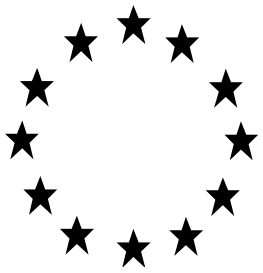
Competent Authority Report



COPPER PYRITHIONE (PT21)

DOCUMENT IIIA 7.1–7.3

Fate

Applicant: API

Rapporteur Member State: Sweden

Draft December 2010

KEMI
Kemikalieinspektionen
Swedish Chemicals Agency

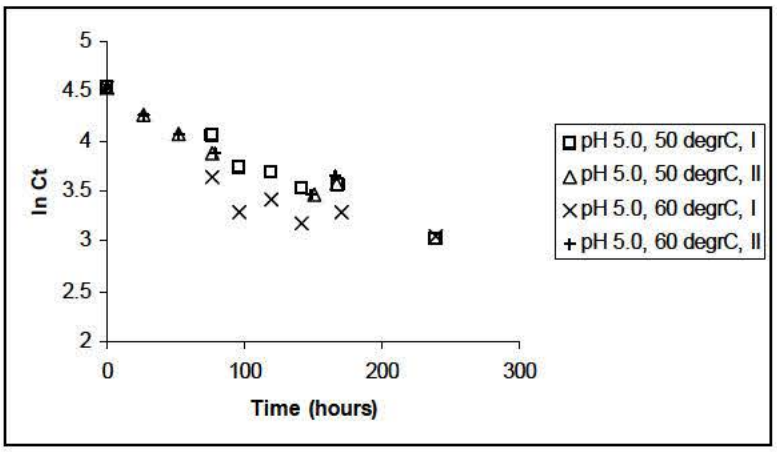
Section A7.1.1.1.1 Hydrolysis as a function of pH and identification of breakdown products

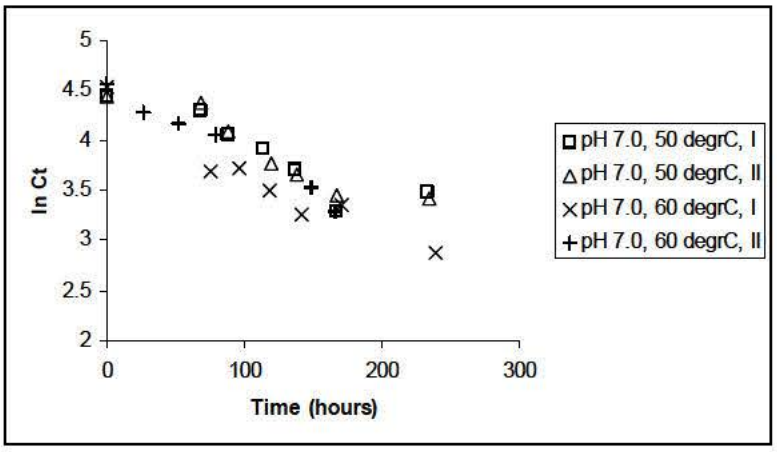
Annex Point IIA7.6.2.1

			Official use only
		1 REFERENCE	
1.1	**Reference**	De Wolf JM, De Bie AThHJ (2003) Abiotic degradation of copper pyrithione in aqueous solutions using [14C]-copper pyrithione according to OECD guideline 111. TNO Nutrition and Food Research, Report No. V4477, November 28, 2003 (unpublished)	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Yoshitomi Fine Chemicals, Ltd.	
1.2.2	Companies with letter of access	-	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Yes, OECD 111	
2.2	**GLP**	Yes	
2.3	**Deviations**	No	X
		3 MATERIALS AND METHODS	
3.1	**Test material**	Radio-labelled copper pyrithione ([^{14}C]-Copper Pyrithione)	X
3.1.1	Lot/Batch number	3362-120	
3.1.2	Specification	Specific activity of radio-labelled test material: 28.68 mCi/mmol	
3.1.3	Purity	Radio-labelled test material (radiochemical purity): > 95%.	X
3.1.4	Further relevant properties	The test material is photodegradable and was stored under protection from light	
3.2	**Reference substance**	No	X
3.2.1	Initial concentration of reference substance		
3.3	**Test solution**	See table A7_1_1_1_1-1 and A7_1_1_1_1-2	X
3.4	**Testing procedure**		
3.4.1	Test system	See table A7_1_1_1_1-3 The tests were carried out in the dark to avoid photolytic interference. Oxygen was exluded by bubbling nitrogen through the test solutions for 5 min. The effectiveness of the measures taken to exclude the occurrence of biodegradation was checked in a test for sterility by incubating samples of the test solutions on multi medium agar plates.	X
3.4.2	Temperature	50 and 60 °C	X
3.4.3	pH	5.0 ± 0.2, 7.0 ± 0.2, and 9.0 ± 0.2	X
3.4.4	Duration of the test	0 – 240.0 h, for specific test durations see tables A7_1_1_1_1-4a to f	

Section A7.1.1.1.1 Hydrolysis as a function of pH and identification of breakdown products

Annex Point IIA7.6.2.1

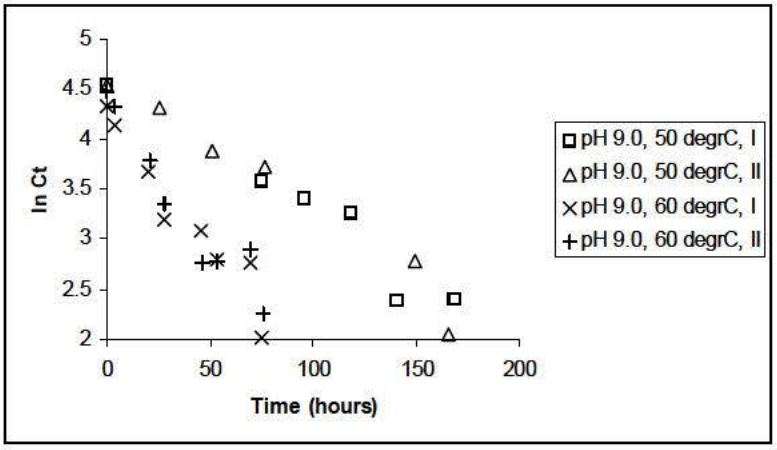
3.4.5	Number of replicates	2 series	
3.4.6	Sampling	The concentration of [^{14}C]-copper pyrithione was determined at t = 0 and six other time points (see tables A7_1_1_1_1-4a to f)	
3.4.7	Analytical methods	HPLC with radiometric detection	X
3.5	**Preliminary test**	Yes, at pH 5.0, 7.0, and 9.0 and 50 °C	
		4 RESULTS	
4.1	**Concentration and hydrolysis values**	See tables A7_1_1_1_1-4a to f	X
4.2	**Hydrolysis rate constant (k_h)**	See table A7_1_1_1_1-5 .	X
4.3	**Dissipation time**	See table A7_1_1_1_1-6	X
4.4	**Concentration – time data**	 Concentration-time data at pH 5.0.	



Concentration-time data at pH 7.0.

Section A7.1.1.1.1
Annex Point IIA7.6.2.1

Hydrolysis as a function of pH and identification of breakdown products



Concentration-time data at pH 9.0.

4.5	**Specification of the transformation products**	The identity of the metabolites is investigated in [redacted] (2003a, b) and [redacted] (2005) (see section A7.1.2).	

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	OECD 111 was followed	X
5.2	**Results and discussion**	The half-life of the hydrolysis of [^{14}C]-copper pyrithione is dependent on pH and temperature. Copper pyrithione is most stable in water at pH 7.0 and 50 °C (half-life of 134 h).	X
5.2.1	k_H	See table A7_1_1_1_1-5	
5.2.2	DT_{50}	See table A7_1_1_1_1-6	
5.2.3	r^2	Not reported	
5.3	**Conclusion**	Validity criteria were fulfilled. Although the test substance degraded via hydrolysis, the hydrolysis rate is still much lower than the photolysis rate and therefore hydrolysis is only of importance when the test substance is not exposed to light.	X
5.3.1	Reliability	1	X
5.3.2	Deficiencies	No	X

Section A7.1.1.1.1 Hydrolysis as a function of pH and identification of breakdown products

Annex Point IIA7.6.2.1

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date

[redacted]

Materials and Methods

[redacted]

Section A7.1.1.1.1
Annex Point IIA7.6.2.1

Hydrolysis as a function of pH and identification of breakdown products

[redacted]

Results and discussion

[redacted]

4.2

Section A7.1.1.1.1
Annex Point IIA7.6.2.1

Hydrolysis as a function of pH and identification of breakdown products

The "k_h" presented in the study summary and the study report correspond to the

[redacted]

[redacted]				

[redacted]

Section A7.1.1.1.1 Hydrolysis as a function of pH and identification of breakdown products

Annex Point IIA7.6.2.1

[redacted]

Conclusion [redacted]

Reliability [redacted]

Acceptability [redacted]

Remarks [redacted]

Table A7_1_1_1_1-1: Type and composition of buffer solutions

pH	Type of buffer (final molarity)	Composition
5	0.05 M	250 mL of 0.1 M monopotassium citrate made up to 0.5 L with water
7	0.05 M	250 mL of 0.1 M monopotassium citrate made up to 0.5 L with water
9	0.05 M	250 mL of 0.1 M boric acid made up to 0.5 L with water

Table A7_1_1_1_1-2: Description of test solution

Criteria	Details
Purity of water	Demineralised, sterile water
Preparation of test medium	A stock solution containing 8.8 µg [^{14}C]-copper pyrithione/mL methanol was prepared by dissolving 3 mg [^{14}C]-copper pyrithione in 10 mL dichloromethane. 50 µL aliquots of this solution were diluted with methanol to obtain the required concentration. 2.5 mL of this stock solution was transferred to 500 mL sterile buffer solutions of pH 5.0, 7.0, and 9.0 and homogenised.
Test concentrations (µg a.i./L)	44 µg [^{14}C]-copper pyrithione/L buffer solution
Temperature (°C)	50 and 60 °C
Controls	In order to determine the between-run variation of retention times, a control sample, containing 44 µg [^{14}C]-copper pyrithione/L buffer solution (pH 7.0) was stored in the refrigerator and analysed on each day of analysis of the study samples
Identity and concentration of co-solvent	Methanol (0.5 % v/v)
Replicates	2 series

Table A7_1_1_1_1-3: Description of test system

Glassware	Sterilised 20-mL sample vials and teflon-coated closures
Other equipment	Calibrated pH electrodes, thermostatically controlled enclosure
Method of sterilization	Glassware was sterilised at 120 °C for at least 30 min before use; buffer solutions were sterilised by filtration over a 0.45 µm filter

Table A7_1_1_1_1-4a: Hydrolysis of test compound and transformation products, expressed as percentage of initial concentrations, at pH 5 and 50 °C

Series I							
Compound	**Sampling times (hours)**						
	0	**76.3**	**97.0**	**119.4**	**142.3**	**168.4**	**240.0**
Parent compound	92.9 95.4	58.2	42.0	40.0	34.0	35.5	20.5
Transformation product 2		2.3	6.8	7.8	10.7	9.4	16.5
Transformation product 3	7.1 4.6	39.5	51.1	52.1	55.4	55.1	63.0
Total % recovery[1)]						82	

Series II						
Compound	**Sampling times (hours)**					
	0	**27.0**	**52.1**	**76.7**	**151.0**	**167.0**
Parent compound	93.7	71.4	59.0	48.3	32.1	38.8 32.5
Transformation product 2			3.8	8.1	16.0	11.2 11.9
Transformation product 3	6.3	28.6	37.3	43.6	51.9	50.0 55.6
Total % recovery[1)]						

[1)] The recovery of radioactivity was between 90 and 110%, unless otherwise stated.

Table A7_1_1_1_1-4b: Hydrolysis of test compound and transformation products, expressed as percentage of initial concentrations, at pH 5 and 60 °C

Series I							
Compound	**Sampling times (hours)**						
	0	**76.6**	**97.0**	**119.4**	**142.3**	**170.6**	**240.0**
Parent compound	92.9 95.4	38.1	27.0	30.5	23.9	27.0	21.3
Transformation product 2		11.0	18.2	24.0	26.4	26.1	29.5
Transformation product 3	7.1 4.6	50.9	54.8	45.4	49.8	46.9	49.2
Total % recovery[1)]							111

Series II						
Compound	**Sampling times (hours)**					
	0	**26.7**	**51.8**	**78.7**	**148.7**	**166.7**
Parent compound	93.7	71.4	59.0	48.3	32.1	38.8
Transformation product 2			3.8	8.1	16.0	11.2
Transformation product 3	6.3	28.6	37.3	43.6	51.9	50.0
Total % recovery[1)]						

[1)] The recovery of radioactivity was between 90 and 110%, unless otherwise stated.

Table A7_1_1_1_1-4c: Hydrolysis of test compound and transformation products, expressed as percentage of initial concentrations, at pH 7 and 50 °C

Series I							
Compound	**Sampling times (hours)**						
	0.1	**68.1**	**88.5**	**114.3**	**137.7**	**167.3**	**233.6**
Parent compound	85.1	73.3	58.1	50.0	40.7	26.8	32.4
Transformation product 2			31.7	38.2	43.1	58.5	51.1
Transformation product 3	14.9	26.7	10.3	11.8	16.3	14.7	16.5
Total % recovery[1)]							
Series II							
Compound	**Sampling times (hours)**						
	0.1	**68.1**	**88.9**	**120.0**	**138.2**	**167.7**	**234.6**
Parent compound	85.1	79.1	60.1	43.2	38.7	31.7	30.7
Transformation product 2			25.7	39.1	48.0	53.7	55.0
Transformation product 3	14.9	20.9	14.2	17.7	13.3	14.6	14.3
Total % recovery[1)]							

[1)] The recovery of radioactivity was between 90 and 110%, unless otherwise stated.

Table A7_1_1_1_1-4d: Hydrolysis of test compound and transformation products, expressed as percentage of initial concentrations, at pH 7 and 60 °C

Series I							
Compound	**Sampling times (hours)**						
	0	**75.7**	**96.4**	**118.7**	**141.7**	**170.6**	**239.4**
Parent compound	94.0	40.0	41.3	32.9	25.9	28.9	17.9
Transformation product 2		36.8	37.5	47.2	46.0	44.8	56.6
Transformation product 3	6.0	23.3	21.2	19.9	28.1	26.7	25.5
Total % recovery[1)]							116

Series II						
Compound	**Sampling times (hours)**					
	0	**26.7**	**51.8**	**79.2**	**148.7**	**166.7**
Parent compound	96.0	72.0	64.9	57.9	34.0	26.8
Transformation product 2		12.1	18.4	24.2	45.8	51.7
Transformation product 3	4.0	15.9	64.9	17.9	20.3	21.5
Total % recovery[1)]					111	116

[1)] The recovery of radioactivity was between 90 and 110%, unless otherwise stated.

Table A7_1_1_1_1-4e: Hydrolysis of test compound and transformation products, expressed as percentage of initial concentrations, at pH 9 and 50 °C

Series I						
Compound	**Sampling times (hours)**					
	0	**75.3**	**96.0**	**118.4**	**141.3**	**169.1**
Parent compound	93.1 94.6	36.0	30.3	26.1	10.9	11.0
Transformation product 1		37.0	40.0	38.4	51.2	48.6
Transformation product 2		1.8	2.0	3.4	7.6	
Transformation product 3	6.9 5.4	25.1	27.7	32.1	30.3	40.4
Total % recovery[1)]						82
Series II						
Compound	**Sampling times (hours)**					
	0	**25.7**	**50.8**	**77.0**	**149.7**	**165.7**
Parent compound	93.7	75.3	48.2	41.1	16.1	7.7
Transformation product 1		16.6	27.0	29.8	50.3	53.9
Transformation product 2			3.6	8.2	5.0	
Transformation product 3	6.3	8.1	21.3	20.9	28.6	38.4
Total % recovery[1)]						

[1)] The recovery of radioactivity was between 90 and 110%, unless otherwise stated.

Table A7_1_1_1_1-4f: Hydrolysis of test compound and transformation products, expressed as percentage of initial concentrations, at pH 7 and 60 °C

Series I								
Compound	**Sampling times (hours)**							
	0	**4.2**	**20.4**	**27.7**	**45.7**	**53.3**	**69.4**	**75.3**
Parent compound	76.0	63.1	39.2	24.3	21.8	16.4	15.9	7.5
Transformation product 1			26.1	47.6	33.3	35.3	46.9	41.7
Transformation product 2	24.0	36.9	34.7	24.3	44.9	48.3	37.2	50.9
Transformation product 3	24.0	36.9	60.8	71.9	78.2	83.6	84.1	92.5
Total % recovery[1)]								
Series II								
Compound	**Sampling times (hours)**							
	0	**4.2**	**20.8**	**28.1**	**46.2**	**53.7**	**69.8**	**76.0**
Parent compound	88.1	75.8	43.9	28.8	15.8	16.2	18.2	9.6
Transformation product 1			25.5	39.2	38.3	41.2	40.4	36.9
Transformation product 2	11.9	24.2	30.6	28.8	45.9	42.6	41.4	53.5
Total % recovery[1)]								

[1)] The recovery of radioactivity was between 90 and 110%, unless otherwise stated.

Table A7_1_1_1_1-5: Hydrolysis rate constants (k_h) as a function of pH and temperature and the correlation coefficient for each set of experiments

pH	Temperature (°C)	Correlation coefficient	Hydrolysis rate constant (* 10^{-6} sec^{-1})
5.0	50	0.98	1.75
		0.96	1.56
	60	0.90	1.82
		0.97	2.04
7.0	50	0.93	1.43
		0.93	1.45
	60	0.96	1.82
		0.99	1.99
9.0	50	0.98	3.65
		0.98	3.90
	60	0.96	7.24
		0.95	7.39

Table A7_1_1_1_1-6: Mean DT50s (hours) of parent compound at pH 5, pH 7 and pH 9 at 50 and 60 °C

	pH 5			**pH 7**			**pH 9**		
	50 °C	**60 °C**	**20 °C[1]**	**50 °C**	**60 °C**	**20 °C[1]**	**50 °C**	**60 °C**	**20 °C[1]**
Parent compound	116	100	192	134	101	336	51.1	26.3	480

[1] Calculated by use of the Arrhenius relationship

Section A7.1.1.1.2 Phototransformation in water including identity of transformation products

Annex Point IIA7.6.2.2

			Official use only
		1 REFERENCE	
1.1	**Reference**	De Vette HQM, Van Es C (2002a) A study on the photolysis of copper pyrithione in aqueous solutions using [^{14}C] copper pyrithione (OECD Proposal, SETAC-Europe and EU Commission Directive 95/36/EC). TNO Chemistry, Report No. 2422/10, August 27, 2002 (unpublished)	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Yoshitomi Fine Chemicals, Ltd.	
1.2.2	Companies with letter of access	-	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Yes, OECD Proposal for a new guideline and the SETAC-Europe procedure as specified by the EU Commission Directive 95/36/EC	X
2.2	**GLP**	Yes	
2.3	**Deviations**	No	
		3 MATERIALS AND METHODS	
3.1	**Test material**	Radio-labelled copper pyrithione ([^{14}C]-copper pyrithione)	
3.1.1	Lot/Batch number	3362-120	
3.1.2	Specification	Specific activity of radio-labelled test material: 28.680 mCi/mmol.	X
3.1.3	Purity	Radio-labelled test material (radiochemical purity): 99.0%.	
3.1.4	Radiolabelling	Copper Omadine Pyridine-2,6-^{14}C	X
3.1.5	UV/VIS absorption spectra and absorbance value	Not available	
3.1.6	Further relevant properties	Not applicable	
3.2	**Reference substances**	No	
3.3	**Test solution**	See table A7_1_1_1_2-1	X
3.4	**Testing procedure**		
3.4.1	Test system	See table A7_1_1_1_2-2.	X
3.4.2	Properties of light source	See table A7_1_1_1_2-2	X
3.4.3	Determination of irradiance	Not reported	X
3.4.4	Temperature	20 ± 3 °C	
3.4.5	pH	7.0	

Section A7.1.1.1.2 Phototransformation in water including identity of transformation products

Annex Point IIA7.6.2.2

3.4.6	Duration of the test	Irradiated samples: 300 sec; dark controls: 60 min	
3.4.7	Number of replicates	2	
3.4.8	Sampling	The irradiated test solutions were samped after 0, 20, 40, 60, 90, 120, and 300 sec. The dark control was taken immediately after incubation and after 30 and 60 min of incubation.	X
3.4.9	Analytical methods	LSC and HPLC	X
3.5	**Transformation products**	Transformation products tested: Yes	X
3.5.1	Method of analysis for transformation products	HPLC	X

4 RESULTS

4.1 Screening test

Preliminary test: Amounts of [^{14}C] copper pyrithione and metabolites as percentage of the initial radioactivity in irradiated aqueous solutions (average of duplicates) and dark control (DC) as detected by HPLC:

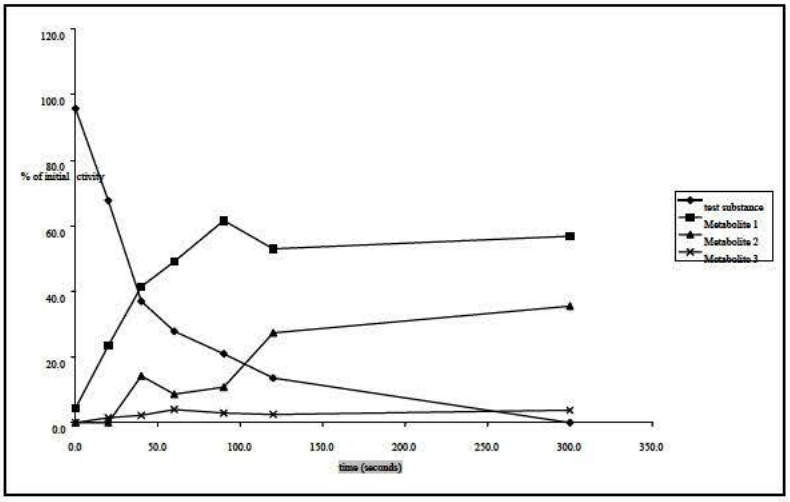
Time (h)	Test substance	Metabolite 1	Metabolite 2	Metabolite 3	Sum
0.0	91.0	9.0	0.0	0.0	100.0
0.5	14.8	45.7	33.1	1.5	95.0
1.0	1.6	68.9	39.7	0.0	110.2
2.0 DC	99.8	5.7	0.0	0.0	105.5

4.2 Actinometer data Not applicable X

4.3 Controls Initial (C_0) and final ($C_{60\ min}$) concentrations of [^{14}C]-copper pyrithione were 95.7 and 90.4% of the initial radioactivity.

4.4 Photolysis data X

4.4.1 Concentration values



X

Amounts of copper pyrithione and its metabolites in irradiated aqueous solutions as mean percentage of the initial radioactivity detected by HPLC-analysis.

Section A7.1.1.1.2 Phototransformation in water including identity of transformation products

Annex Point IIA7.6.2.2

4.4.2	Mass balance	Recovery of radiolabelled test substance at different time points (DC is dark control): Mean overall recovery: 94.1 ± 5.4% for the test system and 95.3 ± 3.6% for the dark control	
4.4.3	k^c_p	0.020 ± 0.002 sec^{-1}	X
4.4.4	Kinetic order	First order	
4.4.5	k^c_p / k^a_p	Not applicable	X
4.4.6	Reaction quantum yield (ϕ^c_E)	Not applicable	
4.4.7	k_{pE}	Not applicable	X
4.4.8	Half-life ($t_{1/2E}$)	34.1 sec	X

Time (s)	DPM total	Recovery
0.0	155600	100.0
0.0 DC	142000	91.3
20	144050	92.6
40	147475	94.8
60	139225	89.5
90	149750	96.2
120	149925	96.4
300	149400	96.0
30 min DC	150050	96.4
60 min DC	152600	98.1

4.5	**Specification of the transformation products**	The maximum amount of the metabolite 1 with a retention time of approximately 8 min. was 61.6% of the initial activity and the metabolite 2 with a retention time of approximately 6 min. was 35.5%. The maximum amount of the third metabolite with a retention time of approximately 14 min. was 3.7%. The identity of the metabolites is investigated in [redacted] (2003a, b) and [redacted] (2005) (see section A7.1.2).	X
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	The OECD Proposal for a new guideline and the SETAC-Europe procedure as specified by the EU Commission Directive 95/36/EC were followed	X
5.2	**Results and discussion**	[^{14}C]copper pyrithione in aqueous solutions demonstrated a very rapid degradation when irradiated. The half-life under the chosen conditions was 34.1 sec.	
5.2.1	k^c_p	0.020 ± 0.002 sec^{-1}	
5.2.2	K_{pE}	Not applicable	
5.2.3	ϕ^c_E	Not applicable	
5.2.4	$t_{1/2E}$	34.1 sec	X
5.3	**Conclusion**	Validity criteria were fulfilled. The very rapid photolysis of [^{14}C]copper pyrithione indicates that metabolites were also present in the test media used in the toxicity tests. Therefore, it is expected that the observed effects resulted from the mixture of parent compound and its metabolites.	X
5.3.1	Reliability	1	X
5.3.2	Deficiencies	No	

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date

Materials and Methods

[redacted]

4.4.7

According to Equation 13 of the US EPA guideline, $k_{pE} = k_p / 2.2$ for test tubes

[redacted]

Results and discussion

[redacted]

Conclusion

[redacted]

Reliability

[redacted]

Acceptability

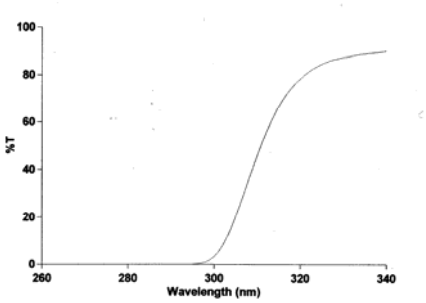
[redacted]

Remarks	[redacted]

Table A7_1_1_1_2-1: Description of test solution and controls

Criteria	Details
Purity of water	0.05 M phosphate buffer solution of pH 7 (hydrolysis rat in this solution is much lower than the expected rate of photolysis)
Preparation of test chemical solution	An amount (approximately 3.9 mg) of [^{14}C] copper pyrithione was dissolved in 15 mL of dichloromethane. From this solution, 0.7 mL was mixed with 9.0 mL of methanol and this solution was used as stock solution. An aliquot (50 µL) was pippeted in each test vessel containing 9.95 mL of phosphate buffer. The final concentration was 77.2 ng/mL.
Test concentrations (µg a.s./L)	77.2
Temperature (°C)	20 ± 3 °C
Preparation of a.s. solution	See preparation of test chemical solution
Controls	Additional flasks with aqueous solution with the same concentration of the test substance were kept in the dark in order to distinguish between photochemical degradation and other reactions.
Identity and concentration of co-solvent	Dichloromethane (0.5 % v/v)

Table A7_1_1_1_2-2: Description of test system

Criteria	Details
Laboratory equipment	Open scintillation vials
Test apparatus	LSC and HPLC
Properties of artificial light source:	
Nature of light source	Xenon lamp at a distance of ca. 26.5 cm and a capacity of 800 W
Emission wavelenght spectrum	
Light intensity	34.5 µmol/s^{-1} · m^{-2}
Filters	Wavelengths < 290 nm were excluded
Properties of natural sunlight:	Not applicable
Latitude	-
Hours of daylight	-
,Time of year	-
Light intensity	-
Solar irradiance (L_λ)	-

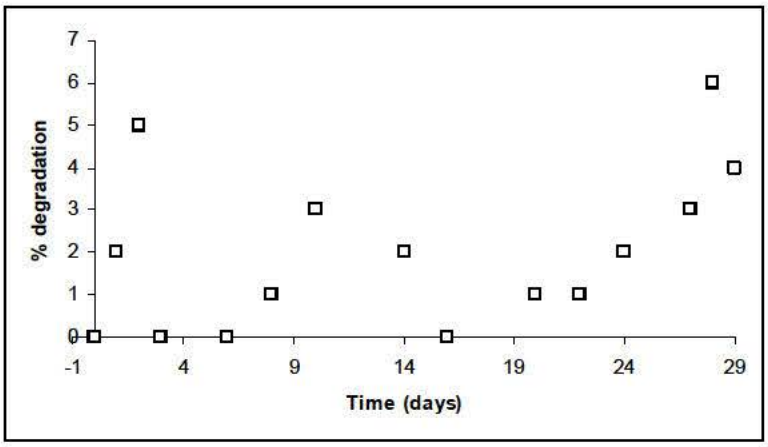
Section A7.1.1.2.1 Biodegradability (ready)

Annex Point IIA7.6.1.1

			Official use only
		1 REFERENCE	
1.1	**Reference**	Mead C (2000) Copper pyrithione: assessment of ready biodegradability; CO_2 evolution test. Safepharm Laboratories Limited, Report No: ECCMR00517, January 18, 2000 (unpublished)	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Yoshitomi Fine Chemicals, Ltd.	
1.2.2	Companies with letter of access	-	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Yes, OECD 301B, EC C.4, and OPPTS 835.3110	
2.2	**GLP**	Yes	
2.3	**Deviations**	No	
		3 MATERIALS AND METHODS	
3.1	**Test material**	Copper pyrithione	
3.1.1	Lot/Batch number	990210	X
3.1.2	Specification	As given in section 2	X
3.1.3	Purity	As given in section 2	X
3.1.4	Further relevant properties	The test material is photodegradable and was stored under protection from light	
3.1.5	Composition of Product		
3.1.6	TS inhibitory to microorganisms	Yes, toxicity was observed in the culture medium at 10 mg C/L. In the respiration inhibition test, a 3-h EC50 of 15 mg/L was found.	X
3.1.7	Specific chemical analysis	TOC analyser (Ionics 1555B and Dohrman DC-190)	
3.2	**Reference substance**	Yes, sodium benzoate	
3.2.1	Initial concentration of reference substance	17.1 mg/L	X
3.3	**Testing procedure**		
3.3.1	Inoculum / test species	See table A7_1_1_2_1-1	X
3.3.2	Test system	See table A7_1_1_2_1-2	X
3.3.3	Test conditions	See table A7_1_1_2_1-3	X
3.3.4	Method of preparation of test solution	The test substance was directly dispersed in culture medium	X

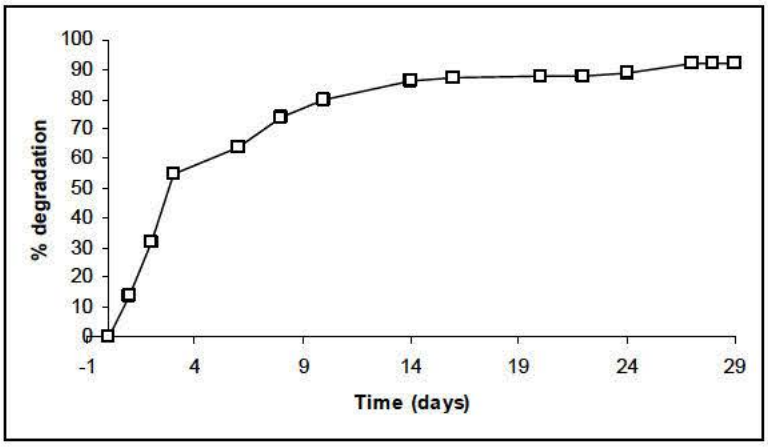
Section A7.1.1.2.1 Biodegradability (ready)

Annex Point IIA7.6.1.1

3.3.5	Initial TS concentration	13.2 mg/L (nominal concentration)	X
3.3.6	Duration of test	29 d	
3.3.7	Analytical parameter	CO_2 evolution	X
3.3.8	Sampling	The first CO_2 absorber vessel was sampled on days 0, 1, 2, 3, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 27, 28, and 29. The second absorber vessel was sampled on days 0 and 29.	
3.3.9	Intermediates/ degradation products	Not identified	
3.3.10	Nitrate/nitrite measurement	No	X
3.3.11	Controls	Control without test substance, control with standard material, and toxicity control	X
3.3.12	Statistics	The percentage degradation was calculated according to the equations given in OECD 301B	X
		4 RESULTS	
4.1	**Degradation of test substance**		
4.1.1	Graph	 Course of degradation of copper pyrithione against time	X
4.1.2	Degradation	6% degradation after 28 days	X
4.1.3	Other observations	In an initial experiment at a concentration of 10 mg C/L, the test substance showed toxicity to the sewage sludge microorganisms used in the study	X
4.1.4	Degradation of TS in abiotic control	Not applicable	

Section A7.1.1.2.1 Biodegradability (ready)

Annex Point IIA7.6.1.1

4.1.5	Degradation of reference substance	 Course of degradation of sodium benzoate against time	
4.1.6	Intermediates/ degradation products	Not applicable	

5 APPLICANT'S SUMMARY AND CONCLUSION

5.1	**Materials and methods**	OECD 301B, EC C.4, and OPPTS 835.3110 were followed	
5.2	**Results and discussion**	The test substance attained 6% degradation after 28 d	X
5.3	**Conclusion**	Validity criteria were fulfilled, except that the IC/TC ratio of the test media exceeded 5% (see table A7_1_1_2_1-4). This was probably due to the low level of TC added and is not considered to have influenced the results of the test. The test substance cannot be considered to be readily biodegradable in 29 d under the conditions of the test. Although ≥ 25% degradation was observed in the toxicity control after 14 days (as required by the OECD guideline), inhibition of the inoculum cannot be excluded as the degradation in the toxicity control (test substance plus sodium benzoate) is less than the sum of the degradation in the test substance treatment and the sodium benzoate treatment separately (71% versus 96% after 28 days, respectively).	
5.3.1	Reliability	1	X
5.3.2	Deficiencies	Yes, the IC/TC ratio of the test media exceeded, but this is not considered to have influenced the results of the test.	

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date

Materials and Methods

[redacted]

Results and discussion

[redacted]

Conclusion

[redacted]

Reliability

[redacted]

Acceptability

[redacted]

Remarks

[redacted]

Table A7_1_1_2_1-1: Inoculum / Test organism

Criteria	Details
Nature	Activated sludge
Species	Mixed population of activated sewage sludge micro-organisms
Strain	Not applicable
Source	Sewage treatment plant treating predominantly domestic sewage
Sampling site	Severn Trent Water Plc sewage treatment plant at Belper, Derbyshire, UK
Laboratory culture	No, the activated sewage sludge sample was used on the day of collection
Method of cultivation	Not applicable
Preparation of inoculum for exposure	Sample of sludge was washed three times by settlement and resuspension in culture medium to remove any excessive amounts of DOC possibly present
Pretreatment	Continuous aeration upon receipt
Initial cell concentration	30 mg suspended solids/L

Table A7_1_1_2_1-2: Test system

Criteria	Details
Culturing apparatus	5-L glass culture vessels containing 3 L of test solution
Number of culture flasks/concentration	2 for the control, the reference material and each test concentration and 1 for the toxicity control (test substance and reference material)
Aeration device	CO_2-free air was produced by passing compressed air through a glass column containing self indicating soda lime (Carbosorb®) granules
Measuring equipment	CO_2 produced by degradation was collected in two 500-mLDreschel bottles containing 350 mL of 0.05 M NaOH.
Test performed in closed vessels	Yes

Table A7_1_1_2_1-3: Test conditions

Criteria	Details
Composition of medium	Culture medium according to OECD 301B, prepared by adding minerals to purified water
Additional substrate	No
Test temperature	21 °C
pH	Not reported
Aeration of dilution water	Yes, ca. 40 mL/min
Suspended solids concentration	30 mg/L
Other relevant criteria	The test solution was stirred and the test was performed in the dark

Table A7_1_1_2_1-45: Pass levels and validity criteria for tests on ready biodegradability

	fulfilled	not fulfilled
Pass levels		
70% removal of DOC resp. 60% removal of ThOD or $ThCO_2$		x
Pass values reached within 10-d window (within 28-d test period) - not applicable to MITI-I-Test - 14-d window acceptable for Closed-Bottle-Test		x
Criteria for validity		
Difference of extremes of replicate values of TS removal at plateau (at the end of test or end of 10-d window) < 20%	Not reported	Not reported
Percentage of removal of reference substance reaches pass level by day 14	x	

Section A7.1.1.2.2 Annex Point IIA7.6.1.2	Biodegradability (inherent)	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [X]	**Technically not feasible [ ]** **Scientifically unjustified [X]**	X
Limited exposure [X]	**Other justification [ ]**	X
Detailed justification:	The inherent biodegradability was not determined, because a water/sediment study in sea water was performed (see section A7.1.1.2.3).	x
Undertaking of intended data submission [ ]		
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Evaluation of applicant's justification	[redacted]	
Conclusion		
Remarks		

Section A7.1.1.2.3 Marine water/sediment degradation study

Annex Point IIA7.6.1.3

			Official use only
		1 REFERENCE	
1.1	**Reference**	Bowmer CT, De Vette HQM (2003) A marine water/sediment degradation study using [^{14}C] labelled copper pyrithione (OECD 308 & SETAC-Europe). TNO Chemistry, Report No: 2422/07, November 6, 2003 (unpublished)	
1.2	**Data protection**	Yes	
1.2.1	Data owner	Yoshitomi Fine Chemicals, Ltd.	
1.2.2	Companies with letter of access	-	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Yes, OECD 308 and the SETAC Europe guidelines as specified by the EU Commission Directive 95/36/EC	
2.2	**GLP**	Yes	
2.3	**Deviations**	Yes, the organic matter contents of the two marine sediments differ from the content recommended by the test guidelines for freshwater sediments. Since no properties for the selection of marine water/sediments are given in the guidelines, sediments which best represent coastal benthic conditions were chosen (one with low and one with a higher organic matter content).	X
		3 MATERIALS AND METHODS	
3.1	**Test material**	Non-radiolabelled test material (used in fumigation tests): Copper pyrithione Radiolabelled test material (used in degradation tests): [^{14}C]-Copper Pyrithione (Copper Omadine, [Pyridine-2,6-^{14}C])	
3.1.1	Lot/Batch number	Unlabelled test material: Y104 E. Radio-labelled test material: 3362-120.	
3.1.2	Specification	Non-radiolabelled test material: as given in section 2 Radiolabelled test material: specific activity 28.680 mCi/mmol	
3.1.3	Purity	Non-radiolabelled test material: 99.9% (as given in section 2) Radio-labelled test material (radiochemical purity): 99.0%	
3.1.4	Further relevant properties	The test material is photodegradable and was stored under protection from light	
3.1.5	Composition of Product		
3.1.6	TS inhibitory to microorganisms	Yes, in the ready biodegradability test, toxicity was observed in the culture medium at 10 mg C/L. In the respiration inhibition test, a 3-h EC50 of 15 mg/L was found.	X
3.1.7	Specific chemical analysis	LSC and HPLC	X

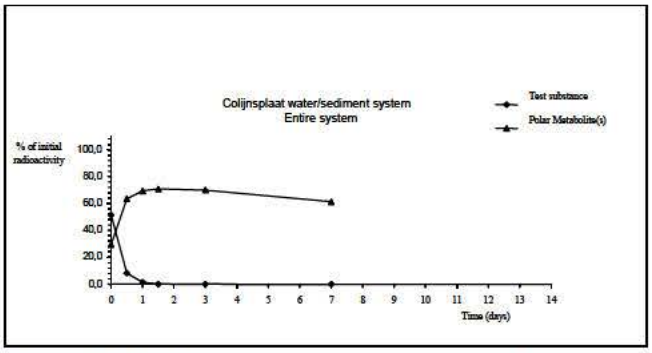
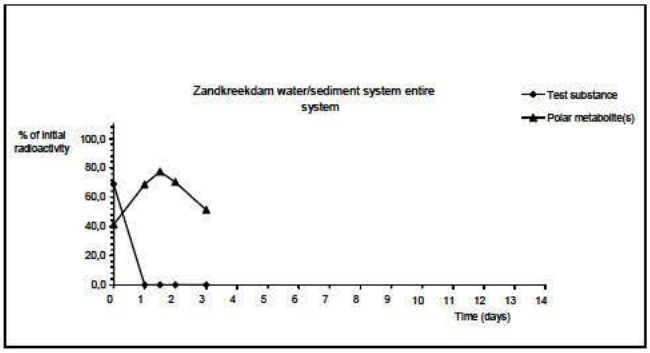
Section A7.1.1.2.3 Marine water/sediment degradation study

Annex Point IIA7.6.1.3

3.2	**Reference substance**	No	
3.2.1	Initial concentration of reference substance		
3.3	**Testing procedure**		
3.3.1	Inoculum / test species	See table A7_1_1_2_3-1 Anaerobic water conditions do not exist in the environment and are therefore not relevant. Anaerobic sediment conditions do exist in the environment, but the present water/sediment study already accounts for that as the sediment has got an anaerobic phase. As copper pyrithione biodegrades very quickly under aerobic conditions and exposure of the anaerobic sediment compartment is unlikely, an anaerobic water/sediment study is not considered necessary.	X
3.3.2	Test system	See table A7_1_1_2_3-3	
3.3.3	Test conditions	See table A7_1_1_2_3-4	X
3.3.4	Method of preparation of test solution	The test substance was dissolved in isopropanol (0.016% v/v)	X
3.3.5	Initial TS concentration	0.083 mg/L (Colijnsplaat), 0.082 mg/L (Zandkreekdam), and 0.084 mg/L (TNO) radiolabelled copper pyrithione	X
3.3.6	Duration of test	7 d	
3.3.7	Analytical parameter	[^{14}C]CO_2 evolution, dissolved radioactivity present in aqueous phase, extractable radioactivity present in sediment phase, and unextractable radioactivity (bound residue) present in sediment phase	
3.3.8	Sampling	Duplicate test flasks containing the marine water/sediment systems were taken after 0, 0.5, 1, 1.5, 2, 3, 7, and 14 d.	X
3.3.9	Intermediates/ degradation products	Not identified	X
3.3.10	Nitrate/nitrite measurement	Not applicable	
3.3.11	Controls	A reference water/sediment system (freshwater) was tested	X
3.3.12	Statistics	A mass balance was calculated for each sampling point. DT50 and DT90 values were calculated using Jandel TableCurve™ 2D (version 4) software assuming first-order kinetics.	

4 RESULTS

4.1 Degradation of test substance

4.1.1	Graph	 Course of degradation against time for Colijnsplaat water/sediment system	X
		 Course of degradation against time for Zandkreekdam water/sediment system	
4.1.2	Degradation	In the entire Colijnsplaat system, [^{14}C]copper pyrithione decreased from 51.5% of the initial activity to 0.0% after 1.5 d of incubation. In the entire Zandkreekdam system, the test substance decreased from 69.0% at the start to 0.0% after 1 d of incubation. An apparently single metabolite was formed (or a group of polar metabolites) accounting for 70.9% of the initial radioactivity after 1.5 d (Colijnsplaat) and 77.4% after 1.5 d (Zandkreekdam). DT50 values for the aqueous phase and the entire system were 4.6 and 1.3 h for Colijnsplaat and 3.7 and 1.3 h for Zandkreekdam, respectively.	X
4.1.3	Other observations	After 15 d, microbial biomass had decreased from 174 mg/kg (dw) to 59 mg/kg (34 % of start value) in Colijnsplaat sediment and to 134 mg/kg (77 % of start value) in Zandkreekdam sediment. For TNO sediment, microbial biomass had doubled to 409 mg/kg. The sediments were considered to be microbially active during the test, although a variable inhibition of microbial activity was observed in the marine sediments.	
4.1.4	Degradation of TS in abiotic control	Not applicable	
4.1.5	Degradation of reference substance	Not applicable	
4.1.6	Intermediates/ degradation	In all three water/sediment systems, nearly all test material degraded into a metabolite. However, the observed HPLC peak may represent	

	products	more than one co-eluted fraction in the aqueous phase. Bound residues were observed in all three sediments. The identity of the metabolites is investigated in [redacted] (2003a, b) and [redacted] (2005) (see section A7.1.2).	
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	OECD 308 and the SETAC Europe guidelines as specified by the EU Commission Directive 95/36/EC were followed	
5.2	**Results and discussion**	The test substance was rapidly degraded at 15 °C; after 1.5 d of incubation, all test substance was transformed into one or a group of polar metabolites in both marine water/sediment systems. DT50 values for the aqueous phase and the entire system were 4.6 and 1.3 h for Colijnsplaat and 3.7 and 1.3 h for Zandkreekdam, respectively.	X
5.3	**Conclusion**	Validity criteria can be considered as fulfilled (recovery of radiolabelled test material between 90 and 110%)	
5.3.1	Reliability	1	X
5.3.2	Deficiencies	No	

Evaluation by Competent Authorities

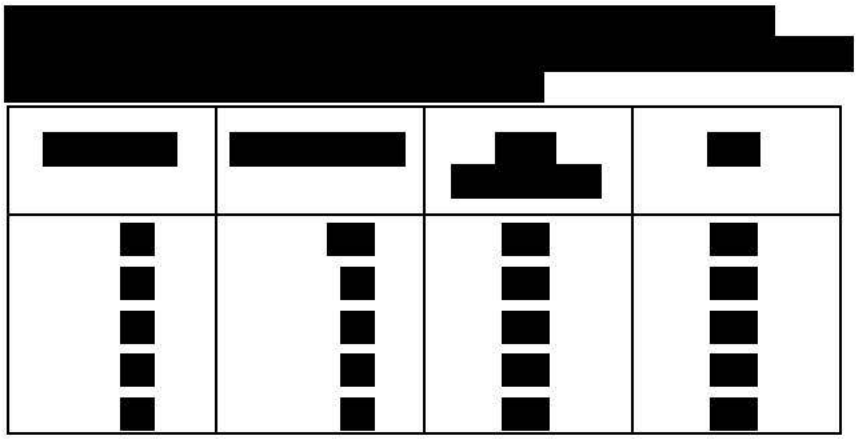
EVALUATION BY RAPPORTEUR MEMBER STATE

Date [redacted]

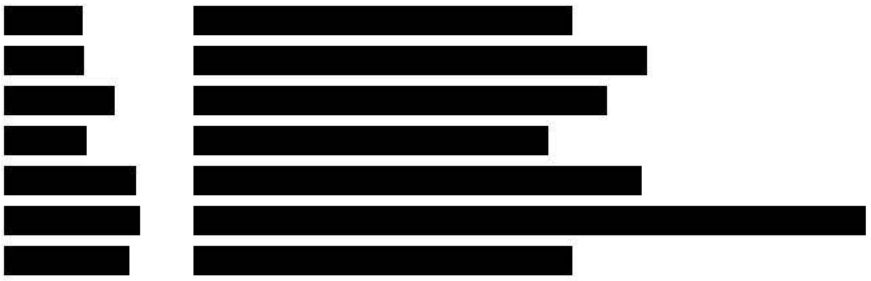
Materials and Methods [redacted]

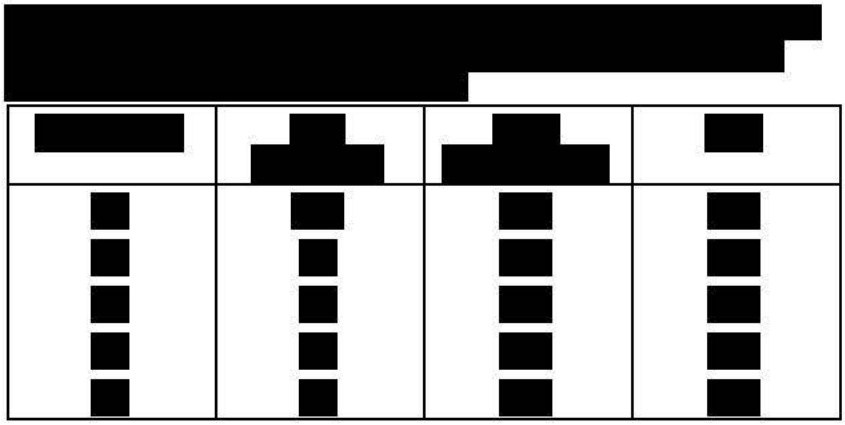
3.3.4

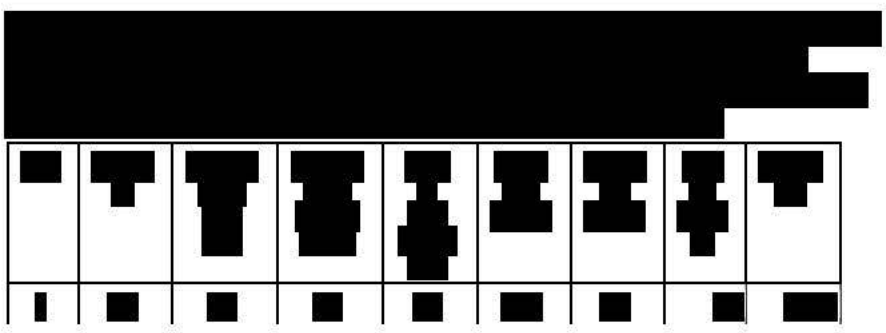
Results and discussion

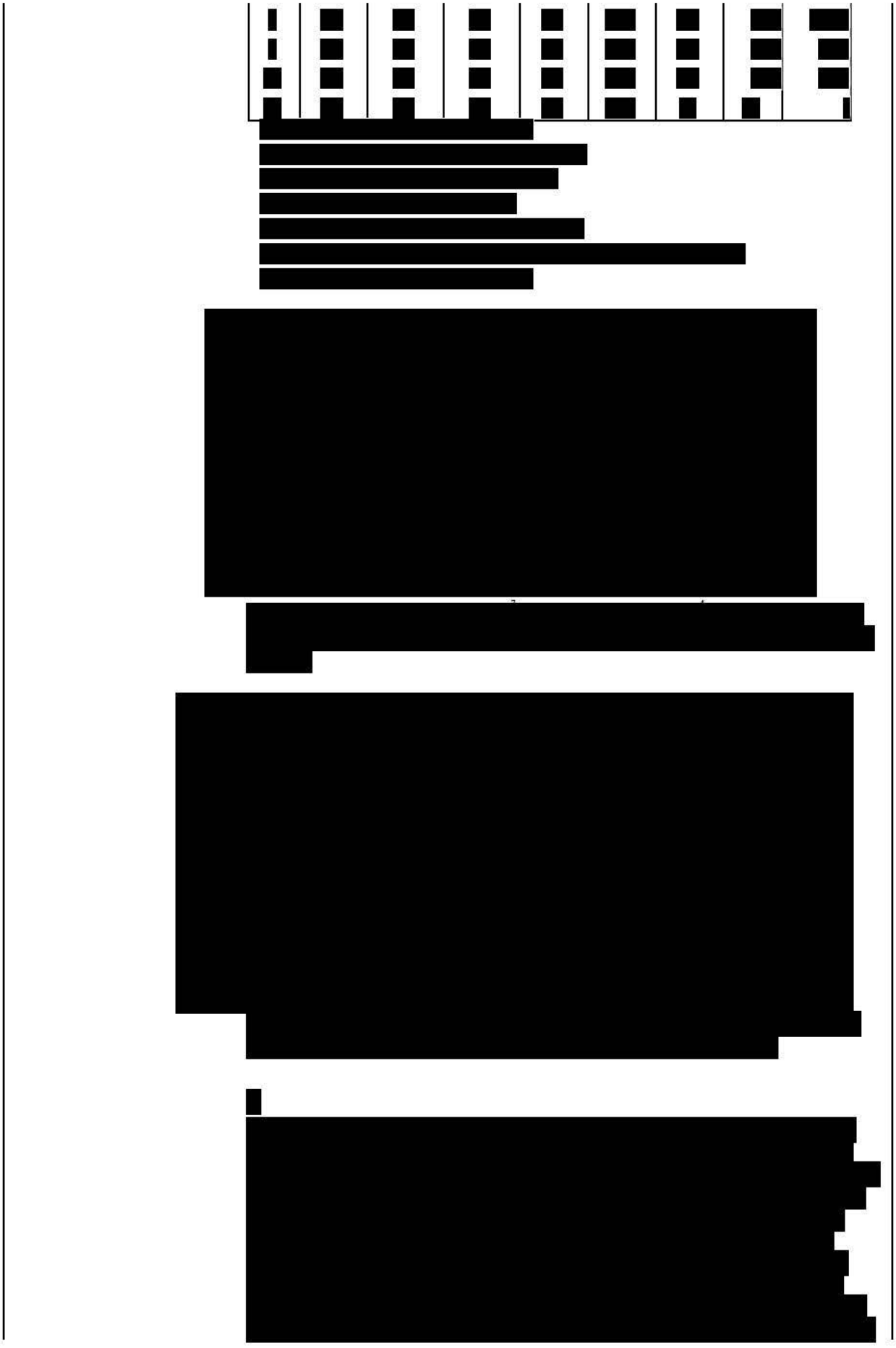


		CO_2 trap	CO_2 in water	forma tion	phase	phase	resid ue	









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[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]

[redacted]

Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

Table A7_1_1_2_3-1: Inoculum / Test organism

Criteria	Details
Nature	Two marine water/sediment systems (Colijnsplaat and Zandkreekdam) and one reference freshwater/sediment system (TNO). The characteristics of the three sediments are given in table A7_1_1_2_3-2.
Species	Mixed population present in field samples
Strain	Not applicable
Source	Marine field samples, representative of coastal areas in terms of grain size, organic matter and silt/clay content. Freshwater field samples frequently used as reference in tests of this type at TNO
Sampling site	Marine water and sediment samples were taken from coastal areas of Colijnsplaat and Zandkreekdam. Freshwater reference water and sediment was taken from the North-Eastern part of the ditch surrounding the TNO premises at Schoemakerstraat 97, Delft, the Netherlands. Sediment samples were taken from the top 5 cm layer (approximately).
Laboratory culture	No, samples were pre-incubated in the laboratory prior to use in the test
Method of cultivation	Not applicable
Preparation of substrate for exposure	Sediment samples were allowed to settle, the supernatants were drawn off, the sediments were passed through a 2 mm sieve and the dry solid contents were determined. Marine water samples were sieved at 0.1 mm to remove zooplankton and fortified with sea salt to ca. 31‰.
Pretreatment	Water/sediment systems were acclimatised for up to 35 days at 15 ± 2 °C with some temporary increased to 20 °C, in the dark and on a slowly revolving rotary shaker
Initial cell concentration	174 mg biomass/kg dry sediment (mean for the three sediments)

Table A7_1_1_2_3-2: Composition of the three sediments used in the present study

	Unit	Colijnsplaat water/sediment system	Zandkreekdam water/sediment system	TNO water/sediment system
Origin		Colijnsplaat	Zandkreekdam	Delft
Country		The Netherlands	The Netherlands	The Netherlands
Date of sampling		1 February 2001	1 February 2001	2 February 2001
63µm – 2mm	%	54.14	80.04	42.28
2µm - 63µm (silt)[1]	%	30.02	12.99	28.67
<2µm (clay)	%	15.84	6.97	29.05
pH (1:5) in water		8.6	8.7	8.0
pH (1:5) in 1M KCl		8.6	8.7	7.8
pH (1:5) in 0.01M $CaCl_2$		7.3	7.7	7.3
Critical Electrolyte Concentration (CEC)	mEq/100g	8.7	2.1	22.2
Organic Carbon	%	1.5	0.8	3.3
Organic Matter[2]	%	2.6	1.4	5.6
$Phosphorus_{total}$	mg/kg	783.6	437.1	365.0
$Nitrogen_{total}$	mg/kg	1498.1	546.0	2701.8

[1] Silt is defined as having a grain size of between 63µm and 4µm and that of clay as < 4µm on the basis of gravimetric analysis of sieved fractions. As silt/clay is used here as the operative description of the sediments, the fact that a 2µm in place of a 4µm sieve was used is not of importance.

[2] Organic matter is calculated as ca. 1.7 times the organic carbon content.

Table A7_1_1_2_3-3: Test system

Criteria	Details
Culturing apparatus	Fumigation test for the determination of biomass: 250-mL flasks containing a total amount of 200 mL sediment and surface water. Flasks were filled with 91.7 g wet sediment and 171 mL seawater (Colijnsplaat), 87.6 g wet sediment and 171 mL seawater (Zandkreekdam), and 44.4 g wet sediment and 175.6 mL ditch water (TNO). Degradation test: 1000-mL cylindrical incubation flasks (biometer flasks) with a soda lime column for trapping evolved CO_2 which also contained an oil-covered, quartz-wool layer for trapping volatile metabolites. Flasks were filled with sediment and water to achieve a ratio of 1:4 for the marine systems. For Colijnsplaat, flasks were filled with 275 g wet sediment containing 118 g pore water and 513 g water. For Zandkreekdam, 260 g wet sediment containing 80 g pore water and 513 water was used. For the TNO systems, 133 g of wet sediment containing 73 g pore water and 527 g water was used.
Number of culture flasks/concentration	3 (fumigation test); 2 (degradation test)
Aeration device	Not reported
Measuring equipment	LSC and HPLC
Test performed in closed vessels due to significant volatility of TS	Yes, vessels were closed with a soda lime column for trapping evolved CO_2 which also contained an oil-covered, quartz-wool layer for trapping volatile metabolites

Table A7_1_1_2_3-4: Test conditions

Criteria	Details
Composition of medium	Natural sea- and freshwater and corresponding sediment
Additional substrate	No
Test temperature	15 ± 2 °C
pH of aqueous phase (minimum – maximum)	Colijnsplaat: 7.8 – 8.2 Zandkreekdam: 7.8 – 8.3 TNO: 7.9 – 8.6
Aeration of dilution water	No
Suspended solids concentration	Not reported
Other relevant citeria	The test systems were placed on a slowly revolving rotary shaker

Section A7.1.1.2.4/01 Fate and behaviour in water – Speciation of copper pyrithione

			Official use only
		1 REFERENCE	
1.1	**Reference**	Kramer KJ (2008) Chemical speciation of copper pyrithione in sea and surface waters. MERMAYDE, Report No. MM-1051, August 27, 2008 (unpublished)	X
1.2	**Data protection**	Yes	
1.2.1	Data owner	API Corporation	
1.2.2	Companies with letter of access	-	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	No, not applicable	
2.2	**GLP**	No	
2.3	**Deviations**	No	
		3 MATERIALS AND METHODS	
3.1	**Test material**	Speciation modelling with Copper pyrithione	
3.1.1	Lot/Batch number	Not applicable	
3.1.2	Specification	Not applicable	
3.1.3	Purity	Not applicable	
3.1.4	Further relevant properties	Not applicable	
3.2	**Reference substance**	Not applicable	
3.2.1	Initial concentration of reference substance	-	
3.3	**Test solution**		
3.4	**Testing procedure**		
3.4.1	Test system	The mathematical speciation modelling program CHEAQS Pro has been set according to the following input criteria: pH: fixed for each medium Ionic strength: calculated Convergence criterion: 0.010% (1.00E-04 M) Precipitation equilibria: Not included Adsorption equilibria: Not included Redox equilibria: Not included Organic complexation: Included; model used: Cabaniss & Shuman (1988a, 1988b)	

Section A7.1.1.2.4/01 Fate and behaviour in water – Speciation of copper pyrithione

		Not extrapolated to other metals than Cu Components entered as: total concentration (H+ as free activity) Dataset: NIST, 2004	
3.4.2	Components	Copper (Cu) and pyrithione (PT) shall be included in the set of components. Other elements can be included when they are expected to seriously interfere with the species distribution. A first obvious additional cationic component is the proton H+. For other cations the elements shall be selected on the basis firstly of stability constant (to form (metal)PTn complexes) and presence, the concentration in the environment. For the following elements the stability constants have been defined and the stability of the PT complexes is considered to increase: Na<Mn<Fe<Co<Ni<Zn<Cu. As a result only Zn was included in the model calculations. Based on earlier studies it is known that copper forms (mixed) complexes with OH-, CO_3^{2-} and SO_4^{2-}. Cl^- has been added because of its importance for the calculation of the ionic strength by the program. The OH- is automatically introduced from the pH. These ligands have been included in the components list. Copper is known to form strong complexes with organic matter in natural waters. For complexation with natural organic matter (dissolved organic carbon, DOC), an approximation has been used in CHEAQS Pro.	X
3.4.3	Species	The following species were defined and added to the program. **Species** / **log K** HPT 4.67 $CuPT_2$ 8.5 ‘ $ZnPT^+$ 5.9 $ZnPT_2$ 5.4 $FePT_3$ 4.7 “	X
3.4.4	Duration of the test	The characteristics of the aquatic media are presented in Table 7.1.1.2.4_1 for the components identified above.	X
		4 RESULTS	
4.1	**Cu speciation**	Focusing first on the Cu-speciation – thus the relative distribution of copper over the Cu-containing cation and complexes - at high concentrations of PT nearly all PT is bound in CuPT2, with 0% contribution for the Cu2+ and the CuDOC. With decreasing [PT], this changes to an increase in concentrations of Cu2+ and CuDOC. For free copper the relative contribution of Cu2+ at S=35 increases to 3.4% for decreasing [PT], for S=0 only up to 0.34%. This is the result of the increase of DOC from 0.5 mg (at S=35) to 5 mg (at S=0). This is confirmed by the CuDOC concentrations: at S=35, maximum CuDOC levels reach 31.8% whereas at S=0 it levels off at 91.2%, emphasising the importance of the complexing capacity of the DOC. For the entire range of salinities in the five waters at PT concentrations of 1.0E-02 M and above, >99% of the copper is bound into CuPT2. At a concentration of 1.0E-03 M PT, a considerable amount of the copper is bound in the CuPT2 complex, but this depends on the salinity, or better the effect of the increased DOC (S=35: 61.9%, S=0: 39% bound in CuPT2). At a [PT] level of 1.0E-04 M or below, hardly any copper is bound to PT (< 1.0E-10 M CuPT2).	

Section A7.1.1.2.4/01 Fate and behaviour in water – Speciation of copper pyrithione

4.2	**PT speciation**	For the PT-species distribution – thus the relative distribution of PT over the PTcontaining anion and complexes - the picture looks rather simple. For the five waters and nearly all PT-concentrations the free PT- is the dominant species (<99%). This means that also in absolute terms practically all PT is in this form. Only at very low [PT], ≤1.0E-6 M, and especially at S=0, some PT is bound into the ZnPT+ ion (up to 17.5% at 1.0E-10 M at S=0). Only a tiny fraction, less than 0.1% is present as HPT.	
4.3	**Relative distribution**	For the relative distribution in the speciation of Cu, no difference between the pyrithione concentration levels 1.0E-05 M and 1.0E-07 M exists. Both show a relatively high contribution of CuDOC, but only at the lowest copper concentrations. At higher Cu concentrations the fraction CuDOC becomes of less importance. This tendency is also shown for the fraction free Cu2+. For the relative distribution in the speciation of PT, in most situations the dominant species is PT-. However, at the higher concentrations of copper (1.0E-02 to 1.0E-4 M) as well as high concentrations of PT (1.0E-01 to 1.0E-03 M) there is a shift towards the CuPT2 complex, with a maximum contribution of nearly 62% of the PT-concentration at [Cu(total)]=1.00E-02 M and [PT(total)]=1.00E-03 M. In an absolute sense, there is an increase of CuPT2 with increasing concentrations of Cu and PT.	
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	The mathematical speciation modelling program CHEAQS Pro has been used.	
5.2	**Conclusion**	From the modelling studies it becomes clear that the speciation of copper is only to some level affected by an increase in the concentration pyrithione (PT). Only at higher concentrations of PT a considerable part of the Cu may be in the CuPT2 complex, provided the concentration of Cu is also high. The ligand PT- clearly competes with natural organic matter (DOC) to form trace metal complexes. This leads to lowering the free copper (Cu2+) concentration. The species distribution of pyrithione shows that the dominant species is the free ligand PT-, followed by the zinc species ZnPT+. Addition of copper to the system, e.g. as co-biocide in the paint matrix – does not lead to different conclusions: higher concentrations of Cu and PT favour the formation of CuPT2.	
5.2.1	Reliability	2	X
5.2.2	Deficiencies	No GLP study, modelling.	X

Section A7.1.1.2.4/01 Fate and behaviour in water – Speciation of copper pyrithione

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date

Materials and Methods

Section A7.1.1.2.4/01 Fate and behaviour in water – Speciation of copper pyrithione

Results and discussion

[redacted]

Conclusion

Reliability

[redacted]

Acceptability

Remarks

[redacted]

Table 7.1.1.2.4_1. Components used in the calculations and definition of their concentration for the different waters (concentration in mol/l (M) unless indicated otherwise)

	sea/ocean	coastal	estuarine		fresh
S	35	25	15	5	0
components					
pH	8.1	8.0	7.8	7.7	7.7
H	7.94E-09	1.00E-08	1.58E-08	2.00E-08	2.00E-08
Mg	5.20E-02	3.73E-02	2.25E-02	7.78E-03	4.12E-04
Ca	1.01E-02	7.62E-03	5.17E-03	2.72E-03	1.50E-03
Cu(II)	1.57E-08	3.01E-08	4.45E-08	5.89E-08	6.61E-08
Zn(II)	1.53E-07	2.58E-07	3.63E-07	4.68E-07	5.20E-07
HCO3	2.27E-03	2.40E-03	2.52E-03	2.64E-03	2.70E-03
SO4	8.26E-02	5.92E-02	3.57E-02	1.22E-02	5.21E-04
Cl	5.33E-01	3.81E-01	2.29E-01	7.70E-02	1.02E-03
DOC (mg/l)	0.50	1.79	3.07	4.36	5.00

Section A7.1.1.2.4/02 Fate and behaviour in water – Speciation of copper pyrithione

			Official use only
		1 REFERENCE	
1.1	**Reference**	Kramer KJ (2009) Chemical speciation of copper pyrithione in sea and surface waters. MERMAYDE, Report No. MM-1051a, March 19, 2009 (unpublished)	X
1.2	**Data protection**	Yes	
1.2.1	Data owner	API Corporation	
1.2.2	Companies with letter of access	-	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	No, not applicable	
2.2	**GLP**	No	
2.3	**Deviations**	No	
		3 MATERIALS AND METHODS	
3.1	**Test material**	Speciation modelling with Copper pyrithione	
3.1.1	Lot/Batch number	Not applicable	
3.1.2	Specification	Not applicable	
3.1.3	Purity	Not applicable	
3.1.4	Further relevant properties	Not applicable	
3.2	**Reference substance**	Not applicable	
3.2.1	Initial concentration of reference substance	-	
3.3	**Test solution**		
3.4	**Testing procedure**		
3.4.1	Test system	The mathematical speciation modelling program CHEAQS Pro has been set according to the following input criteria: pH: fixed for each medium Ionic strength: calculated Convergence criterion: 0.010% (1.00E-04 M) Precipitation equilibria: Not included Adsorption equilibria: Not included Redox equilibria: Not included Organic complexation: Included; model used: Cabaniss & Shuman (1988a, 1988b)	

Section A7.1.1.2.4/02 Fate and behaviour in water – Speciation of copper pyrithione

Not extrapolated to other metals than Cu

Components entered as: total concentration (H+ as free activity)

Dataset: NIST, 2004; added the PT complexes for hydrogen, copper and zinc

3.4.2 Components

Copper (Cu) and pyrithione (PT) shall be included in the set of components. Other elements can be included when they are expected to seriously interfere with the species distribution. A first obvious additional cationic component is the proton H+. For other cations the elements shall be selected on the basis firstly of stability constant (to form (metal)PTn complexes) and presence, the concentration in the environment. For the following elements the stability constants have been defined and the stability of the PT complexes is considered to increase: Na<Mn<Fe<Co<Ni<Zn<Cu. As a result only Zn was included in the model calculations. In natural waters major compounds shall be included for the speciation of copper and H+, namely Mg and Ca. Based on earlier studies it is known that copper forms (mixed) complexes with OH-, CO_3^{2-} and SO_4^{2-}. Cl^- has been added because of its importance for the calculation of the ionic strength by the program. The OH- is automatically introduced from the pH. These ligands have been included in the components list. Also, pyrithione has been entered as a component. Copper is known to form strong complexes with organic matter in natural waters. For complexation with natural organic matter (dissolved organic carbon, DOC), an approximation has been used in CHEAQS Pro.

3.4.3 Species

The following species were defined and added to the program.

Species	log K	
HPT	4.67	
$CuPT^+$	8.5	'
$CuPT_2$	9.0	"
$ZnPT^+$	5.9	
$ZnPT_2$	5.4	
$FePT_3$	4.7	"'

3.4.4 Duration of the test

The characteristics of the aquatic media are presented in Table 7.1.1.2.4_1 for the components identified above.

4 RESULTS

4.1 Cu speciation

Focusing first on the Cu-speciation – thus the relative distribution of copper over the Cu-containing cation and complexes - at high concentrations of PT nearly all PT is bound in CuPT+, with 0% contribution for the Cu2+ and the CuDOC. With decreasing [PT], this changes to a slight increase in concentrations of Cu2+ and a considerable increase in CuDOC. This is the result of the increase of DOC from 0.5 mg (at S=35) to 5 mg (at S=0) and emphasizes the importance of the complexing capacity of the DOC.

For the entire range of salinities in the seven waters tested at PT concentrations of 1.0E-03 M and above, >90% of the copper is bound into CuPT+. At lower concentrations of PT, the relative contribution of CuPT+ is lowered, in favour of notably CuDOC. Only at high concentration of PT, CuPT2 is formed.

Section A7.1.1.2.4/02 Fate and behaviour in water – Speciation of copper pyrithione

4.2	**PT speciation**	For the PT-species distribution – thus the relative distribution of PT over the PT- anion and PTcontaining complexes - the picture looks rather simple. For the seven waters and nearly all PT-concentrations the free PT- is the dominant species (>95%). This means that also in absolute terms practically all PT is in this form. At low [PT], ≤1.0E-4 M, there is a trend towards the formation of ZnPT+. Only a tiny fraction, less than 0.1% is present as HPT.
4.3	**Relative distribution**	For the relative distribution in the speciation of Cu, it is shown that at high PT (1.0E-01 M),, the majority (approx. 85%) of the copper is bound as CuPT+ complex, and nearly all of the rest in CuPT2 (approx 14%). Lowering the PT to 1.0E-03 M there is a shift towards CuPT+, accounting for >98% of the total copper. At 1.0E-05 M PT the CuPT+ is only dominant at the lower copper concentrations (<1.0E-05 M Cu). At higher concentrations of Cu there is too much copper to be totally complexed by PT and the majority is bound in inorganic copper complexes, such as hydroxides and carbonates. At the lowest PT 1.0E-07 M, the organic Cu(DOC) is the most abundant form, except for the highest CU, where the inorganic forms take over. For the relative distribution in the speciation of PT, at the highest PT the dominant species is PT-. This is also true for situations where both PT and Cu are low. At PT=1.0E-03 for the highest Cu, CuPT+ takes over from PT- as the most abundant PT species. This trend is continues when lowering the PT. ZnPT+ is only marginally important, always <1% fo the total PT, and at maximum at the lowest Cu.
4.4	**Comparison with ecotoxicological studies**	For the seawater, assuming a low DOC concentration, the species distribution will be a recombination towards CuPT+ in case of abundant PT. In freshwater, which tends to have a higher concentration of DOC, CuPT+ is abundant only at the highest concentrations of PT. At lower concentrations Cu will bind to DOC, thus lowering its toxicity.
	5	**APPLICANT'S SUMMARY AND CONCLUSION**
5.1	**Materials and methods**	The mathematical speciation modelling program CHEAQS Pro has been used.
5.2	**Conclusion**	From the modelling studies it becomes clear that CuPT2 in water dissociates into Cu2+ and 2PT- ions, which may recombine to single CuPT+ ion as well as other copper species. The speciation of copper is affected by an increase in the concentration pyrithione (PT). The ligand PT- clearly competes with natural organic matter (DOC) to form trace metal complexes. Addition of copper to the system, e.g. as co-biocide in the paint matrix – does not lead to different conclusions: higher concentrations of Cu and PT favour the formation of CuPT+. At lower PT the organic Cu(DOC) becomes more dominant.
5.2.1	Reliability	2
5.2.2	Deficiencies	No GLP study, modelling.

Section A7.1.1.2.4/02 Fate and behaviour in water – Speciation of copper pyrithione

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date [redacted]

Materials and Methods [redacted]

Results and discussion [redacted]

Conclusion

Reliability

Acceptability [redacted]

Remarks [redacted]

Table 7.1.1.2.4_1. Components used in the calculations and definition of their concentration for the different waters (concentration in mol/l (M) unless indicated otherwise)

	sea/ocean		coastal		estuarine		fresh
S	35	30	25	20	15	5	0
components							
pH	8.1	8.1	8.0	7.9	7.8	7.7	7.7
H	7.94E-09	7.94E-09	1.00E-08	1.26E-08	1.58E-08	2.00E-08	2.00E-08
Mg	5.20E-02	4.46E-02	3.73E-02	2.99E-02	2.25E-02	7.78E-03	4.12E-04
Ca	1.01E-02	8.84E-03	7.62E-03	6.39E-03	5.17E-03	2.72E-03	1.50E-03
Cu(II)	1.57E-08	2.29E-08	3.01E-08	3.73E-08	4.45E-08	5.89E-08	6.61E-08
Zn(II)	1.53E-07	2.05E-07	2.58E-07	3.10E-07	3.63E-07	4.68E-07	5.20E-07
HCO3	2.27E-03	2.33E-03	2.40E-03	2.46E-03	2.52E-03	2.64E-03	2.70E-03
SO4	8.26E-02	7.09E-02	5.92E-02	4.74E-02	3.57E-02	1.22E-02	5.21E-04
Cl	5.33E-01	4.57E-01	3.81E-01	3.05E-01	2.29E-01	7.70E-02	1.02E-03
DOC (mg/l)	0.50	1.14	1.79	2.43	3.07	4.36	5.00

Section 7.1.2 Annex Point IIIA XII 2.1	Rate and route of degradation in aquatic systems including identification of metabolites and degradation products	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [X]** **Other justification [ ]**	X
Detailed justification:	Biodegradation in biological sewage treatment plants (section 7.1.2.1.1 and 7.1.2.1.2) is not applicable because the substance will not be discharged to sewage treatment plants due to its use as an antifouling (see also Doc IIB, In a ship-yard waste water is usually collected in a basin or reservoir. Water has to be purified before discharge, residue will be removed as chemical waste.). Further, biodegradation in freshwater (section 7.1.2.2.1 and 7.1.2.2.2) is not applicable since the a.s. is only to be used on marine ships. Alternatively, a water/sediment study with seawater and marine sediment is performed (see section A7.1.1.2.3). Therefore, such studies do not seem to be necessary.	
Undertaking of intended data submission [ ]		
Evaluation by Competent Authorities		
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Evaluation of applicant's justification	[redacted]	

[redacted]	[redacted]
Conclusion	[redacted]
Remarks	

Section A7.1.2/01 Metabolite identification (study 1 of 3)

Annex Point IIIA XII.2.1

See section A6.2 for the identification of metabolites formed in mammalian toxicity studies.

			Official use only
		1 REFERENCE	
1.1	**Reference**	[redacted] (2003a) Structural elucidation of [^{14}C]-Copper Pyrithione degradation products in rat excreta and in environmental matrices. TNO Chemistry, Report No. V4584, September 2003 (unpublished)	X
1.2	**Data protection**	Yes	
1.2.1	Data owner	Yoshitomi Fine Chemicals, Ltd.	
1.2.2	Companies with letter of access	-	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	OECD Draft Document (2000). Proposal for a new guideline: phototransformation of chemicals in water – direct and indirect photolysis. SETAC-Europe. Procedures for assessing the environmental fate and ecotoxicity of pesticides.	X
2.2	**GLP**	Yes	
2.3	**Deviations**	No	
		3 MATERIALS AND METHODS	
3.1	**Test material**	Radio-labelled copper pyrithione ([^{14}C]-Copper Pyrithione) and samples from a previously performed marine water/sediment degradation study (for materials and methods, see section A7.1.1.2.3)	
3.1.1	Lot/Batch number	Radio-labelled test material: 3362-120	
3.1.2	Specification	Specific activity of radio-labelled test material: 28.680 mCi/mmol.	
3.1.2.1	Description	Not reported	
3.1.2.2	Purity	Radio-labelled test material (radiochemical purity): 96.4%.	
3.1.2.3	Stability	As given in section 2	
3.1.2.4	Radiolabelling	[Pyridine-2,6-^{14}C]	
3.2	**Reference substance**	No	
3.2.1	Initial concentration of reference substance		
3.3	**Test solution**	Hydrolysis: see table A7_1_2-1/01 and A7_1_2-2/01 Photolysis: see table A7_1_2-4/01	X
3.4	**Testing procedure**		
3.4.1	Test system	Hydrolysis: see table A7_1_2-3/01. The test was carried out in the dark to avoid photolytic interference. Oxygen was exluded by bubbling	

Section A7.1.2/01 Metabolite identification (study 1 of 3)

Annex Point IIIA XII.2.1

		nitrogen through the test solutions. Photolysis: see table A7_1_2-5/01	X
3.4.2	Temperature	Hydrolysis: 50 °C Photolysis: room temperature	
3.4.3	pH	Hydrolysis: 5.0, 7.0, and 9.0 Photolysis: 7	
3.4.4	Duration of the test	Hydrolysis: 96 h Photolysis: 5 min	
3.4.5	Number of replicates	Not reported	
3.4.6	Sampling	Hydrolysis: at t = 0 and 96 h Photolysis: at t = 1, 2.5, and 5 min	**X**
3.4.7	Analytical methods	LSC and HPLC	X

4 RESULTS AND DISCUSSION

4.1 Specification of the transformation products

In the hydrolysis experiment, the test substance concentrations ranged from 33.7 – 37.7 µg [^{14}C]-copper pyrithione. After 96 h, the parent compound was degraded by more than 98% in all pH solutions. X a

In the photolysis experiment, the test substance concentrations ranged from 80.3 – 87.3 µg [^{14}C]-copper pyrithione. After 5 min, the parent compound was degraded by more than 92%. X b

The following major degradation products were found (maximum concentrations are given):

Metabolite	pH	% of applied radioactivity	Approximated retention time (min)
Hydrolysis			
P1	5.0	45.7	4.3 – 4.6
P4	5.0	25.3	24.6 – 25.8
H7	7.0	66.3	8.8 – 9.4
	9.0	58.2	8.8 – 9.4
P2	7.0	10.5	15.3 – 16.1
H8	9.0	11.0	12.6 – 13.5
Photolysis			
P1	7	31.6	4.3 – 4.6
P2	7	12.5[1)]	15.3 – 16.1
P3	7	30[2)]	19.7 – 20.9
Water/sediment			
B12		45.8	10.1 – 11.1
H8		42.3	12.6 – 13.5

X c

Section A7.1.2/01 Metabolite identification (study 1 of 3)

Annex Point IIIA XII.2.1

		[1] At t = 2.5 min (lower amounts were detected at t = 1 and 5 min) [2] Only detected at t = 1 min. The peak shape of the hydrolysis products H7 and H8 was relatively broad, and therefore, it might be possible that these peaks consist of more than one degradation product. In the photolysis experiment, the formation of the hydrophilic transformation product P1 was preceded by the formation of two intermediate products (P2 and P3). Similar degradation patterns were observed for the two water/sediment systems. The degradation products formed (B12 and H8) could not clearly be separated on the HPLC system. Therefore, it might be possible that the detected peaks represent more than one degradation product. It could not be revealed if metabolite H7 and B12 are identical, nor whether H8 in the hydrolysis sample is identical to H8 in the water/sediment sample. Although the degradation products were not identified yet, recommendations on the isolation and structural elucidation of these products were given (see section A7.1.2/02 and /03 for summaries).	X d
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	Degradation products were obtained from hydrolysis and photolysis tests and from a previously performed marine water/sediment degradation study. In the present study, the degradation tests were performed according to OECD Draft Document (2000), Proposal for a new guideline: phototransformation of chemicals in water – direct and indirect photolysis and SETAC-Europe, Procedures for assessing the environmental fate and ecotoxicity of pesticides. Degradation products were analysed by LSC and HPLC.	X
5.2	**Results and discussion**	Extensive degradation of [^{14}C]-copper pyrithione was detected in all samples analysed. A total of seven degradation products were found to occur at a level above 10% of the total added radioactivity. These products were labelled P1, P2, P3, P4, H7, H8, and B12. The products were not identified yet, but recommendations on the isolation and structural elucidation of these products were given.	X
5.3	**Conclusion**	A total of seven major degradation products were formed in the hydrolysis, photolysis, and water/sediment degradation studies. The products were not identified yet, but recommendations on the isolation and structural elucidation of these products were given.	X
5.3.1	Reliability	1	
5.3.2	Deficiencies	No	

Section A7.1.2/01 Metabolite identification (study 1 of 3)

Annex Point IIIA XII.2.1

Evaluation by Competent Authorities	
EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]
Materials and Methods	[redacted]

Section A7.1.2/01 Metabolite identification (study 1 of 3)

Annex Point IIIA XII.2.1

	[redacted]
Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted] 6.

Table A7_1_2-1/01: Type and composition of buffer solutions used in the hydrolysis test

pH	Type of buffer (final molarity)	Composition
5.0	0.05 M	46.7 mL of 0.1 M NaOH and 50 mL of 0.1 M monopotassium citrate was added to 100 mL Milli-Q water
7.0	0.04 M	88.8 mL of 0.1 M NaOH and 150 mL of 0.1 M monopotassium phosphate was added to 300 mL Milli-Q water
9.0	0.04 M	63.9 mL of 0.1 M NaOH and 150 mL of 0.1 M boric acid (in 0.1 M KCl) was added to 300 mL Milli-Q water

Table A7_1_2-2/01: Description of test solution used in the hydrolysis test

Criteria	Details
Purity of water	Milli-Q water
Preparation of test medium	A stock solution of the test substance was dissolved in sterile buffer solution
Test concentrations (µg a.s./L)	44 µg [^{14}C]-copper pyrithione/L buffer solution
Temperature (°C)	50 °C
Controls	-
Identity and concentration of co-solvent	-
Replicates	-

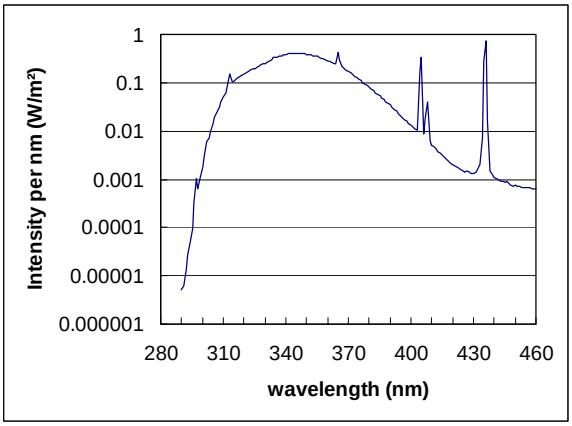
Table A7_1_2-3/01: Description of test system used in the hydrolysis test

Glassware	Sterilised glassware (type of glassware was not reported)
Other equipment	Thermostatically controlled water bath
Method of sterilization	Glassware was sterilised at 120 °C before use; buffer solutions were sterilised by filtration over a 0.45 µm filter

Table A7_1_2-4/01: Description of test solution and controls used in the photolysis test

Criteria	Details
Purity of water	0.04 M phosphate buffer solution of pH 7
Preparation of test chemical solution	A stock solution of the test substance was dissolved in sterile buffer solution
Test concentrations (µg a.s./L)	100 µg [^{14}C]-copper pyrithione/L buffer solution
Temperature (°C)	room temperature
Preparation of a.s. solution	See preparation of test chemical solution
Controls	Not applicable
Identity and concentration of co-solvent	Not applicable

Table A7_1_2-5/01: Description of test system used in the photolysis test

Criteria	Details
Laboratory equipment	Closed plastic vessels
Test apparatus	LSC and HPLC
Properties of artificial light source:	
Nature of light source	Philips TL CLEO Natural sunlamp
Emission wavelenght spectrum	
Light intensity	Not reported
Filters	Wavelengths < 290 nm were excluded
Properties of natural sunlight:	Not applicable
Latitude	-
Hours of daylight	-
Time of year	-
Light intensity	-
Solar irradiance (L_λ)	-

Section A7.1.2/02 Metabolite identification (study 2 of 3)

Annex Point IIIA XII.2.1

			Official use only
		1 REFERENCE	
1.1	**Reference**	[redacted] (2003b) Structural elucidation of seven transformation products of [^{14}C]-copper pyrithione, formed by photolysis, hydrolysis and in a water-sediment degradation study. TNO Chemistry, Report No. V5034, September 2003 (unpublished)	
1.2	**Data protection**	Yes	
1.2.1	Data owner	API Corporation, Japan	
1.2.2	Companies with letter of access	-	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	OECD Draft Document (2000). Proposal for a new guideline: phototransformation of chemicals in water – direct and indirect photolysis OECD Revised Guideline 111	
2.2	**GLP**	Yes	
2.3	**Deviations**	No	
		3 MATERIALS AND METHODS	
3.1	**Test material**	Radio-labelled copper pyrithione ([^{14}C]-Copper Pyrithione) and samples from a previously performed marine water/sediment degradation study (for materials and methods, see section A7.1.1.2.3)	X
3.1.1	Lot/Batch number	3362-120	
3.1.2	Specification	Specific activity: 28.680 mCi/mmol.	
3.1.2.1	Description	Green crystalline powder	
3.1.2.2	Purity	Radiochemical purity: 96.4%	X
3.1.2.3	Stability	As given in section 2	
3.1.2.4	Radiolabelling	[Pyridine-2,6-^{14}C]	
3.2	**Reference substance**	Unlabelled copper pyrithione, 2-mercaptopyridine, and 2-mercaptopyridine-1-oxide	
3.2.1	Initial concentration of reference substance		
3.3	**Test solution**	Photolysis: see table A7_1_2-1/02 Hydrolysis: see table A7_1_2-3/02 and A7_1_2-4/02	
3.4	**Testing procedure**		
3.4.1	Test system	Photolysis: see table A7_1_2-2/02 Hydrolysis: see table A7_1_2-5/02. The test was carried out in the dark	

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		to avoid photolytic interference. Oxygen was exluded by bubbling nitrogen through the test solutions. A short literature survey led to candidate structures for which the exact atomic masses were calculated. Fragmentation patterns in the ion-source were determined for three reference compounds (copper pyrithione, 2-mercaptopyridine, and 2-mercaptopyridine-1-oxide). First, ionic mass traces of all possible fragments in the degradation samples were compared with the trace of the radioactive signal to identify relevant mass signals specific for degradation products of [^{14}C]-copper pyrithione. Additionally, full scan spectra were investigated at the elution time of each radioactive peak to control for unaccounted degradation structures. Tandem MS experiments were conducted with two freeze-dried sampels.	
3.4.2	Temperature	Photolysis: 20 ± 1 °C Hydrolysis: 50 °C	
3.4.3	pH	Photolysis: 7.0 Hydrolysis: 5.0 and 9.0	
3.4.4	Duration of the test	Photolysis: 5 min Hydrolysis: 96 h	
3.4.5	Number of replicates	Photolysis: 3	
3.4.6	Sampling	Photolysis: at t = 0, 1, and 5 min Hydrolysis: at t = 96 h	
3.4.7	Analytical methods	LSC, HPLC, and LC-MS	X
		4 RESULTS AND DISCUSSION	
4.1	**Specification of the transformation products**	In the hydrolysis experiment, the test substance concentrations ranged from 182 – 192 µg/L (expressed as Parent Compound Equivalent (PCE)). In the photolysis experiment, the test substance concentrations ranged from 178 – 183 µg/L (expressed as PCE). The following major degradation products were found: Hydrolysis (pH 5.0): P1, P4 Hydrolysis (pH 9.0): H7 Photolysis (pH 7.0): P1, P6 H8 was a minor degradation product in the hydrolysis (pH 9) test; P2, P4, P5, and H9 are minor degradation products found in the photolysis test. The following degradation products were tentatively assigned to structures: P4: pyrithione disulfide. P5: pyrithione-S,S'-mercaptopyridine The structures of the other products (P1, P2, P6, H7, H8, and H9) were not elucidated. The identity of P4 found in the photolysis sample could not be confirmed by mass spectra data, only by retention time. Clean-up of the water/sediment samples was not successful. Therefore,	

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		they could not be analysed by LC-MS and the structures of B12 and H8 remain unresolved.
		5 APPLICANT'S SUMMARY AND CONCLUSION
5.1	**Materials and methods**	Degradation products were obtained from hydrolysis and photolysis tests and from a previously performed marine water/sediment degradation study. In the present study, the degradation tests were performed according to OECD 308, OECD Draft Document (2000), Proposal for a new guideline: phototransformation of chemicals in water – direct and indirect photolysis and OECD Revised Guideline 111. Degradation products were analysed by LSC, HPLC, and LC-MS.
5.2	**Results and discussion**	Degradation products P4 and P5 were tentatively identified as pyrithione disulfide and pyrithione-S,S'-mercaptopyridine, respectively. The structures of the other products (P1, P2, P6, H7, H8, and H9) were not elucidated. The metabolites B12 and H8 obtained from the marine water/sediment degradation study were not identified because the clean-up of the water/sediment samples was not successful.
5.3	**Conclusion**	Degradation products P4 and P5 were tentatively identified as pyrithione disulfide and pyrithione-S,S'-mercaptopyridine, respectively. The products P1, P2, P6, H7, H8, H9, and B12 were not identified.
5.3.1	Reliability	1
5.3.2	Deficiencies	No

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date

Materials and Methods

Results and discussion

Conclusion

Reliability

Acceptability	[redacted]
Remarks	[redacted]

Table A7_1_2-1/02: Description of test solution and controls used in the photolysis test

Criteria	Details
Purity of water	0.08 M phosphate buffer solution of pH 7.0
Preparation of test chemical solution	A stock solution of the test substance was dissolved in sterile buffer solution
Test concentrations (µg a.s./L)	200 µg [^{14}C]-copper pyrithione/L buffer solution
Temperature (°C)	20 ± 3 °C
Preparation of a.s. solution	See preparation of test chemical solution
Controls	Additional flasks with aqueous solution with the same concentration of the test substance were kept in the dark in order to distinguish between photochemical degradation and other reactions.
Identity and concentration of co-solvent	Not applicable

Table A7_1_2-2/02: Description of test system used in the photolysis test

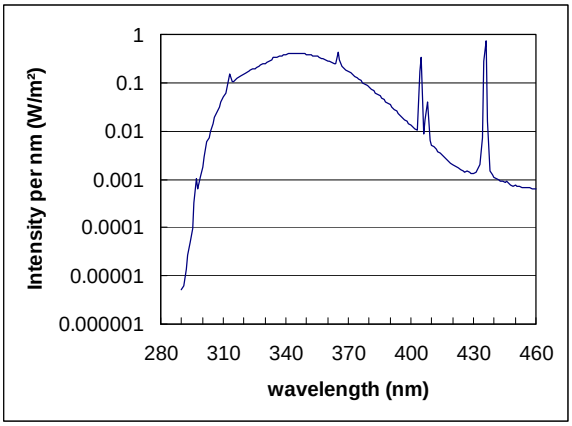
Criteria	Details
Laboratory equipment	Closed glass vials
Test apparatus	LSC, HPLC, and LC-MS
Properties of artificial light source:	
Nature of light source	Philips TL CLEO Natural sunlamp
Emission wavelenght spectrum	
Light intensity	Not reported
Filters	Wavelengths < 290 nm were excluded
Properties of natural sunlight:	Not applicable
Latitude	-
Hours of daylight	-
Time of year	-
Light intensity	-
Solar irradiance (L_λ)	-

Table A7_1_2-3/02: Type and composition of buffer solutions used in the hydrolysis test

pH	Type of buffer (final molarity)	Composition
5.0	0.03 M	50 mL of 0.1 M tripotassium citrate was adjusted to pH 5.0 with HCl and filled up 200 mL with deionised water
9.0	0.03 M	50 mL of 0.1 M boric acid (in 0.1 M KCl) was adjusted to pH 9.0 with 0.1 M NaOH and filled up to 200 mL deionised water

Table A7_1_2-4/02: Description of test solution used in the hydrolysis test

Criteria	Details
Purity of water	Deionised water
Preparation of test medium	A stock solution of the test substance was dissolved in sterile buffer solution
Test concentrations (µg a.s./L)	200 µg [^{14}C]-copper pyrithione/L buffer solution
Temperature (°C)	50 ± 1 °C
Controls	-
Identity and concentration of co-solvent	-
Replicates	-

Table A7_1_2-5/02: Description of test system used in the hydrolysis test

Glassware	Not reported
Other equipment	Thermostatically controlled water bath
Method of sterilization	Buffer solutions were sterilised by filtration over a 0.45 µm filter

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			Official use only
		1 REFERENCE	
1.1	**Reference**	[redacted] (2005) Structural elucidation of hydrophilic transformation products of [^{14}C]-copper pyrithione, formed by photolysis, hydrolysis and in a water-sediment degradation study. TNO Quality of Life, Report No. V5764, June 2005 (unpublished)	
1.2	**Data protection**	Yes	
1.2.1	Data owner	API Corporation, Japan	
1.2.2	Companies with letter of access	-	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	OECD 308 OECD Draft Document (2000). Proposal for a new guideline: phototransformation of chemicals in water – direct and indirect photolysis OECD Revised Guideline 111	
2.2	**GLP**	Yes	
2.3	**Deviations**	No	
		3 MATERIALS AND METHODS	
3.1	**Test material**	Radio-labelled copper pyrithione ([^{14}C]-Copper Pyrithione)	
3.1.1	Lot/Batch number	3362-120	
3.1.2	Specification	Specific activity: 28.7 mCi/mmol.	
3.1.2.1	Description	As given in section 2.	
3.1.2.2	Purity	Radiochemical purity: 95.3%	X
3.1.2.3	Stability	As given in section 2	
3.1.2.4	Radiolabelling	[Pyridine-2,6-^{14}C]	
3.2	**Reference substance**	Pyridine-2-sulfonic acid, ammonium pyridine-2-sulphinate, pyridine-2-sulphonic acid N-oxide, 2-mercaptopyridine	
3.2.1	Initial concentration of reference substance		
3.3	**Test solution**	Photolysis: see table A7_1_2-1/03 Hydrolysis: see table A7_1_2-3/03 and A7_1_2-4/03 Water/sediment: see table A7_1_2-6/03	X
3.4	**Testing procedure**		
3.4.1	Test system	Photolysis: see table A7_1_2-2/03 Hydrolysis: see table A7_1_2-5/03. The test was carried out in the dark to avoid photolytic interference. Oxygen was exluded by bubbling	

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		nitrogen through the test solutions. Water/sediment: see table A7_1_2-7/03 and A7_1_2-8/03 The structural identity of four metabolites of copper pyrithione, P1 (from photolysis), H7 (from hydrolysis at pH 9.0), B12 and H8 (from marine water/sediment study) was investigated.	
3.4.2	Temperature	Photolysis: 20 °C Hydrolysis: 50 ± 3 °C Water/sediment:	
3.4.3	pH	Photolysis: 7.0 Hydrolysis: 9.0 Water/sediment: not reported	
3.4.4	Duration of the test	Photolysis: 30 min Hydrolysis: 96 h Water/sediment: 3 d	
3.4.5	Number of replicates	Photolysis: 3 Water/sediment: 3 exposed and 1 control	
3.4.6	Sampling	Photolysis: at t = 30 min Hydrolysis: at t = 96 h Water/sediment: 3 d	
3.4.7	Analytical methods	LSC, HPLC, and LC-MS	X
		4 RESULTS AND DISCUSSION	
4.1	**Specification of the transformation products**	The following total [^{14}C] radioactivity concentrations were determined: 206 – 233 µg Eq/L (photolysis), 227 – 232 µg Eq/L (hydrolysis), 139 – 147 µg Eq/L (water/sediment). The following degradation products were found: Photolysis: P1, H7, H9, P4, P5, P6, and a less hydrophobic metabolite than H7 Hydrolysis: P1, B12, H7, P4, P5 Water/sediment: B12, H7, P1, P4. The following degradation products were tentatively assigned to structures: H7: pyridine sulfinic acid H9: 2-mercaptopyridine P4: could be bis(2-pyridinyl)sulfonyl 1,1' dioxide, but based on the literature, the most probable structure is bis(2-pyridinyl)disulfide 1,1' dioxide (pyrithione disulfide) P5: No additional information was obtained on this metabolite. In a previous study, this substance was identified as bis(2-pyridinyl)disulfide 1 oxide (mixed disulfide)	

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		Unidentified metabolites: B12: very hydrophilic, pyridine-containing structure P1: very hydrophilic substance under acidic and neutral pH conditions P6: probably a dimer containing pyrithione or mercaptopyridine structures	
		The absence of H8, P2, P3, which were found in previous studies (P3 was only found at t = 1 min), indicates that these are unstable, intermediate metabolites.	
		Based on these findings, [^{14}C]-copper pyrithione expected to degrade as follows:	
		In aqueous solutions, the pyrithione molecules of copper pyrithione (CuPT2) will undergo speciation between a chelated state with either copper or another metal (Fe or Na), the dimer pyrithione disulfide (PT2) and the monomer (PT). The concentration of CuPT2 is therefore dependent on different factors in the aqueous solution like pH, salinity, concentration of other metals etc.	X a
		Two of the hydrophilic metabolites of copper pyrithione were tentatively identified as Pyridine sulfinic acid (PSO2) and 2-mercaptopyridine (PSH). This indicates that further degradation of pyrithione like compounds occurs by losing the N-oxide on the pyridine ring. This degradation step is likely to be irreversible.	
		The sulphur atoms of PSO2 or PSH can be reduced or oxidized, respectively to form other compounds or disulfides.	
		The unidentified metabolites P1 and B12 were hydrophilic under both acid and neutral eluent conditions on the HPLC. They could not be extracted by one of the liquid liquid extraction procedures. Their bioaccumulation potential is therefore expected to be very low.	
		Based on the tentatively identified metabolites of copper pyrithione, it seems that the metabolic pathway of this compound is comparable to the degradation routes reported for zinc pyrithione.	X b
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	Degradation products were obtained from hydrolysis, photolysis, and water/sediment degradation tests. The tests were performed according to OECD 308, OECD Draft Document (2000), Proposal for a new guideline: phototransformation of chemicals in water – direct and indirect photolysis and OECD Revised Guideline 111. Degradation products were analysed by LSC, HPLC, and LC-MS.	
5.2	**Results and discussion**	H7 and H9 were tentatively identified as pyridine sulfinic acid and 2-mercaptopyridine, respectively. P4 is most probably pyrithione disulfide, but its identity remains ambiguous. The identities of B12, P1, and P6 were not elucidated. B12 and P1 were very hydrophilic. The previously detected degradation products H8, P2, and P3 indicate that these are unstable, intermediate metabolites. The metabolic pathway of [^{14}-C]-copper pyrithione appears to be comparable to the degradation routes reported for zinc pyrithione.	X
5.3	**Conclusion**	Degradation products H7 and H9 were tentatively identified as pyridine sulfinic acid and 2-mercaptopyridine, respectively. The identity of P4 remains ambiguous, although literature indicates that its structure is pyrithione disulfide. The products B12, P1, and P6 were not identified.	

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		B12 and P1 were very hydrophilic. The metabolic pathway of [^{14}-C]-copper pyrithione appears to be comparable to the degradation routes reported for zinc pyrithione. Metabolites have been characterised and identified to the extent that is feasible, although identification could not be completed for all major metabolites. Therefore, no further efforts were made.
5.3.1	Reliability	1
5.3.2	Deficiencies	No

Section A7.1.2/03 Metabolite identification (study 3 of 3)

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Evaluation by Competent Authorities	
EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]
Materials and Methods	[redacted]

Section A7.1.2/03 Metabolite identification (study 3 of 3)

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Results and discussion	[redacted]
Conclusion	[redacted]
Reliability	[redacted]
Acceptability	[redacted]
Remarks	[redacted]

Table A7_1_2-1/03: Description of test solution and controls used in the photolysis test

Criteria	Details
Purity of water	0.08 M phosphate buffer solution of pH 7.0
Preparation of test chemical solution	A stock solution of the test substance in DMSO was dissolved in sterile buffer solution
Test concentrations (µg a.s./L)	200 µg [^{14}C]-copper pyrithione/L buffer solution
Temperature (°C)	20 °C
Preparation of a.s. solution	See preparation of test chemical solution
Controls	Not applicable
Identity and concentration of co-solvent	DMSO

Table A7_1_2-2/03: Description of test system used in the photolysis test

Criteria	Details
Laboratory equipment	Closed glass vials
Test apparatus	LSC, HPLC, and LC-MS
Properties of artificial light source:	
Nature of light source	Philips TL CLEO Natural sunlamp
Emission wavelenght spectrum	Not reported
Light intensity	Not reported
Filters	Wavelengths < 290 nm were excluded
Properties of natural sunlight:	Not applicable
Latitude	-
Hours of daylight	-
Time of year	-
Light intensity	-
Solar irradiance (L_λ)	-

Table A7_1_2-3/03: Type and composition of buffer solutions used in the hydrolysis test

pH	Type of buffer (final molarity)	Composition
9.0	0.07 M	50 mL of 0.1 M boric acid (in 0.1 M KCl) was adjusted to pH 9.0 with 21.3 mL of 0.1 M NaOH and filled up to 100 mL deionised water

Table A7_1_2-4/03: Description of test solution used in the hydrolysis test

Criteria	Details
Purity of water	Deionised water
Preparation of test medium	A stock solution of the test substance in DMSO was dissolved in sterile buffer solution
Test concentrations (µg a.s./L)	200 µg [^{14}C]-copper pyrithione/L buffer solution
Temperature (°C)	50 ± 3 °C
Controls	-
Identity and concentration of co-solvent	DMSO
Replicates	-

Table A7_1_2-5/03: Description of test system used in the hydrolysis test

Glassware	Not reported
Other equipment	Thermostatically controlled water bath
Method of sterilization	Buffer solutions were sterilised by filtration over a 0.45 µm filter

Table A7_1_2-6/03: Inoculum used in the water/sediment degradation test

Criteria	Details
Nature	Two marine water/sediment systems: Colijnsplaat: fine sandy sediment with an organic matter content of ca. 2.6% and a silt clay fraction of ca. 15%. Zandkreekdam: silty fine sand sediment with an organic matter content of ca. 1.4% and a silt clay fraction 50% of more.
Source	Field samples of seawater and marine sediment
Sampling site	Marine water and sediment samples were taken from coastal areas of Colijnsplaat and Zandkreekdam in the Netherlands; the top 5 cm layer was sampled. These sediments are representative of coastal benthic conditions from an area not expected to be contaminated by the test substance. Seawater was collected in the North Sea, off the coast of Jacobahaven in Zeeland, the Netherlands
Preparation of substrate for exposure	Sediment samples were passed through a 2 mm sieve, transferred to the laboratory and allowed to settle. The supernatants were drawn off and the dry solid contents were determined. Marine water samples were sieved to remove particles.
Pretreatment	Water/sediment systems were acclimatised for up to two weeks at 20 ± 2 °C in the dark
Test concentration (µg a.s./L)	180 µL of a stock solution was added to each bottle

Table A7_1_2-7/03: Test system used for in the water/sediment degradation test

Criteria	Details
Culturing apparatus	1-L flasks with ca. 400 – 500 g sediment (ww) and a water phase of ca. 650 – 700 mL
Number of culture flasks	3 with test substance and 1 control
Measuring equipment	LSC, HPLC, and LC-MS

Table A7_1_2-8/03: Test conditions of the water/sediment degradation test

Criteria	Details
Composition of medium	Natural seawater and corresponding sediment
Additional substrate	No
Test temperature	20 ± 2 °C
pH of aqueous phase (minimum – maximum)	Not reported
Aeration of dilution water	Yes (the previous study revealed that no volatile organic metabolites were formed)
Suspended solids concentration	Not reported
Other relevant criteria	-

Section A7.1.3 Adsorption / Desorption screening test

Annex Point IIA7.7

			Official use only
		1 REFERENCE	
1.1	**Reference**	De Vette HQM, Van Es C (2002b) A study on the adsorption/desorption of copper pyrithione to two sediment types using [^{14}C] copper pyrithione (OECD 106, SETAC-Europe). TNO Chemistry, Report No: V2422/05, September 5, 2002 (unpublished) including Amendment 01 Hamwijk, C. (2006)	X
1.2	**Data protection**	Yes	
1.2.1	Data owner	Yoshitomi Fine Chemicals, Ltd.	
1.2.2	Companies with letter of access	-	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Yes, the SETAC-Europe procedure and OECD 106, as specified by EU Council Directive 95/36/EC	
2.2	**GLP**	Yes	
2.3	**Deviations**	No	
		3 MATERIALS AND METHODS	
3.1	**Test material**	Radiolabelled copper pyrithione (Copper Omadine Pyridine-2,6-14C)	
3.1.1	Lot/Batch number	3362-120	
3.1.2	Specification	Specific activity: 28.680 mCi/mmol	
3.1.3	Purity	Radiochemical purity: 99.0%	
3.1.4	Further relevant properties		X
3.1.5	Method of analysis	Selected supernatant samples of each sediment treated with the highest concentration of test substance in the adsorption, as well as the first, the second desorption step and extraction solvent, were analysed by means of HPLC.	X
3.2	**Degradation products**	No	
3.2.1	Method of analysis for degradation products		
3.3	**Reference substance**	No	
3.3.1	Method of analysis for reference substance		
3.4	**Soil types**	See table A7_1 _3-1	X
3.5	**Testing procedure**		
3.5.1	Test system	The test was carried out in 20-mL glass scintillation vials closed with	

Section A7.1.3 Adsorption / Desorption screening test

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		screw caps. Two vessels per concentration were used. Reference vials without sediment were also prepared and treated in the same manner as the other vials.	
3.5.2	Test solution and Test conditions	A test series containing 5, 10, 20, 40 and 70 µg/L [14C] copper pyrithione was prepared. Therefore, 42 µL of the stock solution (stock I) was diluted to 250 mL with 0.01M $CaCl_2$. From this solution, the 40 µg/L test solution was prepared by diluting 114 mL with 86 mL of $CaCl_2$. All the other solutions were prepared by mixing 100 mL of the previous concentration with 100 mL of 0.01 M $CaCl_2$.	X a
		Adsorption was determined by placing samples of 2 g dw of each sediment in the vials. Next, 10 mL of each test substance solution was added to duplicate vials with each sediment, resulting for both sediments in a concentration series of 0.025, 0.050, 0.10, 0.20, and 0.35 µg/g (dw). Reference vials without sediment, containing 10 mL of 0.01 M $CaCl_2$ solution only, were also prepared, and treated in the same manner as the other vials. The test and reference vials were shaken for approximately 15 min in a temperature controlled room at 20 ± 2 °C in the dark. The vials were then centrifuged and duplicate samples of the supernatant (1 mL) were pipetted into vials containing 10 mL scintillation fluid and counted. The concentration of test substance at equilibrium (Ceq) was calculated from the LSC measurements.	X b
3.6	**Test performance**		
3.6.1	Preliminary test	According to OECD 106: Yes	
3.6.2	Screening test: Adsorption	According to OECD 106: Yes, however the adsorption of five concentrations by two sediments was determined at one time point instead of the adsorption of one concentration by five sediments at several time points	
3.6.3	Screening test: Desorption	According to OECD 106: Desorption was determined by removing the remaining aqueous layer and adding 10.0 mL of 0.01 N $CaCl_2$ solution to each sediment. These vials were shaken for 15 min and after this period the samples were centrifuged and duplicate samples of the supernatant (1 mL) were added to 5 mL of scintillation fluid and counted by LSC. This desorption step was repeated once.	X
3.6.4	Determination of Freundlich ad- and desorption isotherms	According to OECD 106: Yes	
3.6.5	HPLC-method	Selected supernatants, as well as methanol extracts of the sediments originating from the highest concentration were analysed by means of HPLC-RAD.	X
3.6.6	Other test	Not applicable	
		4 RESULTS	
4.1	**Preliminary test**	See table A7_1 _3-2	
4.2	**Screening test: Adsorption**	See table A7_1 _3-3	X
4.3	**Screening test: Desorption**	See table A7_1 _3-4	X

Section A7.1.3 Adsorption / Desorption screening test

Annex Point IIA7.7

4.4	**Calculations**		
4.4.1	Ka , Kd	For ^{14}C copper pyrithione and radiolabeled transformation products: Zandkreekdam : Ka = 1.7 mL/g, Kd = 10.2 mL/g Colijnsplaat : Ka = 10.3 mL/g, Kd = 21.0 mL/g	X
4.4.2	Ka_{oc}, Kd_{oc}	For ^{14}C copper pyrithione and radiolabeled transformation products: Zandkreekdam: Ka_{oc} = 276 mL/g, Kd_{oc} = 1656 mL/g (Ka_{om} = 162 mL/g) Colijnsplaat: Ka_{oc} = 3442 mL/g, Kd_{oc} = 7018 mL/g (Ka_{om} = 2024 mL/g)	X
4.5	**Degradation product(s)**	See table A7_1_3-5	
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	The SETAC-Europe procedure and OECD 106, as specified by EU Council Directive 95/36/EC were followed. However, the adsorption of five concentrations by two soils was determined at one time point instead of the adsorption of one concentration by five soils at several time points.	X
5.2	**Results and discussion**	The K_a, K_d, Ka_{oc} and K_a/K_d values given below in sections 5.2.2 – 5.2.5 are all based on LSC measurements and are therefore for ^{14}C copper pyrithione and radiolabeled transformation products. LSC is an unspecific technique which cannot differentiate between the test substance and its transformation products. Selected supernatants, as well as methanol extracts of the sediments originating from the highest concentration were analysed by means of HPLC-RAD. The results showed that, in spite of the short incubation time (15 min), the test substance was not stable in both Zandkreekdam and Colijnsplaat sediment. In some cases, the unstability can be taken into account by analyzing both phases (water and sediment). However, in the present study, the identity of the radiolabeled substance that was adsorbed to the sediment could not be determined due to the relatively high percentage of bound residue . The results showed that ^{14}C copper pyrithione and radiolabeled transformation products are easily adsorbed to sediments. The adsorption coefficients (Ka_{oc}) show that copper pyrithione and radiolabeled transformation products can be considered as immobile. The radiolabeled material was not easily desorbed from both sediments. Therefore, the adsorption appeared to be irreversible in both systems. The parent compound was easily degraded into a more polar metabolite. The recovery of radioactivity appeared to be 99.6% - 111.6%. The recovery of the radioactivity in the supernatant after the adsorption/desorption test was 70.6% for the Zandkreekdam and 42.1% for the Colijnsplaat, whereas 4.6% and 1.8% was desorbed with the extraction solvent, respectively. Finally, 24.4% and 67.7%, respectively, remained as unextractable radioactivity (bound residue) in the sediments.	Xa Xb
5.2.1	Adsorbed a.s. [%]	Not reported	
5.2.2	K_a	For ^{14}C copper pyrithione and radiolabeled transformation products: 1.7 mL/g (Zandkreekdam) 10.3 mL/g (Colijnsplaat)	X
5.2.3	K_d	For ^{14}C copper pyrithione and radiolabeled transformation products:	X

Section A7.1.3 Adsorption / Desorption screening test

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		10.2 mL/g (Zandkreekdam) 21.0 mL/g (Colijnsplaat)	
5.2.4	Ka_{oc}	For ^{14}C copper pyrithione and radiolabeled transformation products: 276 mL/g (Zandkreekdam) 3442 mL/g (Colijnsplaat)	X
5.2.5	Ka/Kd	0.167 (Zandkreekdam) 0.490 (Colijnsplaat)	X
5.2.6	Degradation products (% of a.s.)	One polar metabolite was found which exceeded 10% of the parent compound (59.1 and 100% of the parent compound in Zandkreekdam and Colijnsplaat sediment, respectively)	X
5.3	**Conclusion**	Validity criteria can be considered as fulfilled. ^{14}C copper pyrithione and radiolabeled transformation products are considered to be immobile, as the adsorption of radiolabeled material appeared to be irreversible in both systems.	X
5.3.1	Reliability	1	
5.3.2	Deficiencies	No	

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date [redacted]

Materials and Methods [redacted]

Section A7.1.3 Adsorption / Desorption screening test

Annex Point IIA7.7

Section A7.1.3 Adsorption / Desorption screening test

Annex Point IIA7.7

Results and discussion

[redacted]

Section A7.1.3 Adsorption / Desorption screening test

Annex Point IIA7.7

[redacted]

Conclusion

[redacted]

Section A7.1.3 Adsorption / Desorption screening test

Annex Point IIA7.7

[redacted]

Reliability

[redacted]

Acceptability

[redacted]

Remarks

[redacted]

Table A7_1_3-1: Classification and physico-chemical properties of sediments used as adsorbents (sediments were sieved through a ≤ 2 mm sieve)

	Soil 1	Soil 2
Soil order	Not reported	Not reported
Soil series	Not reported	Not reported
Classification	Not reported	Not reported
Location	Colijnsplaat, Eastern Scheld Estuary, the Netherlands	Zandkreekdam, Eastern Scheld Estuary, the Netherlands
Horizon	Not reported	Not reported
Sand [%]	95.50	85.03
Silt [%]	2.24	9.68
Clay [%]	2.26	5.29
Organic carbon [%]	0.3	0.6
Carbonate as $CaCO_3$	Not reported	Not reported
insoluble carbonates [%]	Not reported	Not reported
pH (1:5 H_2O)	8.2	8.3
pH (1:5 1 M KCl)	8.8	8.5
pH (1:5 0.01 M $CaCl_2$)	8.1	8.0
Cation exchange capacity (MEQ/100 g)	6.4	6.5
Extractable cations (MEQ/100 g)	Not reported	Not reported
Ca	Not reported	Not reported
Mg	Not reported	Not reported
Na	Not reported	Not reported
K	Not reported	Not reported
H	Not reported	Not reported
Special chemical/mineralogical features	Not reported	Not reported
Clay fraction mineralogy	Not reported	Not reported
Dry matter content (%)	99.6	82.5
Water content (%)	0.4	21.2
Total phosphorus (mg/kg)	197.4	231.7
Total nitrogen (mg/kg)	196.0	419.9

Table A7_1_3-2: Results of preliminary test:

Test substance	^{14}C copper pyrithione
Sample purity	Radiochemical purity: 99.0%
Weighed sediment	Mixed Zandkreekdam and Colijnsplaat sediments (0.4, 2, and 10 g)
Volume of $CaCl_2$ solution	10 mL
Nominal concentration of a.s. final solution	40 µg/L
Analytical concentration final of a.s. solution	135.0 Bq/mL
Concentration of the test solution (show calculation)	An amount of ^{14}C copper pyrithione was added to 3 mL of methanol and 5 mL of dimethylsulfoxide (stock solution I). An aliquote (50 µL) was counted and contained 68.0 kBq. From this solution, 50 µL was diluted to 500 mL 0.01 M $CaCl_2$ solution (stock solution II) and an aliquote (1 mL) was counted by Liquid Scintillation Counting (LSC). The final concentration was 40 µg/L and 135.0 Bq/mL.
Details of the analytical method used:	
Method	LSC
Recovery rate	-
Detection limit	-

Table A7_1 _3-3: Results of screening test - adsorption:

	Zandkreekdam					Colijnsplaat				
Concentration of test material [µg/l]	5.1	10.0	20.7	40.8	70.5	5.1	10.0	20.7	40.8	70.5
After contact of ca. 15 min with soil	1.4	3.1	7.6	17.8	35.3	1.3	2.3	6.8	9.5	20.3
Correction for blank with soil										
Correction for blank without soil	-[1]					-[1]				
Final corrected concentration [mg/l]										
Initial concentration of test solution [µg/L]	5	10	20	40	70	5	10	20	40	70
Decrease in concentration [mg/l]										
Quantity adsorbed [µg]										
Quantity of soil [g of oven-dried equivalent]	2	2	2	2	2	2	2	2	2	2
Quantity adsorbed [µg] per gram of soil	0.02	0.03	0.06	0.11	0.17	0.02	0.04	0.07	0.15	0.24
Test material adsorbed [%]										
Temperature [°C]	20 ± 2 °C					20 ± 2 °C				
Volume of solution recovered after centrifugation [ml]										
Volume of solution not recovered [ml]										
Corresponding quantity of test substance [mg]										
Recovery of test substance [%] (determined in reference vials without sediment)	96.8	95.4	93.6	94.8	95.8	96.5	95.4	93.6	94.8	95.8

[1] The recovery of the test substance in the reference vials without sediment was between 93.6 and 96.8%, which means that the test substance was not adsorbed to the glass.

Table A7_1 _3-4: Results of screening test - desorption:

	Zandkreekdam					Colijnsplaat				
Temperature [°C]	20 ± 2 °C					20 ± 2 °C				
Concentration in combined washings [µg/l]	0.3	0.6	1.1	2.4	3.4	0.2	0.5	1.0	2.1	3.9
Corresponding quantity of test material [µg]	0.003	0.006	0.011	0.024	0.034	0.002	0.005	0.01	0.021	0.039
Quantity desorbed [µg]										
[%] of adsorbed test material, which is desorbed	50	0	17	27	35	0	25	29	20	29
[%] of adsorbed test material, which is not desorbed	50	100	83	73	65	100	75	71	80	71

Table A7_1 _3-5: Degradation products analysed by HPLC:

Sediment	Treatment	Metabolite 1 (%)[a]	^{14}C copper pyrithione (%)[a]
Zandkreekdam	Adsorption	59.1	40.9
Colijnsplaat		100	n.d.
Zandkreekdam	Desorption I	100	n.d.
Colijnsplaat		100	n.d.
Zandkreekdam	Desorption II	100	n.d.
Colijnsplaat		100	n.d.
Zandkreekdam	Methanol	100	n.d.
Colijnsplaat	Extraction		

n.d.: not detectable

a: as percentage in HPLC chromatogram

Section 7.1.4.1 Annex Point IIIA XII 2.2	Field study on accumulation in the sediment	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ]	**Technically not feasible [ ]** **Scientifically unjustified [X]**	
Limited exposure [ ]	**Other justification [ ]**	
Detailed justification:	This study is not considered relevant because the non-extractable residues formed in the water/sediment study do not exceed 70% of the initial dose and the mineralisation rate in the water/sediment system is higher than 5% in 100 days.	
Undertaking of intended data submission [ ]		
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Evaluation of applicant's justification	[redacted]	
Conclusion	[redacted]	
Remarks		

Section A7.2 Annex Point IIIA XII 1	Fate and behaviour in soil	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure [X]**	**Technically not feasible [ ]** **Scientifically unjustified [ ]** **Other justification [ ]**	
Detailed justification:	As no to limited exposure of soil will take place due to the use of the active substance as an anti-fouling, no studies seem to be necessary. See also the environmental exposure assessment (Doc IIB)	
Undertaking of intended data submission [ ]		
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Evaluation of applicant's justification		
Conclusion	[redacted]	
Remarks	[redacted]	

Section A7.3.1 Phototransformation in air (estimation method)

Annex Point IIIA7.5

			Official use only
		1 REFERENCE	
1.1	**Reference**	Hollander JCTh, Paulussen JJC (2005) Determination of the photolysis in air of the active substance copper pyrithione by Atkinson calculation. TNO Chemistry, Report No: V6462, June 1, 2005 (unpublished)	
1.2	**Data protection**	Yes	
1.2.1	Data owner	API Corporation, Japan	
1.2.2	Companies with letter of access	-	
1.2.3	Criteria for data protection	Data submitted to the MS after 13 May 2000 on existing a.s. for the purpose of its entry into Annex I.	
		2 GUIDELINES AND QUALITY ASSURANCE	
2.1	**Guideline study**	Yes, the SETAC Europe Guideline and the EU Directive 95/36/EEC	
2.2	**GLP**	No, this is a theoretical study	
2.3	**Deviations**	No	
		3 MATERIALS AND METHODS	
3.1	**Test material**	Copper pyrithione	X
3.1.1	Lot/Batch number	Not applicable	
3.1.2	Specification	As given in section 2	
3.1.3	Purity	Not applicable	
3.1.4	Radiolabelling	Not applicable	
3.1.5	UV/VIS absorption spectra and absorbance value	Not applicable	
3.1.6	Further relevant properties	Not applicable	
3.2	**Reference substances**	Not applicable	
3.3	**Test solution**	Not applicable	
3.4	**Testing procedure**		
3.4.1	Test system	The photolysis of copper pyrithione in air was determined using Atkinson calculation. The atmospheric decay rate, expressed as half-life, was calculated with the Atmospheric Oxidation Programme AOPWIN©, software package v1.8 (Syracuse Research Corporation).	X a
		The atmospheric decay by hydroxyl radicals was determined by the addition of hydroxyl radicals to the aromatic rings in the two pyrithione ligands in the complex. An average hydroxyl radical concentration of $1.5 \times 10^6/cm^3$ was used in the calculation. No reaction with ozone is calculated because the complex does not contain olefinic or acetylenic bonds.	X b

Section A7.3.1 Phototransformation in air (estimation method)

Annex Point IIIA7.5

3.4.2	Properties of light source	Not applicable	
3.4.3	Determination of irradiance	Not applicable	
3.4.4	Temperature	Not applicable	
3.4.5	pH	Not applicable	
3.4.6	Duration of the test	Not applicable	
3.4.7	Number of replicates	Not applicable	
3.4.8	Sampling	Not applicable	
3.4.9	Analytical methods	Not applicable	
3.5	**Transformation products**	Not applicable	X
3.5.1	Method of analysis for transformation products	Not applicable	X
		4 RESULTS	
4.1	**Screening test**	Not applicable	
4.2	**Actinometer data**	Not applicable	
4.3	**Controls**	Not applicable	
4.4	**Photolysis data**		
4.4.1	Concentration values	Not applicable	
4.4.2	Mass balance	Not applicable	
4.4.3	k^c_p	The overall hydroxyl radical rate is 4.77×10^{-12} cm^3/molecule × sec (2.3854×10^{-12} for each of the pyrithione rings).	
4.4.4	Kinetic order	Not reported	X
4.4.5	k^c_p / k^a_p	Not applicable	
4.4.6	Reaction quantum yield (ϕ^c_E)	Not applicable	
4.4.7	k_{pE}	Not applicable	
4.4.8	Half-life ($t_{1/2E}$)	26.9 h, equivalent to 2.24 day-light periods	X
4.5	**Specification of the transformation products**	Not applicable	X
		5 APPLICANT'S SUMMARY AND CONCLUSION	
5.1	**Materials and methods**	The SETAC Europe Guideline and the EU Directive 95/36/EEC were followed	X
5.2	**Results and discussion**	The reaction with hydroxyl radicals is the only route of decay during daylight (since no olefinic or acetylenic bonds are present). However,	X

Section A7.3.1 Phototransformation in air (estimation method)

Annex Point IIIA7.5

		when copper pyrithione is degraded in e.g. water before being volatilised into the air, the reaction rate in the air is increased very much.	
5.2.1	k^c_p	The overall hydroxyl radical rate is 4.77 × 10-12 cm^3/molecule × sec (2.3854×10^{-12} for each of the pyrithione rings).	X
5.2.2	K_{pE}	Not applicable	
5.2.3	ϕ^c_E	Not applicable	
5.2.4	$t_{1/2E}$	26.9 h, equivalent to 2.24 day-light periods	X
5.3	**Conclusion**	Validity criteria can be considered as fulfilled. Copper pyrithione is expected to degrade rapidly by phototransformation in air.	X
5.3.1	Reliability	1	
5.3.2	Deficiencies	No	

Evaluation by Competent Authorities

EVALUATION BY RAPPORTEUR MEMBER STATE

Date

Materials and Methods

Results and discussion

3.

[redacted]

There seem to be a bug in the structure drawing module of the EPI suite

[redacted]

Conclusion

[redacted]

Reliability

[redacted]

Acceptability

[redacted]

Remarks	[redacted]

Section 7.3.2 Annex Point IIIA XII 3	Fate and behaviour in air, further studies	
	JUSTIFICATION FOR NON-SUBMISSION OF DATA	Official use only
Other existing data [ ] **Limited exposure [ ]**	**Technically not feasible [ ]** **Scientifically unjustified [X]** **Other justification [ ]**	
Detailed justification:	As the active substance is not to be used in preparations for fumigants and it causes no risk to the atmospheric environment, such a study does not seem to be necessary.	X
Undertaking of intended data submission [ ]		
	Evaluation by Competent Authorities	
	EVALUATION BY RAPPORTEUR MEMBER STATE	
Date	[redacted]	
Evaluation of applicant's justification	[redacted]	
Conclusion	[redacted]	
Remarks		