Data Evaluation Report on the phototransformation of chlorothalonil in water

PMRA Submission Number {.....} EPA MRID Number 45710223

Data Requirement: PMRA Data Code:
EPA DP Barcode: D301503
OECD Data Point:
EPA Guideline: 161-2

Test material:
Common name: Chlorothalonil.
Chemical name
IUPAC: Tetrachloroisophthalonitrile.
CAS name: 2,4,5,6-Tetrachloro-1,3-benzenedicarbonitrile.
CAS No: 1897-45-6.
Synonyms: None reported.
SMILES string: Clc1c(c(c(c(c1C#N)Cl)C#N)Cl)Cl.

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CITATION: Kirkpatrick, D. 1996. Chlorothalonil photodegradation in water. Unpublished study performed by Huntingdon Life Sciences Ltd., Cambridgeshire, England, sponsored by Vischim S.r.l., Milano, Italy, and submitted by Huntingdon Life Sciences Ltd., Cambridgeshire, England. HRC Study No.: VCM 42/951419. Experiment initiated July 21, 1994 and completed May 31, 1995 (p. 10). Final report issued on March 12, 1996.

EXECUTIVE SUMMARY

The aqueous phototransformation of [^{14}C]tetrachloroisophthalonitrile (chlorothalonil), at a nominal concentration of 0.3 mg a.i./L, was studied at 25 ± 1°C in sterile aqueous pH 7 (0.01M phosphate) buffered solutions for up to 12 hours under continuous irradiation. The test system used a UV-filtered xenon lamp. The equivalent continuous summer sunlight at 30° North Latitude was calculated from the intensity of the artificial light. The ratio of the intensity of the artificial light to natural sunlight varied because it was measured at different sampling positions at each sampling interval. This experiment was conducted in accordance with USEPA Guidelines for Pesticide Registration, Subdivision N §161-2, and in compliance with USEPA Good Laboratory Practices. The test system consisted of glass vials filled with *ca.* 20 mL of the treated pH 7 buffer solution. The vials were sealed, placed on a water-cooled steel block in the irradiation apparatus, and stirred with a magnetic stir bar. Volatiles were not measured, and dark controls were not prepared in the 12 hour, definitive experiment. Single irradiated test vials were collected at 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, and 12 hours posttreatment and analyzed using LSC. [^{14}C]Residues were identified via one-dimensional TLC and HPLC co-chromotagraphy and comparison of retention times with unlabeled reference standards. [^{14}C]Residues were quantified via HPLC.

Test conditions were reportedly maintained throughout the study (pH ranged from 7.06 to 7.13). However, no further supporting data were provided, and sterility was not determined.

Overall recovery of radiolabeled material averaged 100.6 ± 1.7% (range 97.3-103.5%) of the applied in the irradiated solutions. There was no significant loss of material from the buffer solution with time.

[^{14}C]Chlorothalonil declined from 100.7% of the applied radioactivity at 0 hours posttreatment to 53.2% at 6 hours to a final of 20.9% at 12 days (study termination; outlier of 12.1% at 9 hours). Eight transformation products were observed and named components 1-8. Four major transformation products were observed: components 1, 2, 3, and 7. Component 1 (Rt 2.0 minutes) was measured at a maximum and final value of 29.6% of the applied radioactivity at 12 hours posttreatment (study termination). Component 2 (Rt 3.0 minutes) was measured at a maximum and final value of 17.3% at 12 hours. Component 3 (Rt 4.0 minutes) increased to a maximum value of 10.8% at 9 hours (outlier time interval) and declined to 4.8% at 11 hours and was not resolved at 12 hours. Component 7 (Rt 14.0 minutes) increased to a maximum of 14.3% at 7 hours and declined slightly to 12.6% at 12 hours. Component 7 was identified as an isomer of hydroxy-chloro-1,3-dicyanobenzene via GC/MS analysis in the supplemental experiment with the high-dose irradiated samples. Four minor transformation products were observed: components 4, 5, 6, and 8. Component 4 (Rt 4.5 minutes), component 5 (Rt 5.0 minutes), component 6 (Rt 12.0 minutes), component 8 (Rt 15.5 minutes) were measured at respective maximum values of 4.7% at 12 hours, 3.4% at 6 hours, 4.9% at 9 hours (outlier time interval), and 6.9% at 12 hours. Components 6 and 8 were identified as 4-hydroxy-2,5,6-trichloro-1,3-dicyanobenzene and trichloro-1,3-dicyanobenzene,

respectively, via GC/MS analysis in the supplemental experiment with the high-dose irradiated samples.

Components 1-5 were not conclusively identified in the study, including the three major transformation products components 1-3. The study author reported that chromatographic characterization (which was not provided) identified these components to be highly polar. Therefore, based on that data, the study author suggested that these components were low molecular weight, ring-opened, dechlorinated phototransformation products of chlorothalonil.

Based on first-order linear regression analysis using all data points (except the outlier of 12.1% at 9 hours), the reviewer-calculated half-life of [^{14}C]chorothalonil in the irradiated solution was 7.1 hours (continuous irradiation; or 14.2 hours based on 12-hour light/12-hour dark cycles). Dark controls were not prepared. The study author calculated the half-life of chorothalonil in pH 7 buffered solution as 10.5 hours based on equivalent continuous summer sunlight at 30° North Latitude via first-order reaction kinetics based on all data points (except the outlier). The study author did not report a half-life based on hours of continuous irradiation with the irradiation apparatus.

The **phototransformation half-life** for chlorothalonil at pH 7 is 14.2 hours, based on 12-hour light/12-hour dark cycles. The equivalent continuous summer sunlight at 30° North Latitude was calculated by the study author for each sampling interval. The reviewer was then able to calculate the predicted environmental phototransformation half-life of chlorothalonil by plotting the disappearance of chlorothalonil versus the equivalent continuous summer sunlight at 30° North Latitude. The calculated predicted **environmental phototransformation half-life** of chorothalonil in the irradiated samples is approximately 20.6 hours in the pH 7 buffer solution (10.3 hours based on continuous summer sunlight at 30° North Latitude).

A transformation pathway was proposed by the study author. The parent, chlorothalonil, degraded to 4-hydroxy-2,5,6-trichloro-1,3-dicyanobenzene (component 6), hydroxy-chloro-1,3-dicyanobenzene (component 7), and trichloro-1,3-dicyanobenzene (component 8). 4-Hydroxy-2,5,6-trichloro-1,3-dicyanobenzene, hydroxy-chloro-1,3-dicyanobenzene, and trichloro-1,3-dicyanobenzene degraded to polar, low molecular weight components which, in turn, degraded to CO_2.

Results Synopsis:

		Half-life	Major transformation products	Minor transformation products
25°C;[^{14}C]clodinafop-propargyl; 0-12 hour data; continuous irradiation				
pH 7	Irradiated	7.11 hours	Hydroxy-chloro-1,3-dicyanobenzene isomer (component 7). Components 1, 2, and 3.*	4-Hydroxy-2,5,6-trichloro-1,3-dicyanobenzene (component 6). Trichloro-1,3-dicyanobenzene (component 8). Components 4 and 5.
	Dark	stable**		

* Components 1, 2, and 3 were suggested to be low molecular weight, ring-opened, dechlorinated phototransformation products of chlorothalonil.

**Dark controls were not prepared in the definitive study, but chlorothalonil was stable in the dark control for the 96 hour preliminary study.

Study Acceptability: This photodegradation study conducted using pH 7 sterile buffer solutions is classified as **acceptable**. It is scientifically valid, and can be used to fulfill the requirement for a photolysis in water study. While there were some minor deficiencies in this study, they have not effected the interpretation of the reported data. Dark controls were not prepared for the 12 hour study, all major transformation products were not adequately identified, the sterility of the samples of the 12 hour study was not determined at study termination, and the storage stability of the test samples was not determined. However, the stability of the test substance in the dark control of the 96 hour study indicates that the test substance is not expected to degrade in the time period reported for between sample collection and analysis.

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: This study was conducted in accordance with the USEPA Pesticide Assessment Guidelines for Photodegradation in Water, Subdivision N §161-2, and Annex I to EEC Council Directive 91/414/EEC (pp. 1, 14). The following significant deviations from the Subdivision N §161-2 guidelines were noted:

Dark controls were not prepared in the 12 hour, definitive study. This does not affect the validity of the study.

The major transformation products components 1-3 (maximum values of 10.8% to 29.6% of the applied radioactivity) were not identified. Additionally, the major transformation product component 7 (maximum of 14.3% of the applied) was only identified as an isomer of hydroxy-

chloro-1,3-dicyanobenzene. The mass spectra analysis was not adequate for transformation product identification. Subdivision N guidelines require that a reasonable attempt is made to identify transformation products which are observed at ≥10% of the applied radioactivity. This does not affect the validity of the study.

The sterility of the samples of the 12 hour, definitive study was not determined at study termination. Subdivision N guidelines require that the sterility of the test samples is assured in the study. This does not affect the validity of the study.

COMPLIANCE: This study was conducted in compliance with USEPA (40 CFR Part 160), British, EC Council, OECD, and Japanese Good Laboratory Practices (1983 and 1989; 1986 and 1989; 1986; 1992; 1984; p. 3). Signed and dated Data Confidentiality, GLP, Certificate of Authenticity, and Quality Assurance statements were provided (pp. 2-5).

A. MATERIALS

1. Test Materials [^{14}C]Tetrachloroisophthalonitrile (chlorothalonil; pp. 11, 16).

Chemical Structures: See DER Attachment 2.

Description: Crystalline solid (p. 11).

Purity: Radiochemical purity: >97% (by TLC; p. 16; Appendix 6, p. 76).
Lot No.: CFQ 7386 (p. 11).
Analytical purity: Not reported.
Specific activity: 3.8 MBq/mg, 102.6 µCi/mg.
Location of the radiolabel: Uniformly in the phenyl ring (Appendix 5, p. 62).

Storage conditions: Test material was stored at <-15°C in the dark according to the study protocol (Appendix 5, p. 62).

Physico-chemical properties of chlorothalonil.

Parameter	Values	Comments
Molecular Formula	$C_8Cl_4N_2$	
Molecular weight	265.9 g/mole	
Water solubility	0.6 mg/L	In acetone, 20 g/L.
Melting point	250-251°C	
Density	Not reported.	
Vapor pressure	Not reported.	
UV absorption	Not reported.	The UV/Vis spectra was provided in Appendix 2, Figure 2, p. 55 of the study report.
pK_a	Not reported.	
K_{ow}/log K_{ow}	Not reported.	
Stability of compound at room temperature	Not reported.	

Data obtained from p. 11 of the study report.

2. Buffer Solution: The following buffer solutions were prepared:

Table 1: Description of buffer solutions.

pH	Type and final molarity of buffer	Composition
7	0.01M phosphate	1.56 g of sodium dihydrogen orthophosphate was dissolved in 900 mL of Super Purity Water*. After the pH was adjusted to *ca.* 7.0 with aqueous sodium hydroxide, the volume was adjusted to 1000 mL with Super Purity Water. Further pH adjustment was not necessary.

Data obtained from p. 15 of the study report.

* Specifications for Super Purity Water were provided in Appendix 3, p. 56 of the study report.

3. Details of light source:

Table 2: Artificial light source.

Property	Details
Type of lamp used:	Xenon arc lamp (Suntest Accelerated Exposure Unit, Heraeus Equipment Limited, UK). The irradiation apparatus is shown in Figure 1, p. 35 of the study report.
Emission wavelength spectrum:	290-400 nm.
Light intensity:	Approximately 0-90 $\mu W/cm^2$ between 300 and 400 nm.[1]
Filters used:	UV filters eliminated radiation <290 nm.
Relationship to natural sunlight:	The average mid-day intensity of the natural sunlight on April 25, 1995 at Huntingdon Research Centre, Cambridgeshire, England (52°21' north latitude) was measured as 2610 $\mu W/cm^2$. The intensity of the sunlight was corrected to reflect the difference in intensity of sunlight at 30°N during the summer (ratio 0.77), and that radiation from the sun in June is *ca.* 75% of the peak radiation intensity over 12 hours. However, the number of hours equivalent to continuous summer sunlight at 30°N latitude at each sampling interval varied because they were calculated based on measurements from different sample positions; the reviewer-calculated ratio of equivalent hours averaged 1.28 (see Reviewer's Comments and DER Attachment 1). The emission spectrum of the artificial light to natural sunlight was similar. A graphical comparison was provided in Figure 2, p. 36 of the study report.

Data obtained from pp. 14 and 21-23; Table III, p. 29 in the study report.
1 Approximated by the reviewer based on Figure 2, p. 36 of the study report.

B. EXPERIMENTAL CONDITIONS:

1. Preliminary experiments: No preliminary experiments were reported.

2. Experimental conditions:

Table 3: Experimental design.

Parameter		Details
Duration of the test:		12 hours (continuous irradiation).
Application rate:	Nominal:	0.3 mg a.i./L
	Measured:	Not reported.
Dark controls used (Yes/No):		No.
Replications	Dark controls:	Dark controls were not prepared in the 12 hour, definitive study.
	Irradiated:	One test vial was removed from the irradiation apparatus at each sampling interval.
Preparation of the test medium	Volume used/ treatment:	The [^{14}C]chlorothalonil dose solution (concentration 0.1-0.2 mg/mL, acetonitrile solvent) was dissolved in the pH 7 buffer (concentration 0.3 mg/L, unreported volume of buffer).
	Method of sterilization:	The buffer solution, test vials, other equipment (pipets, stir bars, etc.), and glassware were sterilized by autoclaving for 20 minutes at 121°C. Aseptic procedures were used throughout the experiment.
	Co-solvent, if any:	Acetonitrile, 1%.
Test apparatus (Type/material/ volume):	Dark controls:	Dark controls were not prepared in the 12 hour, definitive study.
	Irradiated:	An aliquot (*ca.* 20 mL) of the treated buffer solution was pipetted into cylindrical, borosilicate glass vials (2.5 cm i.d. x 8.0 cm h). The vials were sealed and placed on a water-cooled steel block in the irradiation apparatus and stirred with a Teflon-coated magnetic stir bar. Illustrations of the incubation set and test apparatus were provided in Figure 1, p. 35 and Figure 3, p. 37 of the study report.
Details of traps for CO_2 and organic volatiles, if any:	Dark controls:	Dark controls were not prepared in the definitive study.
	Irradiated:	Volatiles were not trapped in the definitive study.
If no traps were used, is the system closed/open?		Closed.
Any indication of the test material adsorbing to the walls of the test apparatus?		Not indicated.
Experimental conditions.	Temperature (°C):	25 ± 1°C (mean temperature, 25.2°C).
	Duration of light/ darkness:	Continuous irradiation.

Parameter	Details
Other details, if any:	The test vials (cylindrical, borosilicate glass vials) were equipped with side-arms. The side-arms were sealed during the definitive study.

Data obtained from pp. 15-17 in the study report.

3. Supplementary experiments: 96-hour study: The aqueous phototransformation of [^{14}C]chlorothalonil, at a nominal concentration of 0.3 mg a.i./L, was studied at 25 ± 1°C (mean temperature 24.9°C for all samples) in sterile aqueous pH 7 (0.01M phosphate) buffered solutions for up to 96 hours under continuous irradiation (equivalent to 121.6 hours of continuous summer sunlight at 30° North Latitude; pp. 14-16). The test system was the same as that which was used in the definitive study. Cylindrical, borosilicate glass vials (2.5 cm i.d. x 8.0 cm h) filled with *ca.* 20 mL of the treated pH 7 buffer solution. The irradiation samples were placed on a water-cooled steel block in the irradiation apparatus and stirred with a magnetic stir bar. The dark controls were stirred continuously in the dark, temperature-controlled room. Both the irradiation samples and dark controls were fitted with individual volatile-trap apparatuses. Sterile, humidified air was drawn through the headspace of a pair of test vessels (flow rate 5 mL/minute), and volatiles were trapped by a 2-(2-ethoxyethanol) trap and two KOH traps (for carbon dioxide), consecutively. Microbiological filters (0.2 µm) were incorporated on either side of each pair of test vessels to ensure sterility. Duplicate irradiated and non-irradiated test vials were collected at 0 (dark controls only), 12, 24, 48, and 96 hours posttreatment and analyzed using LSC. The 2-(2-ethoxyethanol) and KOH trap solutions were collected and analyzed at every sampling interval, except day 0. The pH was measured at every sampling interval. The pH ranged 7.06 to 7.17 for the irradiated samples and 7.04 to 7.21 for the dark controls throughout the study (pp. 17, 23; Appendix 1, p. 46). The sterility was determined at every sampling interval. Samples remained sterile throughout the experiment (pp 17, 23). All samples were stored in the freezer at <-15°C. The parent was only identified in the dark controls via HPLC (Methods B; pp. 19-20). Other [^{14}C]residues were not identified via one-dimensional TLC, HPLC, or HPLC-APCI MS analysis.

High level irradiation: In order to provide sufficient material to identify phototransformation products, a set of high concentration samples (0.3 mg a.i./mL; 10% ethanol by volume) were prepared in pH 7 buffer (0.01M phosphate) and irradiated for 5 to 16 hours under the same conditions as those described in the definitive study (p. 17). After incubation, samples were placed in the freezer at <-15°C prior to analysis (unreported length of storage). The identities of the parent and major transformation products, which were observed in the definitive study, were determined and confirmed by HPLC-APCI MS analysis (pp. 19-21). The HPLC system (Method A) was equipped with an Zorbax R_xC_8 column (250 mm x 4.6 mm; particle size not reported), gradient mobile phase consisting of (A) 20 mM ammonium formate pH 3 and (B) acetonitrile [percent A:B; 0 minutes 75:25 and 20 minutes 0:100], flow rate 1.5 mL/min, and UV/Vis (254 nm) and radioactivity detectors. The atmospheric pressure chemical ionization (APCI) MS analysis was performed using a TSQ7000 Finnigan MAT mass spectrometer in negative ion mode. The m/z scan was from 100 to 400.

Quantum Yield: In order to determine the quantum yield, aliquots (*ca.* 20 mL) of a *p*-nitroanisole (PNA)/pyridine actinometer solution was prepared in the same borosilicate test vials which were used in the definitive experiment (p. 17). The irradiated actinometry samples were irradiated simultaneously with the irradiated samples of the definitive experiment (i.e., 25 ± 1°C, continuously stirred). At each sampling interval of the definitive experiment, one actinometry sample was removed for analysis. The dark actinometry samples were maintained at 25 ± 1°C in the dark for 24 hours. A dark sample was analyzed at 0 and 24 hours. The actinometry samples were analyzed by HPLC (Method C; pp. 19-20). The quantum yield was determined to be 2.03×10^{-2} by the study author (p. 25; calculations were provided in Appendix 2, pp. 47-55).

4. Sampling:

Table 4: Sampling details.

Parameters		Details
Sampling intervals:		0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, and 12 hours posttreatment.
Sampling method:	Dark	Dark controls were not prepared in the definitive study.
	Irradiated	At each sampling interval, one test vial was removed from the water-cooled steel block in the irradiation apparatus.
Method of collection of volatile compounds, if any:	Dark	Dark controls were not prepared in the definitive study.
	Irradiated	Volatiles were not trapped in the definitive study.
Sampling intervals/times for: Sterility check: pH measurement:		 None. At every sampling interval.
Sample storage before analysis:		All samples, except the 12-hour, were analyzed on the day of sampling.
Other observations, if any:		None.

Data obtained from pp. 16-17, 23; and Appendix 1, p. 46 of the study report.

C. ANALYTICAL METHODS:

Extraction/clean up/concentration methods, if used: Each test vessel was re-weighed, and acetonitrile (2 mL) added aseptically to dissolve any insoluble radioactive photodegradates prior to analysis (p. 17).

Volatile residue determination: Volatiles were not trapped in the definitive study.

Total ^{14}C measurement: Total [^{14}C]residues in solution were determined by LSC analysis of the test solutions (unreported number and volume of aliquots for analysis; p. 18).

Derivatization method, if used: A derivatization method was not employed.

Identification and quantification of the parent: Chlorothalonil was identified by one-dimensional TLC analysis (p. 18). The TLC was performed with silica gel plates (0.25 mm thickness; 254 F) developed in hexane:ethyl acetate:acetic acid (90:10:1, v/v/v; solvent system code: A), hexane:dichloromethane (1:1, v/v; solvent system code: B), and toluene:acetone (4:1, v:v; solvent system code: D). Reverse TLC was performed with octadecyl silane (ODS) plates (0.2 mm thickness) developed in methanol:water (9:1, v:v; solvent system code: C). The samples were co-chromatographed with an unlabeled reference standard of chlorothalonil (tetrachloroisophthalonite, Lot No. 14/09/93/1, chemical purity 99.84%; R_f A and B: 0.30; R_f C: 0.50; R_f D: 0.68; pp. 12, 18; Table I, p. 27). The plates were visualized by exposure to UV light (unreported wavelength). Radioactive residues were visualized by radiography. The Fuji BAS2000 Autoradiographic Imaging System was used to confirm the identification via co-chromatography (p. 19).

The quantity of the parent in the aqueous solutions was determined by HPLC analysis of the aqueous solutions (pp. 19-20). The HPLC system (Method A) was equipped with an Zorbax R_xC_8 column (250 mm x 4.6 mm; particle size not reported), gradient mobile phase consisting of (A) 20 mM ammonium formate pH 3 and (B) acetonitrile [percent A:B; 0 minutes 75:25 and 20 minutes 0:100], flow rate 1.5 mL/min, and UV/Vis (254 nm) and radioactivity detectors. [^{14}C]Residues were quantified by collection of 1-minute fractions. Chlorothalonil was identified by comparison of the retention time of the unlabeled chlorothalonil reference standard (Lot No. 14/09/93/1, chemical purity 99.84%; retention time: 15 minutes; pp. 12, 20; Table II, p. 28).

Identification and quantification of transformation products: The transformation products were isolated in the aqueous solutions via one-dimensional TLC and HPLC using the same methods as described for the parent (pp. 18-20). The transformation products were identified by co-chromatography and comparison of the retention time with the following unlabeled reference standards (pp. 12-13, 18, 20; Table I-II, pp. 27-28):

Isophthalonitrile (1,3-dicyanobenzene; chemical purity 99.8%; TLC R_f D: 0.60; HPLC retention time: 9 minutes);

4-Hydroxy-2,5,6-trichloro-1,3-dicyanobenzene (chemical purity not reported; Batch/reference No.: 21/9/93; TLC R_f D: origin; HPLC retention time: 12 minutes);

4-Methoxy-2,5,6-trichloroisophthalonitrile (chemical purity 97.2%; TLC R_f: not reported; HPLC retention time: not reported);

Monoamide of chlorothalonil (3-cyano-2,4,5,6-tetrachlorobenzamide; chemical purity not reported; TLC R_f D: 0.34; HPLC retention time: 10 minutes); and

Diamide of chlorothalonil (2,4,5,6-tetrachloroisophthalamide; chemical purity not reported; TLC R_f D: 0.06; HPLC retention time: 4.5 minutes).

Detection limits (LOD, LOQ) for the parent: The Limits of Detection for the LSC was reported to be twice the background (the value of the background was not reported; p. 18). The Limits of Detection for the HPLC and TLC were not reported. The Limits of Quantification were not reported for the LSC, HPLC, and TLC analyses.

Detection limits (LOD, LOQ) for the transformation products: The Limits of Detection and Quantification were the same as those for the parent.

II. RESULTS AND DISCUSSION:

A. TEST CONDITIONS: The incubation temperature was reported as 25 ± 1°C (mean temperature 25.2°C) for the irradiated solutions during the study. No supporting data were provided (pp. 15-16). The pH ranged from 7.06 to 7.13 (p. 23; Appendix 1, p. 46). The sterility of the irradiated, 12 hour test solutions was not determined during the study. Dark controls were not prepared for the 12 hour, definitive experiment, but were used for the 96 hour study.

B. MATERIAL BALANCE: In the pH 7 sterile buffer solutions, the overall recovery of radiolabeled material averaged 100.6 ± 1.7% (range 97.3-103.5%) of the applied in the irradiated solutions (Table IV, p. 30). There was no significant loss of material from the buffer solution with time.

Table 5: Phototransformation of [^{14}C]chlorothalonil in the irradiated solutions, expressed as percentage of the applied radioactivity, at pH 7 and 25°C.*

Compound	Sampling times (hours)												
	0	1	2	3	4	5	6	7	8	9	10	11	12
Chlorothalonil (Rt 16.5 min)	100.7	83.8	78.8	71.0	68.4	61.7	53.2	49.2	43.1	12.1[1]	48.7	41.0	20.9
1 (Rt 2.0 min)	<0.1	NR	2.6	3.2	3.3	6.0	10.7	12.7	11.0	26.0	13.4	14.0	29.6
2 (Rt 3.0 min)	<0.1	0.8	1.5	1.4	3.3	3.1	6.6	8.2	8.5	15.5	8.2	12.1	17.3
3 (Rt 4.0 min)	<0.1	1.6	NR	1.6	NR	2.7	NR	4.3	5.8	10.8	5.0	4.8	NR
4 (Rt 4.5 min)	<0.1	0.5	1.5	0.5	2	2.0	1.4	1.2	2.4	3.8	2.5	3.0	4.7
5 (Rt 5.0 min)	<0.1	1.7	1.9	2.1	2.2	1.3	3.4	1.0	2.4	1.1	1.0	1.2	1.8
6 (4-hydroxy-2,5,6-trichloro-1,3-dicyanobenzene; ret. time 12.0 min)	<0.1	3.9	3.3	3.4	2.9	2.2	2.2	2.4	2.9	4.9	2.4	2.4	3.9
7 (hydroxy-chloro-1,3-dicyanobenzene; ret. time 14.0 min)	<0.1	3.9	9.1	9.3	11.5	13.2	13.1	14.3	13.2	14.1	12.1	12.0	12.6
8 (trichloro-1,3-dicyanobenzene; ret. time 15.5 min)	<0.1	3.3	3.7	4.9	4.8	5.3	6.1	6.4	6.5	5.8	6.6	6.7	6.9
Others (non-discrete radioactivity)	0.2	1.1	1.2	1.1	1.5	1.7	1.8	2.2	1.7	3.2	1.9	2.0	3.3
Total % recovery (aqueous solution)	100.9	100.8	103.5	98.5	99.8	99.7	102.0	102.4	101.2	97.3	101.9	98.9	101.0
Total volatiles	Volatiles were not measured in the definitive study.												
Total % recovery:	100.9	100.8	103.5	98.5	99.8	99.7	102.0	102.4	101.2	97.3	101.9	98.9	101.0

* Data obtained from Table IV, p. 30 and Table VIII, p. 34 of the study report.
NR = Not resolved.
1 The reviewer omitted this outlier when calculating the half-life of chlorothalonil.

C. TRANSFORMATION OF PARENT COMPOUND: In the irradiated samples in pH 7 buffer solutions at 25°C, [^{14}C]chlorothalonil declined from 100.7% of the applied radioactivity at 0 hours posttreatment to 53.2% at 6 hours, and was 20.9% at 12 days (study termination; Table VII, p. 33).

HALF-LIFE: The calculated half-life of [^{14}C]chorothalonil were based on first-order linear regression analysis (Excel 2000) using all data points, except the outlier of 12.1% at 9 hours. For chorothalonil in pH 7 buffer at 25°C, the calculated the half-life of 7.1 hours of continuous irradiation (14.2 hours of 12-hour light/12-hour dark cycles) for the irradiated solutions.

Half-lives*

Temperature		First order linear			DT50	DT90
		Half-life	Regression equation	r^2		
25°C;[^{14}C]chorothalonil; continuous irradiation						
pH 7	Irradiated	7.1 hours	y = -0.0975x + 4.585	0.8599	10.5 hours[1]	ND
	Dark	Dark controls were not prepared for the definitive study.				

*Half-lives were calculated using data obtained from Table VII, p. 33 of the study report (DER Attachment 1). DT50 value was obtained from p. 24 of the study report (the study author's decay curves were illustrated in Figure 5, p. 39 and Figure 10, p. 44 of the study report).
1 Hours of equivalent continuous summer sunlight at 30° N Latitude.
ND = Not determined.

The **phototransformation half-life** for chlorothalonil at pH 7 is 14.2 hours, based on 12-hour light/12-hour dark cycles.

The study author calculated the equivalent continuous summer sunlight at 30° North Latitude from the intensity of the artificial light by the following equation: {[(duration of artificial irradiation) x (irradiance of artificial light) x (0.77)]/[(2610 $\mu W/cm^{-2}$) x (0.75)]}; where 2610 $\mu W/cm^{-2}$ is the average mid-day intensity of the natural sunlight on April 25, 1995 at Huntingdon Research Centre (52°21' North Latitude), 0.77 is the ratio for the adjustment from 52°21' North Latitude to 30° North Latitude, and 0.75 is the correction for diurnal variation (p. 22). The equivalent continuous summer sunlight at 30° North Latitude was calculated at each sampling interval based on the irradiance of the artificial light at different sampling positions. Since these values did not have a constant, direct relationship to the hours of continuous irradiation with the irradiation apparatus, the predicted environmental phototransformation half-life of chlorothalonil was calculated by plotting the disappearance of chlorothalonil versus time values of the equivalent continuous summer sunlight at 30° North Latitude. Therefore, the predicted **environmental phototransformation half-life** of chorothalonil in the irradiated samples is approximately 20.6 hours in the pH 7 buffer solution (see DER Attachment 1).

TRANSFORMATION PRODUCTS: In the irradiated solutions in pH 7 buffer at 25°C, eight total transformation products were observed and named Components 1-8. Four major transformation

products were observed: components 1, 2, 3, and 7 (Table VIII, p. 34). Component 1 (Rt 2.0 minutes) was measured at a maximum and final value of 29.6% of the applied radioactivity at 12 hours posttreatment (study termination). Component 2 (Rt 3.0 minutes) was measured at a maximum and final value of 17.3% at 12 hours. Component 3 (Rt 4.0 minutes) increased to a maximum value of 10.8% at 9 hours (outlier time interval) and declined to 4.8% at 11 hours and was not resolved at 12 hours. Component 7 (Rt 14.0 minutes) increased to a maximum of 14.3% at 7 hours and declined slightly to 12.6% at 12 hours. Component 7 was identified as an isomer of hydroxy-chloro-1,3-dicyanobenzene via HPLC-APCI MS analysis in the supplemental experiment with the high-dose irradiated samples. Four minor transformation products were observed: components 4, 5, 6, and 8. Component 4 (Rt 4.5 minutes) was measured at a maximum of 4.7% at 12 hours. Component 5 (Rt 5.0 minutes) was measured at a maximum of 3.4% at 6 hours. Component 6 (Rt 12.0 minutes) was measured at a maximum of 4.9% at 9 hours (outlier time interval). Component 8 (Rt 15.5 minutes) was measured at a maximum of 6.9% at 12 hours. Components 6 and 8 were identified as 4-hydroxy-2,5,6-trichloro-1,3-dicyanobenzene and trichloro-1,3-dicyanobenzene, respectively, via HPLC-APCI MS analysis in the supplemental experiment with the high-dose irradiated samples. Other radioactivity (regions of radioactivity without discrete peaks) was measured at a maximum of 3.3% at 12 hours. All components (1-8) were measured at <0.1% at 0 hours; other radioactivity accounted for 0.2% at 0 hours.

Components 1-5 were not conclusively identified in the study, including the three major transformation products components 1-3. The study author reported that chromatographic characterization identified these components to be highly polar (p. 24). Therefore, based on that data, the study author suggested that these components were low molecular weight, ring-opened, dechlorinated phototransformation products of chlorothalonil.

Dark controls were not prepared in the 12 hour, definitive experiment of the study.

VOLATILIZATION: Volatiles were not measured in the 12 hour, definitive study.

TRANSFORMATION PATHWAY: A transformation pathway was provided in Figure 11, p. 45 of the study report. The parent, chlorothalonil, degraded to 4-hydroxy-2,5,6-trichloro-1,3-dicyanobenzene (component 6), hydroxy-chloro-1,3-dicyanobenzene (component 7), and trichloro-1,3-dicyanobenzene (component 8). 4-hydroxy-2,5,6-trichloro-1,3-dicyanobenzene, hydroxy-chloro-1,3-dicyanobenzene, and trichloro-1,3-dicyanobenzene degraded to polar, low molecular weight components which, in turn, degraded to CO_2.

Table 6: Chemical names for the transformation products of chorothalonil.

Applicant's Code Name	CAS Number	Chemical Name	Chemical formula	Molecular weight (g/mol)	SMILES string
Component 6		4-hydroxy-2,5,6-trichloro-1,3-dicyanobenzene	--	--	--
Component 7		hydroxy-chloro-1,3-dicyanobenzene isomer	--	--	--
Component 8		trichloro-1,3-dicyanobenzene	--	--	--

Data obtained from pp. 12-13, 24-25 of the study report.

D. SUPPLEMENTARY EXPERIMENT-RESULTS: 96-hour study: The overall recovery of radiolabeled material averaged 100.9 ± 4.1% (range 93.7-107.8%) of the applied in the irradiated solutions and 104.9 ± 2.3% (range 99.0-108.6%) of the applied in the dark controls (Table IV-V, pp. 30-31). There was no significant loss of material from the buffer solution with time.

In the dark controls in pH 7 buffer solutions at 25°C, [^{14}C]chlorothalonil ranged from 96.2% to 103.6% of the applied radioactivity from 0-96 hours posttreatment (Table VI, p. 32). Chlorothalonil was stable in the dark controls. The study authors reported that no other discrete peaks were observed in the HPLC chromatograms (p. 24; Figure 4, p. 38). Volatiles were measured at maximum averages of 12.0% (96 hours) and 0.3% (48 hours) in the irradiated solutions and dark controls, respectively, in the pH 7 buffer solution (p. 23; Table IV-V, pp. 30-31). The volatiles were characterized as volatilized $^{14}CO_2$ (via barium chloride precipitation; pp. 20, 23). [^{14}C]Residues of the irradiated solutions were not characterized.

The results of the 96-hour study are provided in the following table (Table IV-VI, pp. 30-32):

		Sampling intervals (hours of continuous irradiation)					
		0	6	12	24	48	96
Chlorothalonil	Irradiated	Not analyzed					
	Dark	102.1 ± 0.1	102.0 ± 0.7	98.8 ± 3.6	102.2 ± 0.4	102.7 ± 1.3	101.4 ± 0.7
Buffer	Irradiated	104.4 ± 0.3	105.5 ± 3.0	100.2 ± 1.1	98.7 ± 2.1	93.5 ± 1.2	82.2 ± 0.7
	Dark		105.5 ± 0.6	101.5 ± 3.5	105.2 ± 0.4	107.7 ± 0.9	105.2 ± 0.1
Volatiles	Irradiated	<0.1	0.2 ± 0.0	0.4 ± 0.0	2.6 ± 0.0	6.0 ± 0.0	12.0 ± 0.0
	Dark		<0.1	<0.1	<0.1	0.3 ± 0.0	<0.1
Total Recovery	Irradiated	104.4 ± 0.3	105.7 ± 3.0	100.6 ± 1.1	101.3 ± 2.1	99.5 ± 1.2	94.2 ± 0.7
	Dark		105.5 ± 0.6	101.5 ± 3.5	105.2 ± 0.4	108.0 ± 0.9	105.2 ± 0.1

From the results of the 96-hour study, the study author concluded that the sterility was maintained in the study, chlorothalonil ultimately degraded to carbon dioxide during photolysis, and chlorothalonil was stable in pH 7 buffer solutions in the dark at 25°C (p. 24).

High level irradiation: The identity of 4-hydroxy-2,5,6-chloro-1,3-dicyanobenzene was confirmed by HPLC-APCI MS analysis (p. 24; Figure 7, p. 41). Components 7 and 8 were identified as an isomer of hydroxy-chloro-1,3-dicyanobenzene and trichloro-1,3-dicyanobenzene, respectively (pp. 24-25; Figures 8-9, pp. 42-43).

III. STUDY DEFICIENCIES: The study was scientifically valid, but several significant deviations from Subdivision N guidelines were noted:

1. Dark controls were not prepared for the 12 hour, definitive study. Subdivision N guidelines require that dark controls are included in photodegradation in water studies. This does not affect the validity of the study.

2. Several major transformation products were not identified. Components 1-3 were measured at maximum values of 29.6% (12 hours), 17.3% (12 hours), and 10.8% (9 hours- outlier) of the applied radioactivity, respectively, in the study. Components 1-3 were identified only as low molecular weight, ring-opened, dechlorinated phototransformation products of chlorothalonil, based on chromatographic characterization. Subdivision N guidelines require that a reasonable attempt is made to identify transformation products which are observed at ≥10% of the applied radioactivity. This does not affect the validity of the study.

3. The major transformation product component 7 (maximum 14.3% of the applied at 7 hours) was only identified as an isomer of hydroxy-chloro-1,3-dicyanobenzene. Another method, such as ^{1}H NMR analysis, should have been performed in order to fully identify this major transformation product. The results indicate that mass spectra analysis was not adequate for transformation product identification. Subdivision N guidelines require that a reasonable attempt is made to identify transformation products which are observed at ≥10% of the applied radioactivity. This does not affect the validity of the study.

4. The study report indicated that the test samples were stored at <-15°C (p. 17). No additional information was provided about this storage, specifically the time length of storage or the time point in sample processing which this storage took place. Additionally, the storage stability of the test samples at < -15°C was not determined. These details regarding sample storage should have been included in the study report, especially when considering the high degradation rate of the test material. This does not affect the validity of the study.

IV. REVIEWER'S COMMENTS:

1. The reviewer calculated the ratio of hours equivalent to continuous summer sunlight at latitude 30°N and actual irradiation time (hours) for each sampling interval based on the data provided in Table III, p. 29. The average ratio was 1.28 (range 1.07-1.60; see DER Attachment 1). Using this average ratio, the environmental phototranformation half-life of chlorothalonil was approximately 18.2 hours.

2. The reviewer believed that it was questionable if component 3 (Rt 4.0 minutes) was a true major transformation product. It was only observed above 10% of the applied radioactivity at 9 hours (10.8%; Table VIII, p. 34). At all other time intervals, component 3 was observed at ≤5.8%. Since the 9-hour time interval was an outlier time interval, and not included in the half-life determination of the reviewer or the study author, data from this time interval may be questionable.

3. The Limit of Detection and Quantification for the LSC, HPLC, and HPLC-APCI MS methods were not provided. LODs and LOQs should be reported to allow the reviewer to evaluate the adequacy of the test method.

4. In order to determine the quantum yield, aliquots (*ca.* 20 mL) of a *p*-nitroanisole (PNA)/pyridine actinometer solution was prepared in the same borosilicate test vials which were used in the definitive experiment (p. 17). The irradiated actinometry samples were irradiated simultaneously with the irradiated samples of the definitive experiment (i.e., 25 ± 1°C, continuously stirred). At each sampling interval of the definitive experiment, one actinometry sample was removed for analysis. The dark actinometry samples were maintained at 25 ± 1°C in the dark for 24 hours. A dark sample was analyzed at 0 and 24 hours. The actinometry samples were analyzed by HPLC (Method C; pp. 19-20). The quantum yield was determined to be 2.03 x 10^{-2} by the study author (p. 25; calculations were provided in Appendix 2, pp. 47-55).

5. Both the reviewer and the study author did not include the data from the 9-hour sampling interval when calculating the half-life of chlorothalonil since it was an outlier. However, the study author did not provide any possible explanation for the occurrence of the outlier. Regardless, the material balance for this time interval was very good (97.3% of the applied radioactivity) even though the amount of parent was approximately 30% of the applied radioactivity less than the amounts measured in the time points before and after (8 and 10 hours). Further clarification may be required.

6. The reference standard, 4-methoxy-**2,5,6**-trichloroisophthalonitrile, was incorrectly named as 4-methoxy-**2,4,5**-trichloroisophthalonitrile in the study report (p. 13).

7. The physico-chemical properties of the test substances were incomplete. Density, vapor pressure, UV absorption, K_{ow}/log K_{ow}, pKa, and stability at room temperature were not reported.

8. The UV/Vis spectra was provided in Appendix 2, Figure 2, p. 55 of the study report.

9. Representative HPLC chromatograms for the definitive study were presented in Figure 6, p. 40 of the study report. Figure 10 illustrated the decline of the parent and the production of the phototransformation products (p. 44).

10. The Experimental Protocol was provided in Appendix 5, pp. 59-74 of the study report. Appendix 4 was the "Sample raw data and calculation of radioactivity measurements" (pp. 57-58).

V. REFERENCES:

1. U.S. Environmental Protection Agency. 1982. Pesticide Assessment Guidelines, Subdivision N, Chemistry: Environmental Fate, Section 161-2. Photolysis studies. Office of Pesticide and Toxic Substances, Washington, DC. EPA 540/9-82-021.

2. U.S. Environmental Protection Agency. 1989. FIFRA Accelerated Reregistration, Phase 3 Technical Guidance. Office of the Prevention, Pesticides, and Toxic Substances, Washington, DC. EPA 540/09-90-078.

3. U.S. Environmental Protection Agency. 1993. Pesticide Registration Rejection Rate Analysis - Environmental Fate. Office of the Prevention, Pesticides, and Toxic Substances, Washington, DC. EPA 738-R-93-010.

Attachment 1

Excel Spreadsheets

Chemical Name: Chlorothalonil
PC Code: 081901
MRID: 45710223
Guideline No.: 161-2

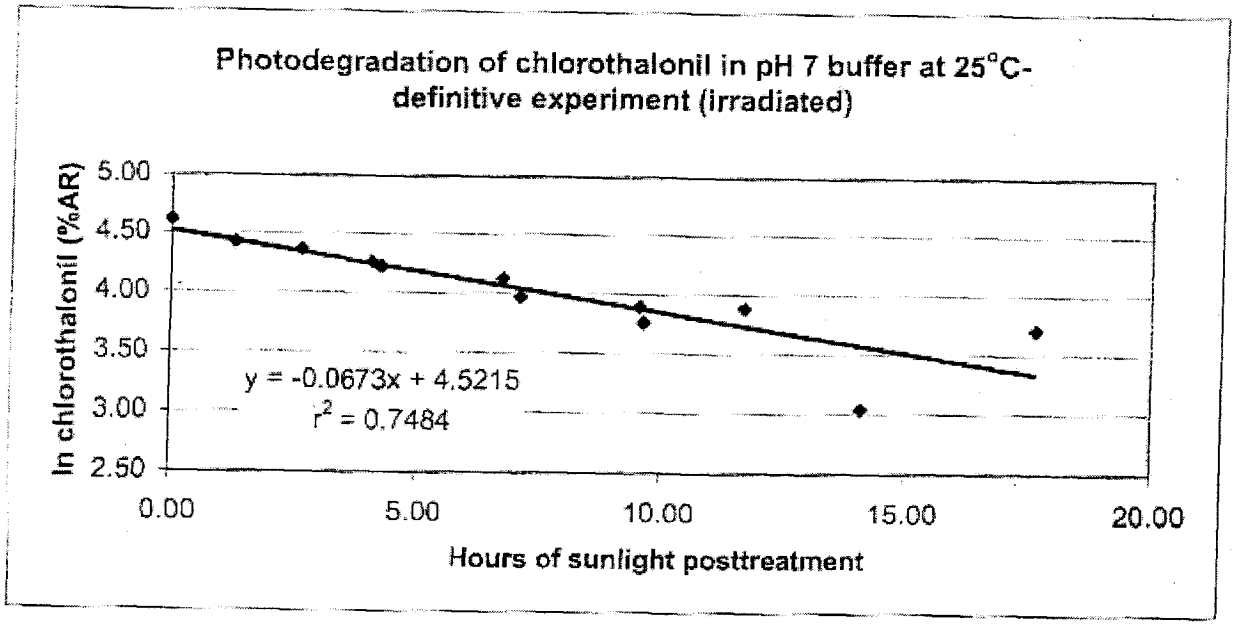
Irradiated

Half-life: 10.30 hours of continuous irradiation under natural sunlight
20.60 hours of 12-hour light/12-hour dark cycles of natural sunlight

pH 7 **25°C**

Irradiation Hours	Sunlight Hours	Chlorothalonil (%AR)	LN Chlorothalonil (%AR)
0	0.00	100.7	4.6121
1	1.27	83.8	4.4284
2	2.60	78.8	4.3669
3	4.07	71.0	4.2627
4	4.26	68.4	4.2254
5	6.75	61.7	4.1223
6	7.10	53.2	3.9741
7	9.55	49.2	3.8959
8	9.63	43.1	3.7635
9	12.28	12.1	
10	11.68	48.7	3.8857
11	17.65	41.0	3.7136
12	14.11	20.9	3.0397

Data obtained from Table VII, p. 33 of the study report.



Chemical Name: Chlorothalonil
PC Code: 081901
MRID: 45710223
Guideline No.: 161-2

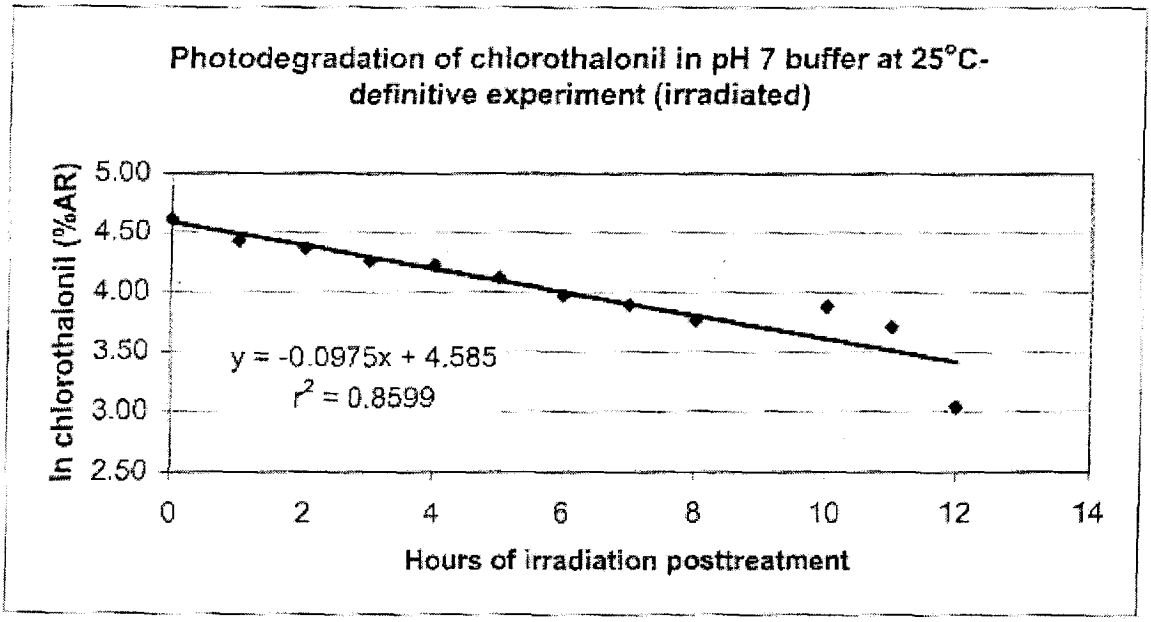
Irradiated

Half-life: 7.11 hours of continuous irradiation
14.22 hours of 12-hour light/12-hour dark cycles

pH 7 **25°C**

Irradiation Hours	Sunlight Hours	Chlorothalonil (%AR)	LN Chlorothalonil (%AR)
0	0.00	100.7	4.6121
1	1.27	83.8	4.4284
2	2.60	78.8	4.3669
3	4.07	71.0	4.2627
4	4.26	68.4	4.2254
5	6.75	61.7	4.1223
6	7.10	53.2	3.9741
7	9.55	49.2	3.8959
8	9.63	43.1	3.7635
9	12.28	12.1	
10	11.68	48.7	3.8857
11	17.65	41.0	3.7136
12	14.11	20.9	3.0397

Data obtained from Table VII, p. 33 of the study report.



Chemical Name: Chlorothalonil
PC Code: 081901
MRID: 45710223
Guideline No.: 161-2

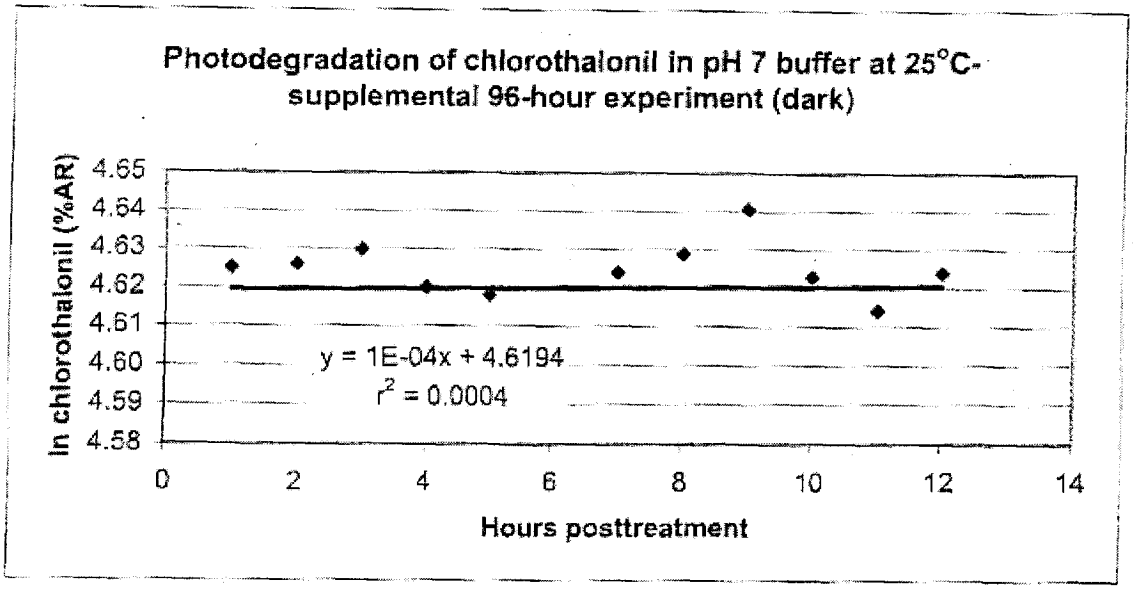
Dark

Half-life: Stable

pH 7 **25°C**

Irradiation Hours	Chlorothalonil (%AR)	LN Chlorothalonil (%AR)
0	102.0	4.6250
0	102.1	4.6260
6	102.5	4.6299
6	101.5	4.6201
12	101.3	4.6181
12	96.2	4.5664
24	101.9	4.6240
24	102.4	4.6289
48	103.6	4.6405
48	101.8	4.6230
96	100.9	4.6141
96	101.9	4.6240

Data obtained from Table VI, p. 32 of the study report.



Chemical Name: Chlorothalonil
PC Code: 081901
MRID: 45710223
Guideline No.: 161-2

Material balance and distribution of radioactivity
Data obtained from Table IV-VI, pp. 30-32 of the study report.
pH 7 **25°C**

Irradiated solutions

Irradiation Hours	Sunlight Hours	Total (%AR)	Mean	SD	Buffer % of applied	Mean	SD
0	0	104.2	104.4	0.3	104.2	104.4	0.3
0	0	104.6			104.6		
6	7.8	103.6	105.7	3.0	103.4	105.5	3.0
6	7.6	107.8			107.6		
12	19.3	101.3	100.6	1.1	100.9	100.2	1.1
12	14.1	99.8			99.4		
24	28.0	102.7	101.3	2.1	100.1	98.7	2.1
24	32.8	99.8			97.2		
48	66.5	100.3	99.5	1.2	94.3	93.5	1.2
48	62.1	98.6			92.6		
96	129.5	93.7	94.2	0.7	81.7	82.2	0.7
96	113.7	94.7			82.7		
Mean		100.9					
SD		4.1					

Dark controls

Irradiation Hours	Total (%AR)	Mean	SD	Buffer % of applied	Mean	SD	Chlorothalonil % of applied	Mean	SD
0	104.2	104.4	0.3	104.2	104.4	0.3	102.0	102.1	0.1
0	104.6			104.6			102.1		
6	105.9	105.5	0.6	105.9	105.5	0.6	102.5	102.0	0.7
6	105.1			105.1			101.5		
12	103.9	101.5	3.5	103.9	101.5	3.5	101.3	98.8	3.6
12	99.0			99.0			96.2		
24	104.9	105.2	0.4	104.9	105.2	0.4	101.9	102.2	0.4
24	105.5			105.5			102.4		
48	108.6	108.0	0.9	108.3	107.7	0.9	103.6	102.7	1.3
48	107.3			107.0			101.8		
96	105.1	105.2	0.1	105.1	105.2	0.1	100.9	101.4	0.7
96	105.2			105.2			101.9		
Mean	104.9								
SD	2.3								

Chemical Name: Chlorothalonil
PC Code: 081901
MRID: 45710223
Guideline No.: 161-2

Defintive Experiment- Irradiated solutions
Material balance
Data obtained from Table IV, p. 30 of the study report.

pH 7 **25°C**

Irradiation Hours	Sunlight Hours	Total (%AR)
0	0.00	100.9
1	1.27	100.8
2	2.60	103.5
3	4.07	98.5
4	4.26	99.8
5	6.75	99.7
6	7.10	102.0
7	9.55	102.4
8	9.63	101.2
9	12.28	97.3
10	11.68	101.9
11	17.65	98.9
12	14.11	101.0
Mean		100.6
SD		1.7

Chemical Name: Chlorothalonil
PC Code: 081901
MRID: 45710223
Guideline No.: 161-2

12 hour irradiation experiment

Actual Irradiation (hours)	Hours Equivalent	Ratio
0	0	
1	1.27	1.27
2	2.60	1.30
3	4.07	1.36
4	4.26	1.07
5	6.75	1.35
6	7.10	1.18
7	9.55	1.36
8	9.63	1.20
9	12.28	1.36
10	11.68	1.17
11	17.65	1.60
12	14.11	1.18
	Average	1.28

Excluding hour 11 (outlier)

Actual Irradiation (hours)	Hours Equivalent	Ratio
0	0	
1	1.27	1.27
2	2.60	1.30
3	4.07	1.36
4	4.26	1.07
5	6.75	1.35
6	7.10	1.18
7	9.55	1.36
8	9.63	1.20
9	12.28	1.36
10	11.68	1.17
11	17.65	
12	14.11	1.18
	Average	1.25

96 hour irradiation experiment

Actual Irradiation (hours)	Hours Equivalent	Ratio
6	7.80	1.30
6	7.60	1.27
12	19.30	1.61
12	14.10	1.18
24	28.00	1.17
24	32.80	1.37
48	66.50	1.39
48	62.10	1.29
96	129.50	1.35
96	113.70	1.18
	Average	1.31

Data obtained from Table III, p. 29 of the study report.