Data Evaluation Report on the phototransformation of halcomid in water

PMRA Submission Number {.....} EPA MRID Number 45369737

Data Requirement: PMRA Data Code:
EPA DP Barcode: D284964
OECD Data Point:
EPA Guideline: 161-2

Test material:
Common name: Halcomid.
Chemical name
IUPAC: N,N-Dimethyldecanoic acid amide.
CAS name: Not reported.
CAS No: Not reported.
Synonyms: None.
SMILES string: O=C(CCCCCCCCC)N(C)C.

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CITATION: Burri, R. 1995. Photodegradation study of [1-^{14}C]N,N-dimethyldecanoic acid amide in water at pH 5. Unpublished study performed by RCC Umweltchemie AG, Itingen/BL, Switzerland, sponsored by Bayer AG, Leverkusen, Germany, and submitted by C. P. Hall Company, Chicago, IL. RCC Project No.: 340312. Study experimental start date July 1, 1993 and study experimental end date December 30, 1993 (p. 14). Final report issued on June 15, 1995.

ADMINISTRATIVE CONCLUSIONS

1) This study is scientifically valid, and satisfies Subdivision N Guideline criteria for photolysis in water (§161-2). No additional aqueous photolysis data are needed at this time.

2) The submitter should note the comments given in Section IV of this Data Evaluation Report, and consider their applicability to the acceptability of future submissions.

SCIENTIFIC CONCLUSIONS

Within experimental limits and for environmental assessment purposes, halcomid was essentially stable (half-life indeterminately long in a 30-day test period) against photolysis in water. A roughly extrapolated, first-order environmental phototransformation half-life is in excess of approximately 15 months. However, because of the slow degradation of halcomid, consequent formation of only minor amounts of unidentified products during a relatively short test period, and the variability of the data, the accuracy of such an extrapolation far beyond the experimental time period is highly uncertain. The observed relative photostability of halcomid is generally consistent with its absorption spectrum.

EXECUTIVE SUMMARY

The aqueous phototransformation of [1-^{14}C]-labeled N,N-dimethyldecanoic acid amide (halcomid), at 0.81-0.94 µg a.i./mL, was studied at 25 ± 1°C in a sterile aqueous pH 5 (0.01M acetate) buffered solution for up to 30 days under intermittent irradiation (12-hour light/12-hour dark cycles). The light source was a UV-filtered xenon lamp (97.0 Klux) that was similar in intensity to natural sunlight in summer on a clear, colorless day (*ca.* 90-100 KLux). This experiment was conducted in accordance with US EPA Pesticide Assessment Guidelines, Subdivision N §161-2, and in compliance with USEPA Good Laboratory Practices.

The test system consisted of two Pyrex glass flasks containing treated buffer solution (150-200 mL) that were attached to a volatile trapping system with the photolysis apparatus. One flask was covered with aluminum foil to serve as the dark control. During irradiation, the flasks were cooled via a water jacket and were stirred constantly using magnetic stir bars. Twice each day (*ca.* 5 minutes each), humidified filtered air was passed through (60 mL/minute) the sample flask, then through polyurethane, 2N NaOH, and ethylene glycol traps. Aliquots (two from the irradiated solution, one from the dark control) of the buffer solutions were collected at 0, 3, 7, 14, 21, and 30 days posttreatment and analyzed using LSC.

At study termination, the sample flasks and tubing were washed with acetone and adsorbed [^{14}C]residues were quantified by LSC. In order to separate, quantify, and identify halcomid and its transformation products, aliquots of the samples were analyzed via one-dimensional TLC.

Areas of radioactivity on the plates were identified by comparison to the location of a halcomid reference standard that was cochromatographed with the samples. The following reference compounds for possible transformation products were included in the study: N,N-dimethyloctanoic acid amide, decanoic acid, decanedioic acid, nonanoic acid, nonanedioic acid, octanoic acid, octanedioic acid, heptanoic acid, heptanedioic acid, hexanoic acid, hexanedioic acid, pentanoic acid, pentanedioic acid, butanoic acid, and butanedioic acid. No reference compounds were cochromatographed with the samples. Further analysis via HPLC was employed to confirm the identification of halcomid.

The overall [^{14}C]residue recoveries averaged 98.8 ± 3.0% (range 93.1-101.7%) of the applied from the dark control and 96.7 ± 4.3% (range 89.4-102.3%) from the irradiated solution. There was no significant loss of material with time.

In both the dark controls and irradiated solutions, halcomid was relatively stable. In the **dark controls**, [^{14}C]halcomid declined from 97.4% at 0 days posttreatment to 89.9% at 30 days posttreatment (study termination). In the **irradiated solutions**, [^{14}C]halcomid declined from 98.5% at 0 days posttreatment to 86.6% at 30 days. No major transformation products were isolated, and no minor transformation products were identified. Three minor discrete areas of radioactivity (M2, M3, and M4) each averaged ≤3.3% of the applied in both the dark control and irradiated solutions. At 30 days posttreatment, volatiles totaled <0.05% and 0.3% of the applied in the dark control and irradiated solutions; residues were not individually quantified by trapping medium. A transformation pathway was not provided.

Based on first-order linear regression analysis (Excel 2000) using all data points, halcomid degraded with half-lives of 141 days in the irradiated samples and 204 days in the dark control. These half-lives are of highly uncertain value because they are extrapolated far beyond the duration of the study (30 days); the r^2 values are only 0.4436 and 0.5362 for the dark control and irradiated experiments, respectively.

Taking the difference between extrapolated first-order regression rate constants (not half-lives) for the irradiated and dark control samples yields an estimated phototransformation half-life of approximately 15.3 months based on the 12-hour light/12-hour dark cycle used in the study. Since the intensity of the artificial light was similar to sunlight, the extrapolated environmental phototransformation half-life is also approximately 15.3 months. However, because of the slow degradation of halcomid, consequent formation of only minor amounts of products during a relatively short test period, and the variability of the data, the accuracy of such an extrapolation far beyond the experimental time period is highly uncertain.

In conclusion, halcomid was relatively stable in the buffer solution and no significant transformation products were formed.

Results Synopsis:

Test medium: Acetate buffer at pH 5.
Source of irradiation: Xenon-arc lamp (12 hour light/dark cycle).
Half-lives (extrapolated from first-order regression):
Irradiated - 140 days (95% confidence interval 85 to 410 days, $r^2 = 0.5362$).
Dark - 203.87 days (95% confidence interval +81 to minus (-) 370 days, $r^2 = 0.4436$). (Minus values mean no degradation.)
Major transformation products/irradiated and dark control:
None identified.
Minor transformation products/irradiated and dark control:
None identified (three minor discrete chromatographic areas).

Study Acceptability: This study is classified as **acceptable**, and satisfies the guideline requirement for a photodegradation in water study.

I. MATERIALS AND METHODS

The page numbers which are referenced in the DER correspond to the page numbers which are found in the lower right-hand corner of the study report. The page numbers which appear at the top right-hand corner were not followed because they did not include all of the pages in the study report.

GUIDELINE FOLLOWED: This study was conducted in accordance with USEPA Pesticide Assessment Guideline Subdivision N §161-1 and amendments (pp. 1, 15). No significant deviations from Subdivision N guidelines were noted.

COMPLIANCE: This study was conducted in compliance with USEPA, OECD, and Swiss Good Laboratory Practices (1989; 1981; 1986; pp. 4, 15). Signed and dated Data Confidentiality, GLP, Certificate of Authenticity, and Quality Assurance statements were provided (pp. 2-4, 7-8).

A. MATERIALS

1. Test Materials [1-^{14}C]Halcomid (pp. 18-19).

Chemical Structures: See DER Attachment.

Description: Colorless liquid (nonradiolabeled, p. 18).

Purity: Radiochemical purity: >98% (97.6% average prior to experiment; p. 19).
Batch No.: A 387.
Analytical purity: Not reported.
Specific activity: 100.5 µCi/mg (3.72 MBq/mg).
Location of the radiolabel: 1-Carbon (carbonyl carbon).

Storage conditions: The test substance was stored in the dark at *ca.* -20°C (p. 19).

Physico-chemical properties of halcomid.

Parameter	Values	Comments
Molecular Formula	Not reported.	
Molecular weight	199.4 g/mole	
Water solubility	270 mg/L.	At 20°C and pH 5.5.
Vapor pressure	Not reported.	
UV absorption	Minimal at wavelengths >290 nm	At pH 7.
pK_a	Not reported.	
K_{ow}/log K_{ow}	Not reported.	
Stability of compound at room temperature	Not reported.	

Data obtained from pp. 18-19 and Figure 19, p. 61, of the study report.

2. Buffer Solution: The following buffer solution was prepared:

Table 1: Description of buffer solutions.

pH	Type and final molarity of buffer	Composition
5	0.01M Acetate	67.8 mL of sodium acetate was combined with *ca.* 32.2 mL of acetic acid. The resulting buffer (0.1M) was diluted 10 fold, and the pH was adjusted to ± 0.1 units.

Data obtained from p. 21 of the study report. The water which was used for the aqueous solutions was bidistilled water (pH 6.0; conductivity, 2.3 µS/cm; hardness, <0.2 mM).

3. Details of light source:

Table 2: Artificial light source.

Property	Details
Type of lamp used:	Xenon arc lamp (Original Hanau Suntest apparatus).
Emission wavelength spectrum:	290-800 nm
Light intensity:	97.0 Klux.
Filters used:	UV filters eliminated radiation <290 nm.
Relationship to natural sunlight:	The intensity of natural sunlight in summer on a clear, colorless day with a vertical incidence of the sun was reported to be *ca.* 90-100 KLux. Therefore, 12 hours of irradiation (or one 12-hour light/12-hour dark cycle) is approximately equivalent to 1 day of natural sunlight. The spectral energy distributions of the artificial light at test initiation and termination were provided in Figures 4-5, pp. 46-47; the spectral energy distribution of the natural summer light was not provided .

Data obtained from pp. 22 and 25, and Figure 2, p. 44, and Figures 4-5, pp. 46-47, in the study report.

B. EXPERIMENTAL CONDITIONS:

1. Preliminary experiments: In a preliminary study (not described), it was determined that the addition of the test substance did not affect the pH of the buffer solution (p. 21).

2. Experimental conditions:

Table 3: Experimental design.

Parameter		Details
Duration of the test:		30 days.
Application rate:	Nominal:	1 µg a.i./mL
	Measured:	Irradiated: 0.94 µg a.i./mL Dark: 0.81 µg a.i./mL
Dark controls used (Yes/No):		Yes.
Replications	Dark controls:	None. One dark control solution was prepared, and this bulk solution was subsampled at each sampling interval.
	Irradiated:	None. One solution was prepared for irradiation, and this bulk solution was subsampled at each sampling interval.
Preparation of the test medium	Volume used/ treatment:	Aliquots (*ca.* 400 µg a.i./aliquot) of the halcomid stock solution were evaporated to near dryness, then dissolved in 400 mL of buffer solution. A portion (150-200 mL) of this solution was used in bulk in the study and repeatedly subsampled.
	Method of sterilization:	The treated test solutions were sterilized by filtration (0.45 µm). Application devices and glassware were sterilized by autoclaving for at least 30 minutes at 120°C.
	Co-solvent, if any:	Acetonitrile, 1% by volume.
Test apparatus (Type/material/ volume):	Dark controls:	A foil-wrapped double-walled Pyrex glass flask (unspecified capacity) containing treated buffer solution (150 mL; *ca.* 3.5 cm depth) were capped with a quartz glass plate, placed in the pbotolysis apparatus, and connected to the volatile trapping system. The solution was stirred continuously throughout the study using a magnetic stir bar. The temperature of the solution was maintained by means of a water jacket connected to a waterbath. An illustration of the test apparatus was provided in Figure 3, p. 45 of the study report.
	Irradiated:	The test system was similar to that of the dark control, except that the sample flask contained 200 mL of solution and was not wrapped in foil.

Parameter		Details
Details of traps for CO_2 and organic volatiles, if any:	Dark controls:	Twice each day (*ca.* 5 minutes each after the end of illumination and dark cycles), humidified filtered air was passed through (60 mL/minute) the sample flask, then through a flask containing polyurethane, a flask containing 2N NaOH, aod a flask containing ethylene glycol. An illustration of trapping apparatus is presented in Figure 3, p. 45 of the study report.
	Irradiated:	
If no traps were used, is the system closed/open?		A volatile trapping system was used.
Any indication of the test material adsorbing to the walls of the test apparatus?		Yes, 3.0 to 4.0% of the applied radioactivity was rinsed from the flask walls at study termination.
Experimental conditions.	Temperature (°C):	Irradiated: 25.0 ± 0.8°C. Dark: 25.0 ± 0.2°C.
	Duration of light/ darkness:	12-hour dark/12-hour light cycles.
Other details, if aoy:		Nooe.

Data obtained from pp. 22-25; Table 1, p. 37; Tables 2-3, pp. 38-39; and Figure 3, p. 45 in the study report.

3. Supplementary experiments: No supplementary experiments were reported.

4. Sampling:

Table 4: Sampling details.

Parameters		Details
Sampling intervals:		0, 3, 7, 14, 21, and 30 days posttreatment.
Sampling method:	Dark	At each sampling interval, one 4-mL aliquot of the bulk dark control solution was collected.
	Irradiated	At each sampling interval, two 4-mL aliquots of the bulk irradiated control solution was collected.
Method of collection of volatile compounds, if any:	Dark	The polyurethane and NaOH trap solutions were collected and replaced with fresh solution at every sampling interval. The ethylene glycol trap was not collected at each sampling interval since the radioactivity remained <0.05% of the applied.
	Irradiated	
Sampling intervals/times for: Sterility check: pH measurement:		Sterility was determined at study initiation and termination. At 0, 14, and 30 days posttreatment
Sample storage before analysis:		Aliquots of samples were analyzed immediately via LSC and TLC. Samples were stored at *ca.* -20°C for ≤1.5 months prior to HPLC analysis.
Other observations, if any:		LSC and TLC analyses were performed for all sampling intervals; however, HPLC analysis was only performed on aqueous samples from 0, 14, and 30 days.

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

C. ANALYTICAL METHODS:

Extraction/clean up/concentration methods, if used: Test solutions were analyzed as collected, without manipulation or modification. At experiment termination, the flasks and glass tubing were washed with acetone (p. 24). The acetone washes were analyzed by LSC for total radioactivity.

Volatile residue determination: Aliquots of the NaOH and ethylene glycol solutions were analyzed by LSC for total radioactivity (p. 26). The polyurethane was extracted twice with acetone, and aliquots of the extracts were analyzed by LSC.

Total ^{14}C measurement: Total [^{14}C]residues were calculated by summing the measured radioactivity in the aqueous solution, volatile traps, and acetone wash.

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

Identification and quantification of the parent: Residues in the aqueous solutions were separated, quantified, and identified by one-dimensional TLC on silica gel plates (5 cm x 20 cm; 0.25 mm thickness; 60 F_{254}) developed in chloroform:acetonitrile:acetic acid (50:50:2, v:v:v; solvent system code: SS 7; p. 27). The samples were cochromatographed with an unlabeled reference standard of halcomid (R_f 0.88; purity 98.8%; pp. 18, 27-28). The plates were visualized by exposure to iodine (parent) and autoradiography. Radioactive residues were quantified by measuring their surface area via the Gaussian fit method.

The identity and concentration of the parent was confirmed via HPLC (pp. 29-30). The HPLC system consisted of a Lichrospher RP 18 column (250 mm x 4.0 mm; 5 µ), a mobile gradient phase consisting of (A) acetonitrile and (B) bidistilled water [A:B, v:v; 0-5 minutes 0:100, 25-30 minutes 100:0, and 30.1-40 minutes 0:100], and UV (205 nm) and radioactive flow detection. Halcomid was identified by comparison of the retention time of the unlabeled reference standard (purity 98.8%; Rt 25.23 minutes; pp. 18, 29-30).

Identification and quantification of transformation products: The transformation products were isolated and quantified in the aqueous solutions of 0, 3, 7, 14, 21, and 30 days posttreatment using TLC as described for the parent (pp. 27-28). The retention times of transformation products were compared to the retention times of the following unlabeled reference standards (pp. 20, 28):

Reference Compound	Ref. Code	Purity (%)	Rf-TLC	Reference Compound	Ref. Code	Purity (%)	Rf-TLC
N,N-Dimethyldecanoic acid amide	None	98.8	0.88	Heptanoic acid	H	>99	0.8
N,N-Dimethyloctanoic acid amide	A	97	0.85	Heptanedioic acid	I	>98	0.46
Decanoic acid	B	>98	0.84	Hexanoic acid	J	>98	0.75
Decanedioic acid	C	>98	0.6	Hexanedioic acid	K	>99	0.4
Nonanoic acid	D	97	0.83	Pentanoic acid	L	>99	0.73
Nonanedioic acid	E	*ca.* 88	0.6	Pentanedioic acid	M	>99	0.32
Octanoic acid	F	>99	0.83	Butanoic acid	N	>99	0.61
Octanedioic acid	G	>99	0.56	Butanedioic acid	O	>99	0.23

The identities of transformation products were confirmed via HPLC as described for the parent (pp. 29-30). The retention times of transformation products were compared to the retention times of the following unlabeled reference standards (pp. 20, 29-30):

Reference Compound	Ref. Code	Purity (%)	Retention time- HPLC
N,N-Dimethyldecanoic acid amide	None	98.8	25.23 minutes
N,N-Dimethyloctanoic acid amide	A	97	22.21 minutes
Decanoic acid	B	>98	24.15 minutes
Decanedioic acid	C	>98	17.21 minutes

Detection limits (LOD, LOQ) for the parent: The Limits of Detection were not reported. The counting error of the LSC reported to be <5%; more specific data were not provided (p. 26). The value of <0.05% was reported as a LOQ for the LSC in Tables 2-3, pp. 38-39. The Limits of Quantification for the TLC and HPLC were *ca.* 0.9% and 3.3% of the applied radioactivity, respectively (pp. 27, 29).

Detection limits (LOD, LOQ) for the transformation products: The Limits of Detection were not reported. The Limits of Quantification were the same as those for the parent.

II. RESULTS AND DISCUSSION:

A. TEST CONDITIONS: The incubation temperatures were reported as 25.0 ± 0.8°C for the irradiated solutions and 25.0 ± 0.2°C for the dark controls; supporting data were not provided (pp. 22, 24-25, 31). The pH was reported to be 5.0 throughout the study. The test solutions were shown to be sterile (0 colonies on agar plates) at study initiation and termination (p. 30).

B. MATERIAL BALANCE: The overall recovery of [^{14}C]residues averaged 96.7 ± 4.3% (range 89.4-102.3%) of the applied in the irradiated solutions and 98.8 ± 3.0% (range 93.1-101.7%) in the dark controls (Tables 2-3, pp. 38-39). There was no significant loss of material from the buffer solution over time.

Table 5: Phototransformation of [^{14}C]halcomid, expressed as percentage of the applied radioactivity (irradiated mean ± SD, n = 2; dark control n = 1), at pH 5 and 25°C.*

Compound		Sampling times (days)					
		0	3	7	14	21	30
Parent (M1; halcomid)[1]	Irradiated	98.5 ± 2.8	94.2 ± 5.0	94.9 ± 1.6	86.2 ± 6.5	83.5 ± 3.7	86.6 ± 5.6
	Dark	97.4	92.1	97.3	94.5	83.6	89.9
Unknown M2 (Rf 0.70-71)[1]	Irradiated	ND	ND	ND	1.4 ± 1.0	3.3 ± 1.2 [4]	2.4 ± 0.7
	Dark	ND	ND	ND	ND	2.2	2.3
Unknown M3 (Rf 0.65)[1]	Irradiated	ND	ND	ND	1.3 ± 0.4	2.6 ± 2.2 [4]	1.6 ± 0.9
	Dark	1.3	1.8	ND	ND	2.2	1.9
Unknown M4 (Rf 0.94[2]-97[3])	Irradiated	1.6 ± 0.2	1.4 ± 0.0	ND	1.0 ± 0.1	ND	ND
	Dark	1.3	1.1	ND	ND	ND	ND
Total % recovery (aqueous solution)	Irradiated	100.0 ± 2.5	95.6 ± 5.0	94.9 ± 1.6	89.8 ± 5.8	87.3 ± 4.2	90.5 ± 5.4
	Dark	100.0	95.0	97.3	94.5	88.0	94.1
Volatiles	Irradiated	NS	<0.05	0.1 ± 0.0	0.1 ± 0.0	0.2 ± 0.0	0.3 ± 0.0
	Dark	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05
Acetone wash (test vessel)[5]	Irradiated	--	3.0	3.0	3.0	3.0	3.0
	Dark	--	4.0	4.0	4.0	4.0	4.0
Acetone wash (tubing)[5]	Irradiated	--	0.2 ± 0.0	0.6 ± 0.0	1.2 ± 0.0	1.9 ± 0.0	2.8 ± 0.0
	Dark	--	0.2	0.4	0.7	1.1	1.7
Total % recovery:	Irradiated	100.0 ± 2.5	98.8 ± 5.0	98.6 ± 1.6	94.1 ± 5.8	92.4 ± 4.2	96.6 ± 5.4
	Dark	100.0	99.2	101.7	99.2	93.1	99.8

* Data obtained from Tables 2-4, pp. 38-40 and Table 6, p. 42 of the study report. For the irradiated samples, n = 2; the reviewer provided the values as mean ± s.d. For the dark controls, n = 1. For the irradiated samples, the study author corrected the recovered percent of radioactivity for water lost via evaporation (8 mL total at day 30) at each sampling interval by multiplying by the "ratio actual volume/theoretical volume" (actual calculations were not provided; p. 30). No evaporation was seen in the dark controls.

ND = Not detected, below the limit of detection.

NS = Not sampled, volatiles were not collected from day 0.

1 The retention time was obtained from the day 30, sample A.

2 The retention time was obtained from the day 0, sample A.

3 The retention time was obtained from the day 3, sample A.

4 M2 and M3 were detected as one peak in replicate B of day 21. The reviewer did not alter the replicate value, 4.1% AR, since no peak percentage information was reported by the study author. Therefore, the mean and s.d. for this sampling interval are inaccurate.

5 The measured radioactivity from the acetone wash of the test vessel at the end of the experiment was added completely to all samples, except day 0 (p. 24). The measured radioactivity from the acetone wash of the tubing at the end of the experiment was added gradually using a linear distribution to all samples, except day 0.

C. TRANSFORMATION OF PARENT COMPOUND: In the dark controls, [^{14}C]halcomid declined from an average 97.4% of the applied at 0 days posttreatment to 83.6% at 21 days and was 89.9% at 30 days posttreatment (study termination; Table 6, p. 42). In the irradiated solutions, [^{14}C]halcomid declined from an average 98.5% of the applied at 0 days posttreatment to 83.5% at 21 days and was 86.6% at 30 days (Table 4, p. 40).

HALF-LIFE: Based on first-order linear regression analysis (Excel 2000) using all data points, halcomid degraded with half-lives of 141 days in the irradiated samples and 204 days in the dark control. These half-lives are of uncertain value because they are extrapolated far beyond the duration of the study, the data are variable, and a single sample was collected from the dark control at each interval. The r^2 values are 0.5362 and 0.4436 for the irradiated and dark experiments, respectively. Although the study author stated that the half-life of halcomid was calculated using first-order reaction kinetics, the values were not included in the MRID because of the low correlation coefficients (p. 33).

Half-lives*

Conditions		First order linear			DT50	DT90
		Half-life	Regression equation	r^2		
pH 5	Irradiated	141.46 days	y = -0.0049x + 4.5659	0.5362	> 30 days	ND
	Dark	203.87 days	y = -0.0034x + 4.5675	0.4436	> 30 days	ND

*Half-lives were calculated by the reviewer using data obtained from Table 4, p. 40 and Table 6, p. 42 of the study report.
ND = Not determined.

The **phototransformation half-life** for halcomid, determined using the equation:

(Ln 2) ÷ [(Ln 2/dark control half-life) - (Ln2/ irradiated half-life)]

is 462 days based on the 12-hour light/12-hour dark cycle used in the study, or 231 days based on continuous irradiation. However, because of the slow degradation of halcomid and the variability of the data, the accuracy of this value is highly uncertain.

The intensity of natural sunlight at the vertical in summer on a clear, colorless day was reported as *ca.* 90-100 KLux, compared to the 97 KLux average intensity of the artificial light. Therefore, 1 day of artificial light is approximately equivalent to 1 day of natural sunlight. The predicted **environmental phototransformation half-life** of halcomid is therefore approximately 462 days.

TRANSFORMATION PRODUCTS: No major transformation products were isolated from either the dark control or the irradiated solutions. No minor transformation products were identified. Unidentified areas of radioactivity M2, M3, and M4 each averaged ≤3.3% of the

applied in the dark control and irradiated solutions during the study (Table 4, p. 40; Table 6, p. 42).

VOLATILIZATION: At 30 days posttreatment, volatiles totaled <0.05% and 0.3% of the applied in the dark control and irradiated solutions; the study author did not distinguish between volatiles trapped in the polyurethane, NaOH, and ethylene glycol (Table 4, p. 40; Table 6, p. 42).

TRANSFORMATION PATHWAY: A transformation pathway was not provided. Halcomid was relatively stable in the buffer solutions; no transformation products were identified.

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

Applicant's Code Name	CAS Number	Chemical Name	Chemical formula	Molecular weight (g/mol)	SMILES string
No transformation products were identified.					

D. SUPPLEMENTARY EXPERIMENT-RESULTS: No supplementary experiments were reported.

III. STUDY DEFICIENCIES: No significant deviations from Subdivision N guidelines were noted.

IV. REVIEWER'S COMMENTS:

1. The material balance for replicate A of the irradiated solution at 21 days posttreatment was 89.4% of the applied. Subdivision N guidelines require that material balances are maintained ≥90% and ≤110%. However, since the material balance of replicate B was 95.3%, the average material balance at 21 days was 92.4% and material balances at later intervals were satisfactory.

2. The results of the HPLC analyses were provided in the following table:

Concentration of halcomid (% of applied radioactivity)			
Sampling times (days)	0	14	30
Irradiated solutions	100.0	89.8	90.5
Dark controls	100.0	94.5	94.1

Data obtained from Table 5, p. 41 and Table 4, p. 42 of the study report.

3. The study author concluded that the test material was stable in the application solution because the radiochemical purity was 97.6% of the applied before application and an average of 98.5% after application (p. 31).

4. Further analysis of the acetone washings (test vessel and tubing) for day 30 of the irradiated solutions and dark controls was performed via TLC (p. 33). Of the total 5.8% of the applied radioactivity of the irradiated solutions, 5.1% was determined to be parent. Of the total 5.7% of the applied radioactivity of the dark controls, 5.3% was determined to be parent.

5. The molar absorption coefficients for halcomid were determined by performing a UV/Vis spectral analysis (wavelengths, 290 and 295 nm) of the furfural test solutions at pH 7 (nominal concentrations, 10 and 100 mg a.i./L; p. 61). The calculated molar absorption coefficients for halcomid were 0 and 40 at 290 and 295 nm, respectively, at a concentration of 10 mg a.i./L and 26 and 32 at 290 and 295 nm, respectively, at a concentration of 100 mg a.i./L. The UV/Vis spectra for halcomid in pH 7 buffer solution was provided in Figure 19, p. 61 of the study report. The study author noted that the low molar absorption coefficients correlate with the observation of photodegradation stability (p. 36).

6. The study author assumed that the adsorption of the test material to the walls of the test vessels occurred during "the first three days" of the experiment (p. 24). Due to this assumption, the radioactivity which was measured in the acetone wash was added completely to every sampling interval after day 0. On the other hand, in the case of the absorption of the test material to the tubing, the study author assumed that the material "accumulated continuously during the incubation" (p. 24). Due to this assumption, the radioactivity which was measured in the acetone wash was added gradually using a linear distribution to every sampling interval after day 0.

7. The study author did not explain why the reference compounds were not co-chromatographed with the aqueous solutions, especially in cases that the R_f of an unidentified transformation product was close to that of a reference compound (e.g. M2, R_f = 0.70-0.71; pentanoic acid, R_f = 0.73; hexanoic acid, R_f = 0.75; p. 28; Table 4, p. 40; Table 6, p. 42). However, the identification of these transformation products was not necessary since they did not exceed 3% of the applied radioactivity.

8. The aliquots of the aqueous solutions which were taken for sterility determinations (0.5-mL) and HPLC analysis (unspecified) were stored at - 20°C for 10 days to 1.5 months (pp. 24, 30). No storage data was provided by the study author; the study author noted that the HPLC storage was irrelevant because this data was not used for quantification (p. 24).

9. The study author noted that one TLC value was reported (0.7%) which was less than the LOQ for the TLC (0.9%; p. 27). The study author explained that this value was obtained from manual peak selection, so automatic peak rejection was omitted.

10. The Limits of Detection for the LSC, TLC, and HPLC methods. LODs should be reported to allow the reviewer to evaluate the adequacy of the test method.

11. Physico-chemical properties such as the molecular formula, vapor pressure, pK_a, and K_{ow} were not reported.

12. The application rate used in the study was not justified by the study author.

13. Representative TLC chromatograms were presented in Figure 1, p. 43, Figures 7-11, pp. 49-53 (irradiated solutions), and Figures 14-16, pp. 56-58 (dark controls) of the study report. Representative HPLC chromatograms were presented in Figure 1, p. 43, Figures 12-13, pp. 54-55 (irradiated solutions), and Figure 17, p. 59 (dark controls) of the study report. Figure 1 contained the TLC and HPLC chromatograms of the non-radiolabeled halcomid reference material.

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.

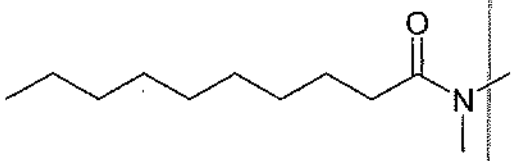
ATTACHMENT

Chemical Structure of Parent
and
Names of Unidentified Reference Compounds

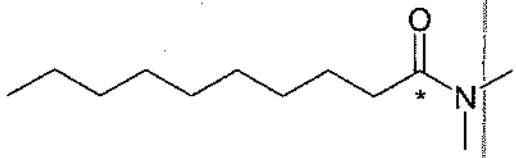
Halcomid

IUPAC name: N,N-Dimethyldecanoic acid amide.
CAS name: Not reported.
CAS No: Not reported.
SMILES string: O=C(CCCCCCCCC)N(C)C

Unlabeled



[1-^{14}C]Halcomid



* Position of radiolabel

Unidentified Reference Compounds

N,N-Dimethyloctanoic acid amide
Structure not provided.
Decanoic acid
Structure not provided.
Decanedioic acid
Structure not provided.
Nonanoic acid
Structure not provided.
Nonanedioic acid
Structure not provided.
Octanoic acid
Structure not provided.
Octanedioic acid
Structure not provided.
Heptanoic acid
Structure not provided.
Heptanedioic acid
Structure not provided.
Hexanoic acid
Structure not provided.
Hexanedioic acid
Structure not provided.
Pentanoic acid
Structure not provided.
Pentanedioic acid
Structure not provided.
Butanoic acid
Structure not provided.
Butanedioic acid
Structure not provided.

Attachment 1

Excel Spreadsheets

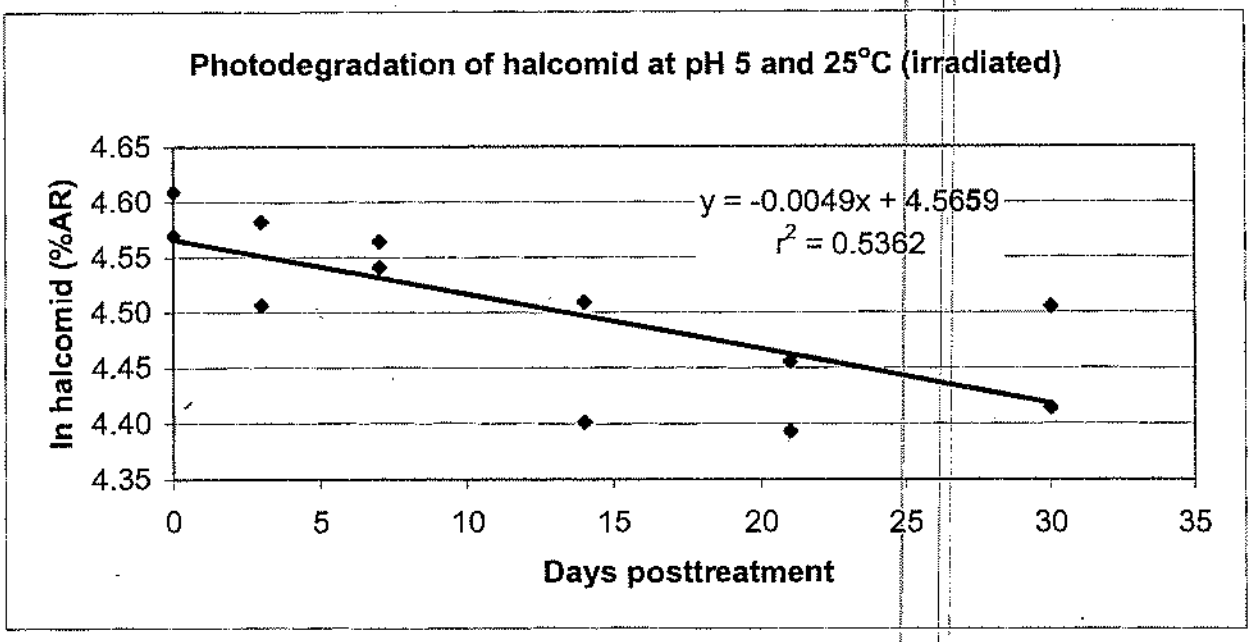
Chemical Name: Halcomid
PC Code: 999999
MRID: 45369737
Guideline No.: 161-2

Half-life: 141.46 days of 12-hour light/12-hour dark cycles

pH 5 **Irradiated**

Days	Halcomid (% AR)	ln Halcomid (%AR)
0	96.5	4.5695
0	100.4	4.6092
3	90.6	4.5065
3	97.7	4.5819
7	93.8	4.5412
7	96.0	4.5643
14	81.6	4.4018
14	90.8	4.5087
21	80.9	4.3932
21	86.1	4.4555
30	82.6	4.4140
30	90.5	4.5053

Data obtained from Table 4, p. 40 of the study report.



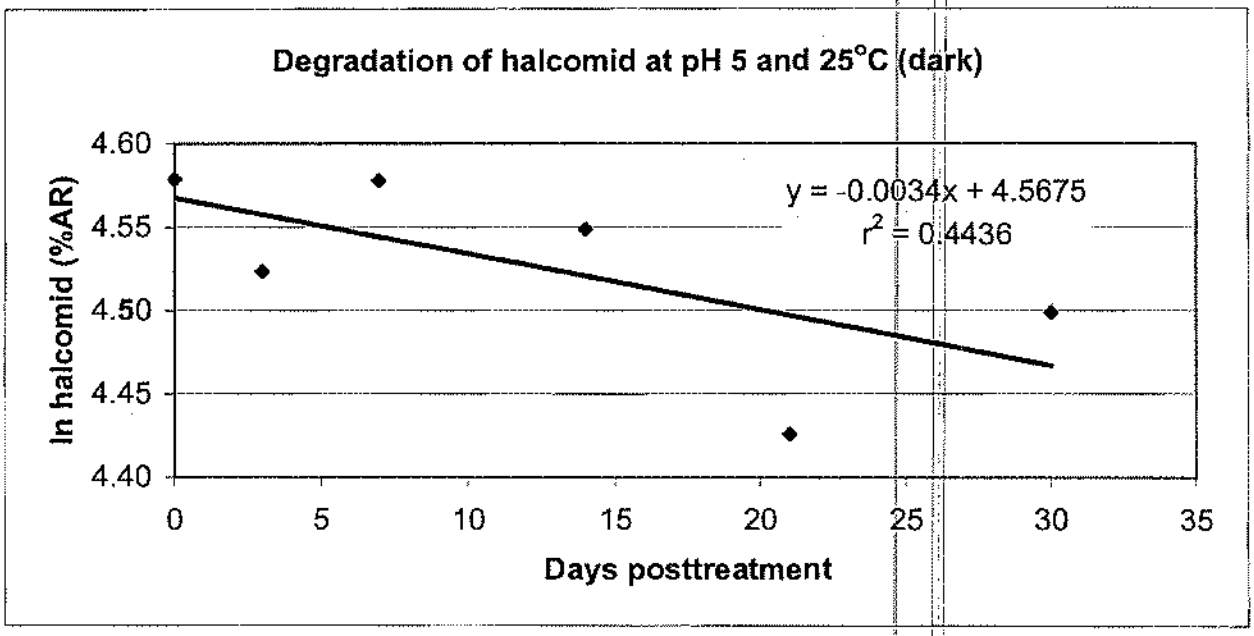
Chemical Name: Halcomid
PC Code: 999999
MRID: 45369737
Guideline No.: 161-2

Half-life: 203.87 days

pH 5 **Dark**

Days	Halcomid (% AR)	ln Halcomid (%AR)
0	97.4	4.5788
3	92.1	4.5229
7	97.3	4.5778
14	94.5	4.5486
21	83.6	4.4260
30	89.9	4.4987

Data obtained from Table 6, p. 42 of the study report.



Chemical Name: Halcomid
PC Code: 999999
MRID: 45369737
Guideline No.: 161-2

Mass Balance in % of applied radioactivity

Irradiated

Days	Aqueous	Mean	SD	Volatiles	Mean	SD	Acetone Wash (Tube)	Mean	SD	Total	Mean	SD
0	98.2	100.0	2.5	0.0			0.0	0.0	0.0	98.2	100.0	2.5
0	101.8			0.0			0.0			101.8		
3	92.0	95.6	5.0	<0.05			0.2	0.2	0.0	95.2	98.8	5.0
3	99.1			<0.05			0.2			102.3		
7	93.8	94.9	1.6	0.1	0.1	0.0	0.6	0.6	0.0	97.5	98.6	1.6
7	96.0			0.1			0.6			99.7		
14	85.7	89.8	5.8	0.1	0.1	0.0	1.2	1.2	0.0	90.0	94.1	5.8
14	93.9			0.1			1.2			98.2		
21	84.3	87.3	4.2	0.2	0.2	0.0	1.9	1.9	0.0	89.4	92.4	4.2
21	90.2			0.2			1.9			95.3		
30	86.7	90.5	5.4	0.3	0.3	0.0	2.8	2.8	0.0	92.8	96.6	5.4
30	94.3			0.3			2.8			100.4		
										96.7	**Mean**	
										4.3	**SD**	

Data obtained from Table 2, p. 38 of the study report.

Dark

Days	Total	
0	100.0	
3	99.2	
7	101.7	
14	99.2	
21	93.1	
30	99.8	
	98.8	**Mean**
	3.0	**SD**

Data obtained from Table 3, p.39 of the study report.

Chemical Name: Halcomid
PC Code: 999999
MRID: 45369737
Guideline No.: 161-2

Distribution of Radioactivity in % of applied radioactivity
Data obtained from Table 4, p. 40 of the study report.

pH 5 25°C

	Parent			Unknown			Unknown			Unknown		
Days	(M1)	Mean	SD	M2	Mean	SD	M3	Mean	SD	M4	Mean	SD
0	96.5	98.5	2.8	0.0	0.0	0.0	0.0	0.0	0.0	1.7	1.6	0.2
0	100.4			0.0			0.0			1.4		
3	90.6	94.2	5.0	0.0	0.0	0.0	0.0	0.0	0.0	1.4	1.4	0.0
3	97.7			0.0			0.0			1.4		
7	93.8	94.9	1.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
7	96.0			0.0			0.0			0.0		
14	81.6	86.2	6.5	2.1	1.4	1.0	1.0	1.3	0.4	1.0	1.0	0.1
14	90.8			0.7			1.5			0.9		
21	80.9	83.5	3.7	2.4	3.3	1.2	1.0	2.6	2.2	0.0	0.0	0.0
21	86.1			4.1			4.1			0.0		
30	82.6	86.6	5.6	1.9	2.4	0.7	2.2	1.6	0.9	0.0	0.0	0.0
30	90.5			2.9			0.9			0.0		

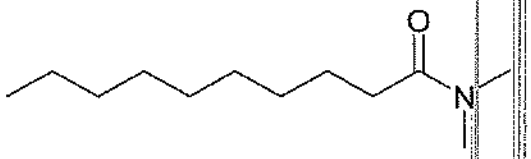
Attachment 2

Structures of Parent and Transformation Products

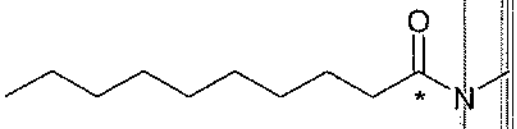
Halcomid

IUPAC name: N,N-Dimethyldecanoic acid amide.
CAS name: Not reported.
CAS No: Not reported.
SMILES string: O=C(CCCCCCCCC)N(C)C

Unlabeled



[1-^{14}C]Halcomid



* Position of radiolabel.

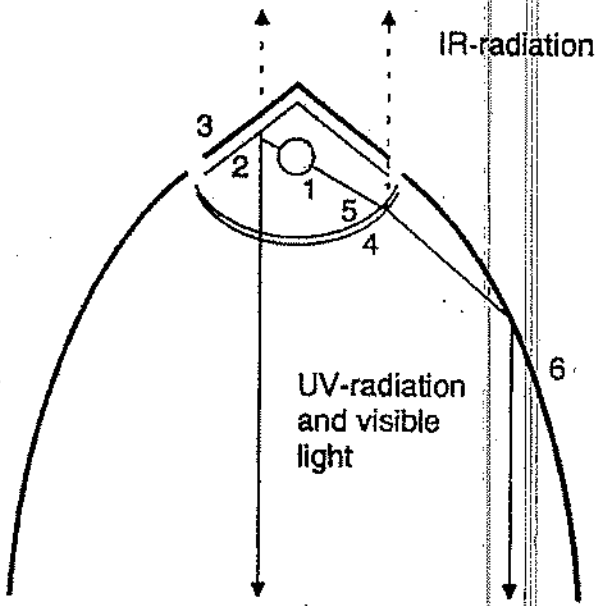
Unidentified Reference Compounds

N,N-Dimethyloctanoic acid amide
Structure not provided.
Decanoic acid
Structure not provided.
Decanedioic acid
Structure not provided.
Nonanoic acid
Structure not provided.
Nonanedioic acid
Structure not provided.
Octanoic acid
Structure not provided.
Octanedioic acid
Structure not provided.
Heptanoic acid
Structure not provided.
Heptanedioic acid
Structure not provided.
Hexanoic acid
Structure not provided.
Hexanedioic acid
Structure not provided.
Pentanoic acid
Structure not provided.
Pentanedioic acid
Structure not provided.
Butanoic acid
Structure not provided.
Butanedioic acid
Structure not provided.

Attachment 3

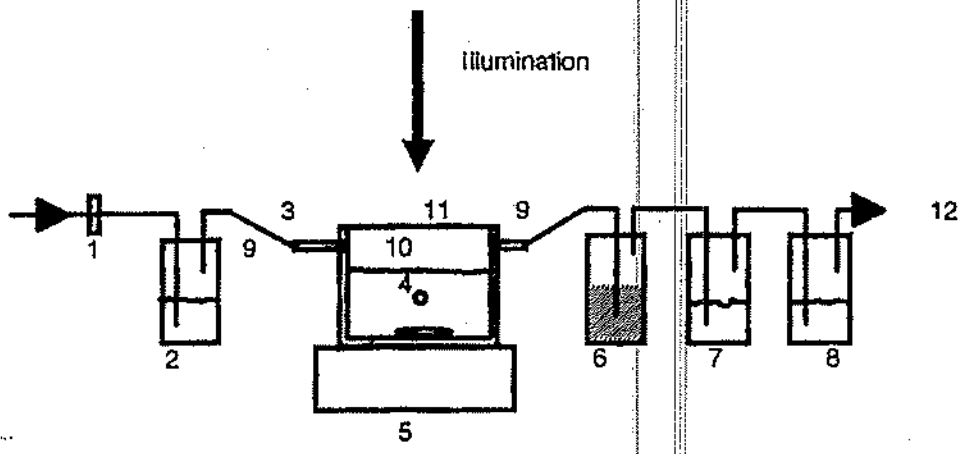
Illustration of Test System
Spectral Energy Disdtributions

Figure 2: Diagram of the Suntest apparatus.



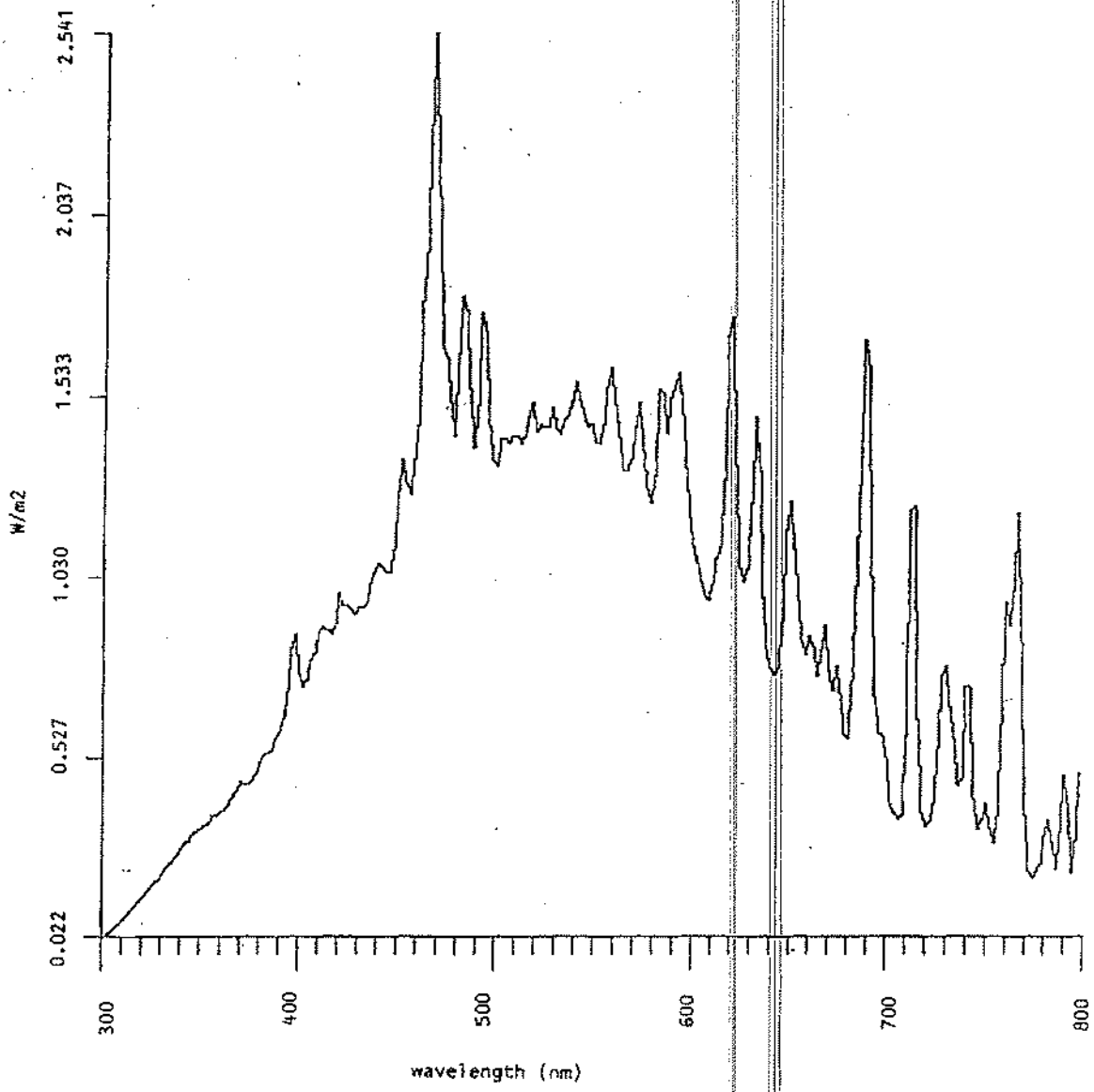
1 XENON burner
2 UV mirror
3 Light mirror
4 Quartz glass dish with selective reflecting coating
5 Supplementary filter made of special UV glass
6 Parabolic reflector

Figure 3: Diagram of the test system.



1 Filter to sterilize the incoming air
2 Sterile bidistilled water to moisten the incoming air
3 Polyurthan piece inserted in the tubing
4 Septum for sample collection
5 Magnetic stirrer
6 Polyurethan inserted into a glass bottle
7 50 ml 2 N NaOH
8 50 ml ethylene glycol
9 Glass tubings connected to the incubation vessel by small pieces of PVC
10 Incubation vessel with double glass wall connected to a waterbath for thermoregulation
11 Quartz glass plate
12 Vacuum pump

Figure 4: Spectral energy distribution of the Suntest apparatus before the study.



RCC PROJECT 340312
N,N-DIMETHYLDECANOIC ACID AMIDE

Figure 5: Spectral energy distribution of the Suntest apparatus after the study.