCF values obtained are less than or equal to values as these were the limits of detection for the BCK calculations i.e. no detectable test item was found in the fish so the BCF is lower than the limit of detection.

The wide range of BCF values is due to the different concentrations used for the two test levels, and are considered as valid.

The study results indicate that the test item does not bioaccumulate.

Study 2:
Bioaccumulation test of AFR-1 in carp (Hori K (1996))
BCF range: 6.8 – 62

The low and variable results are typical of a low bioaccumulating substance and suggest that the test item does not bioaccumulate.

The bioaccumulation criteria (BCF values) that indicate a potential to bioaccumulate are:

DSD: BCF >100

CLP: BCF >500

Two bioconcentration studies have been conducted on the test substance (from two sources). Different analytical methods were used in the studies and both are considered valid. In one study (Noguchi S (1999)) the BCF values are reported to be less than or equal to the limits of detection determined i.e. no detectable test item was found in the fish. In the other study (Hori K (1996)) BCF values have been calculated and the low, variable results are typical of a low BCF substance.

Based on the two study results it is considered that the substance does not bioaccumulate.

5.4 Aquatic Toxicity

Acute toxicity studies:

No acute toxicity recorded up to levels of water solubility (LC50/EC50 values therefore not identified).

Chronic Toxicity studies:

Chronic toxicity studies in fish and daphnia showed an absence of chronic toxicity effects at the solubility limit and chronic toxicity NOEL/NOEC values were determined to be greater than the water solubility limit.

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

Based on the study results available the substance should not be classified for the environment under the DSD criteria or the CLP criteria, based on the arguments described below:

DSD:

The substance is currently classified as R53 (May cause long-term adverse effects in the aquatic environment) under the DSD (Dangerous Substances Directive 67/548/EEC)

Directive 67/548/EEC states the criteria for R53 classification as:

Substances not falling under the criteria listed in this Chapter (Chapter 5 –Classification on the Basis of Environmental Effects), but which on the basis of the available evidence concerning their persistence, potential to accumulate, and predicted or observed environmental fate and behaviour may nevertheless present a long-term and/or delayed danger to the structure and/or functioning of aquatic ecosystems.

For example, poorly water soluble substances, i.e. substances with a solubility of less than 1 mg/l will be covered by this criterion if:

a) they are not readily degradable; and

b) the log Pow is greater than or equal to 3.0 (unless the experimentally determined BCF is less than 100).

This criterion applies to substances unless there exists additional scientific evidence concerning degradation and/or toxicity sufficient to provide an adequate assurance that neither the substance or its degradation products will constitute a potential long term and/or delayed danger to the aquatic environment.

Such additional scientific evidence should normally be based on studies required at Annex VIII and could include

i) a proven potential to degrade rapidly in the aquatic environment.

ii) An absence of chronic toxicity effects at the solubility limit e.g. a no observed effect concentration of greater than the solubility limit determined in a prolonged study with fish or daphnia.

Basis for Proposed Removal of R53:

Based on this criteria the substance meets the following criteria for R53:

- The substance can be considered to be poorly water solubility, based upon the limits of solubility found under test conditions (which are lower than the stated solubility level of 1.88 mg/l from the water solubility study).

- The substance is not readily biodegradable

- The substance has a log Pow >3.0.

However, the results of two bioaccumulation studies indicate the substance does not meet the R53 criteria as the experimentally determined BCF values are less than 100 (result of <159 is not relevant to classification as 159 was the limit of detection) and show the substance does not have potential to bioaccumulate.

Also, a chronic fish study (Early-Life Stage Test) and three chronic daphnia studies (Daphnia Reproduction studies) showed an absence of chronic toxicity effects at the solubility limits determined in the studies.

Therefore, the substance should not be classified as R53 based on the above criteria.

CLP:

The substance is currently classified under the CLP classification as Aquatic Chronic Category 4.

The criteria for classification as Chronic Category 4 states the classification is appropriate where:

poorly soluble substances for which no acute toxicity is recorded at levels 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), indicating a potential to bioaccumulate, 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 evidence of rapid degradation in the environment.

Basis of Proposal Removal of Chronic Category 4:

Based on the criteria above the substance should not be classified in this category as:

- the results of two bioaccumulation studies show the BCF values to be substantially less than 500.
- Chronic toxicity studies in fish and Daphina showed an absence of chronic toxicity effects at the solubility limits determined in the studies. The determined NOEL/NOECs were equal to or greater than the level of water solubility in the relevant studies.

Therefore, the substance should not be classified as Aquatic Chronic Category 4.

Summary of classification:

Based on study data from bioaccumulation studies and chronic toxicity studies (in fish and Daphnia) the substance does not fulfil the criteria required for classification as R53 (under the DSD regulation) or as Aquatic Chronic Category 4 (under the CLP regulation) and as such a proposal has been made to remove the classifications from the substance.

6 OTHER INFORMATION

None applicable.

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