Data Evaluation Report on the hydrolysis of BAS 510 F

PMRA Submission Number {.....} EPA MRID Number 45405205

Data Requirement: PMRA Data Code:
EPA DP Barcode: D278387
OECD Data Point:
EPA Guideline: 161-1

Test material:
Common name: BAS 510 F
Chemical name
IUPAC: 2-Chloro-*N*-(4'-chlorobiphenyl-2-yl)-nicotinamide.
CAS name: 2-Chloro-*N*-(4-chloro[1,1-biphenyl]-2-yl)-3-pyridinecarboxamide.
CAS No: 188425-85-6
Synonyms: Nicobifen, ~~BAS 516 02 F~~
SMILES string:

Primary Reviewer: Mary Thomas
Dynamac Corporation

Signature: Mary Thomas
Date: 1/15/02

QC Reviewer: Joan Harlin
Dynamac Corporation

Signature: Joan L. Harlin
Date: 1/15/02

Secondary Reviewer: Cheryl Sutton
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Company Code: [for PMRA]
Active Code: [for PMRA]
Use Site Category: [for PMRA]
EPA PC Code: 128008

CITATION: von Götz, N. 1999. Hydrolysis of BAS 510 F. Unpublished study performed by BASF Aktiengesellschaft, BASF Agricultural Center Limburgerhof, D-67114 Limburgerhof, Germany and sponsored by BASF Corporation, Agricultural Products, Research Triangle Park, NC. BASF Registration Document Number 1999/11285. Study initiated April 1998 and completed September 17, 1999.

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EXECUTIVE SUMMARY:

The hydrolysis of [diphenyl-U-^{14}C]-labeled 2-chloro-*N*-(4'-chlorobiphenyl-2-yl)-nicotinamide (BAS 510 F) at 3 mg a.i./L was studied in the dark at 25°C in sterile aqueous buffered solutions adjusted to pH 5, 7 and 9 for 30 days. The buffer solutions were only described as commercially available buffer solutions diluted by a factor of 10 to avoid interactions with the test substance. The experiment was conducted in accordance with the US EPA Pesticide Assessment Guidelines, Subdivision N, Section 161-1, and in compliance with the Good Laboratory Practice Regulations. Samples were collected at 0, 6, 11, 15, 20, and 30 days and directly analyzed for BAS 510 F without extraction or concentration using HPLC and HPTLC. Identification was made by comparison to an unlabeled reference standard of BAS 510 F. No transformation products were isolated in any of the buffer solutions.

Total radiocarbon recovery in the pH 5 solution averaged (n = 12) 99.4 ± 0.4% of the applied, in the pH 7 solution averaged 99.5 ± 0.4%, and in the pH 9 solution averaged 99.5 ± 0.4%. [^{14}C]BAS 510 F was stable in all three buffer solutions. The concentration of [^{14}C]BAS 510 F was 100.0% at day 0 and 99.5% of the applied at study termination in the pH 5 solution, 100.0% at day 0 and 100.1% at study termination in the pH 7 solution, and 100.0% at day 0 and 99.8% at study termination in the pH 9 solution. Volatiles were not measured.

Half-life values were not calculated. BAS 510 F was stable (<2% degraded) in all three buffer solutions during the 30 days of incubation.

This study is classified acceptable and satisfies the guideline requirement for an hydrolysis study.

RESULTS SYNOPSIS:

	Half-life	Major transformation products
pH 5	Stable	None
pH 7	Stable	None
pH 9	Stable	None

I. MATERIALS AND METHODS

GUIDELINE FOLLOWED: The study was conducted according to the US EPA Pesticide Assessment Guidelines, Subdivision N, Section 161-1; Commission Directive 94/37/EG amending Council Directive 91/414/EEC; and Appendix 1 to § 19a, Section 1, Chemikaliengesetz of 25 July 1994 (Official Bulletin/Federal Republic of Germany, I 1994, P. 1703). No deviations affected the validity of the study.

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COMPLIANCE: This study was conducted in compliance with Good Laboratory Practice Regulations; Appendix 1 to § 19a, Section 1, Chemikaliengesetz of 25 July 1994 (Official Bulletin/Federal Republic of Germany, I 1994, P. 1703). Signed and dated GLP, Quality Assurance and Data Confidentiality statements were provided.

A. MATERIALS:

1. Test Material [Diphenyl-U-^{14}C]BAS 510 F

Chemical Structure:

Description: Not provided

Purity: Analytical purity: 97-100%
Radiochemical purity: Not provided Batch No. 641-1018
Specific activity: 5.23 MBq/mg
Locations of the label: Uniformly labeled in each phenyl ring

Storage conditions of test chemicals: Not provided

Physico-chemical properties of BAS 510 F:

Parameter	Values	Comments
Water solubility	6 mg/L in water at 20°C	
Vapour pressure/volatility	Not provided	
UV absorption	Not provided	
pK_a	Not provided	
K_{ow}/log K_{ow}	Not provided	
Stability of compound at room temperature, if provided	Not provided	

Data obtained from MRID 45405216, p. 12 of the study report.

2) Buffer Solution:

Table 1: Description of buffer solutions.

pH	Type and final molarity of buffer	Composition
5	Not provided	Not provided
7	Not provided	Not provided
9	Not provided	Not provided

The buffer solutions were commercially available buffer solutions diluted by a factor of 10 to avoid interactions with the test substance (p. 13).

B. EXPERIMENTAL CONDITIONS

1) Preliminary Study: A 5-day study was conducted at 50°C to determine the stability of BAS 510 F in pH 4, 7 and 9 buffer solutions to select optimal sampling intervals for the definitive study. The test solution (360 µL) was added to 50 mL of the diluted buffer solution (not described) and made up to 3 mg/L. The solution was incubated in the dark in a climatic chamber at 50°C for 5 days (p. 14). The samples were collected at 0, 1, 2, 3, 4 and 5 days and analyzed by HPLC and HPTLC. [^{14}C]BAS 510 F was stable at all three pHs during the 5-day study. The concentration of the BAS 510 F was 100.0% of the applied at day 0 and 101.6% at 5 days at pH 4, 100.0% of the applied at day 0 and 100.8% at 5 days at pH 7, and 100.0% of the applied at day 0 and 101.3% at 5 days at pH 9 (Table 1, p. 18).

2) Experimental conditions

Table 2: Experimental parameters

Parameters		Details
Duration of the study		30 days
Test concentrations (mg a.i./L) nominal: measured:		 3 Not reported
No. of replications		2 per sampling interval
Preparation of test medium	volume used/treatment	50 mL of each buffer solution were treated, then 1.5 mL aliquots were transferred to the sample vials.
	method of sterilization	Not reported (but sterilization was confirmed)
	co-solvent (type/concentration)	Acetonitrile/0.72% (360 uL/50 mL)
Test apparatus (type/material/volume)		Autosampler vials; material and volume not specified
Details of traps for volatile, if any		Volatiles were not collected
If no traps were used, is the test system closed/open		Not reported
Is there any indication of the test material adsorbing to the walls of the test apparatus?		Not determined (but no indication of adsorption based on material balances)
Experimental conditions Temperature (°C) Lighting		 25°C Dark
Other details, if any		Temperature range not reported (± 1°C range not confirmed)

Data obtained from pp. 12-14 of the study report.

3). Supplementary Experiments: No supplementary experiments were conducted.

4). Sampling:

Table 3: Sampling details.

Criteria	Details
Sampling intervals for the parent/transformation products	0, 6, 11, 15, 20 and 30 days

Criteria	Details
Sampling method	Entire vials, 2 per pH at each sampling interval
Sampling methods for the volatile compounds, if any	Volatiles not determined
Sampling intervals/times for: pH measurement sterility check	 pH was not measured during the study. Sterility was determined at each sampling interval: 0, 6, 11, 15, 20 and 30 days
Sample storage before analysis	Sample storage details were not provided. It was stated that "if necessary, samples were stored in a freezer before analysis" (p. 14).
Other observation, if any (e.g.: precipitation, color change etc.)	Temperature range not reported (± 1°C range not confirmed)

Data obtained from pp. 14-15 and Table 1, p. 18 of the study report.

C. ANALYTICAL METHODS:

Extraction/clean up/concentration methods, if used: Samples were analyzed directly; no extraction/clean up/concentration methods were used.

Total ^{14}C measurement: Total ^{14}C was analyzed by LSC.

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

Identification and quantification of parent compound: Identification and quantification of [^{14}C]BAS 510 F was performed by reverse-phase HPLC using the following operating conditions: Spherisorb ODS column (250 mm x 8 mm x 4 mm; 5 µm particle size), gradient mobile phase combining (A) water:acetonitrile:formic acid (950:50:1, v:v:v), (B) water:acetonitrile:formic acid (50:950:1, v:v:v) [B (0%) at 0 min., B (inject, acquisition on to 0%) at 10 min., B (100%) at 70 min. and B (100%, acquisition off) at 80 min.], flow rate 1.0 mL/minute; UV (wavelength not reported) and radioactivity detection (p. 12). Identification of parent compound was achieved using by chromatographic comparison of the HPLC retention time with that of an unlabeled reference standard of BAS 510 F. Additional aliquots were analyzed by HPTLC on stationary-phase silica gel plates developed in methanol:acetic acid (100:0.5, v:v), di-isopropyl ether, heptane:di-isopropylether (1:1, v:v), and n-heptane (p. 15). The samples were co-chromatographed with an unlabeled reference standard of BAS 510 F. Following development, areas of radioactivity were detected using a Fuji Imager Fujix BAS 1000.

Identification and quantification of transformation products: No transformation products were identified or quantified.
Detection limits (LOD, LOQ) for parent compound: Detection limits for parent compound were not provided.

Detection limits (LOD, LOQ) for the transformation products: No transformation products were identified or quantified..

II. RESULTS AND DISCUSSION:

A. TEST CONDITIONS: The incubation temperature was reported to be 25°C during the study; however, temperature records were not provided to confirm that the incubation temperature was maintained throughout the study. The pH of the test solutions was not measured during the study. It was stated that the sterility of the samples during the study period was confirmed using a plate count technique; however, sterility data were not provided (p. 16).

B. MASS BALANCE: Total radiocarbon recovery (n = 12) ranged from 98.9% to 100.0% of the applied amount at pH 5, 99.0% to 100.1% of the applied amount at pH 7, and 99.0% to 100.0% of the applied amount at pH 9.

Table 4: Hydrolysis of [^{14}C]BAS 510 F, expressed as percentage of the applied radioactivity (mean ± s.d.), at pH 5.*

Compound		Sampling times (days)					
		0	6	11	15	20	30
BAS 510 F		100.0	99.6	98.9	98.9	99.5	99.5
Transformation product		Not determined					
Unidentified radioactivity, if any							
Volatiles	CO_2						
	volatile organic 1 volatile organic n Total						
Total % recovery		100.0	99.6	98.9	98.9	99.5	99.5

Data obtained from Table 1, p. 18 of the study report.
*Mean values were reported in study report; individual sample data were not provided.

Table 5: Hydrolysis of [^{14}C]BAS 510 F, expressed as percentage of the applied radioactivity (mean ± s.d.), at pH 7.*

Compound		Sampling times (days)					
		0	6	11	15	20	30
BAS 510 F		100.0	99.0	99.3	99.3	99.2	100.1
Transformation product		Not determined					
Unidentified radioactivity, if any							
Volatiles	CO_2						
	volatile organic 1 volatile organic n Total						
Total % recovery		100.0	99.0	99.3	99.3	99.2	100.1

Data obtained from Table 1, p. 18 of the study report.
*Mean values were reported in study report; individual sample data were not provided.

Table 6: Hydrolysis of [^{14}C]BAS 510 F, expressed as percentage of the applied radioactivity (mean ± s.d.), at pH 9.*

Compound		Sampling times (days)					
		0	6	11	15	20	30
BAS 510 F		100.0	99.5	99.0	99.3	99.3	99.8
Transformation product		Not determined					
Unidentified radioactivity, if any							
Volatiles	CO_2						
	volatile organic 1 volatile organic n Total						
Total % recovery		100.0	99.5	99.0	99.3	99.3	99.8

Data obtained from Table 1, p. 18 of the study report.
*Mean values were reported in study report; individual sample data were not provided.

C. TRANSFORMATION OF PARENT COMPOUND: [^{14}C]BAS 510 F was stable in the pH 5, 7, and 9 solutions throughout the 30-day study. The concentration of [^{14}C]BAS 510 F was 100.0% of the applied at day 0 and 99.5% at 30 days at pH 5, 100.0% of the applied at day 0 and 100.1% at 30 days at pH 7, and 100.0% of the applied at day 0 and 99.8% at 30 days at pH 9.

TRANSFORMATION PRODUCTS: No transformation products were identified in pH 5, 7 and 9 buffer solutions. Volatiles were not measured.

PATHWAYS: A hydrolytic pathway was not proposed. BAS 510 F was stable (<2% degraded) in pH 5, 7 and 9 buffer solutions during the 30 days of incubation.

Table 7: Chemical names and CAS numbers for the transformation products of [diphenyl-^{14}C]BAS 510 F.

Applicant's Code Name	CAS Number	CAS and/or IUPAC Chemical Name(s)	Chemical formula	Molecular weight	SMILES string
Not applicable					

HALF-LIFE: No attempt was made to calculate half-lives, either by the study author or the reviewer. BAS 510 F was stable during the 30 days of the study; any value extrapolated from these data would be of limited value.

Half-lives/DT50

pH	First order/other half-life			DT50 (unit)	DT90 (unit)
	half-life (unit)	Regression equation	r^2		
5	Not determined (parent compound was stable at all pH values)				
7					
9					

D. SUPPLEMENTARY EXPERIMENT-RESULTS: Supplementary experiments were not conducted.

III. STUDY DEFICIENCIES: None of the study deficiencies noted are considered to be of sufficient concern to cause the study to be judged scientifically invalid. The study fulfills Subdivision N Guideline §161-1.

IV. REVIEWER'S COMMENTS:

1. Complete details of the experimental design were not provided. It was not reported how the samples were maintained in darkness or where the samples were kept during the study. It was not specified whether the system was open or closed. The method used to sterilize the buffer solution was not specified; rather, it was only stated that "all material used during the study and all buffer solutions were sterilized prior to the experiments' (p. 13). The type,

molarity, and composition of the buffer solutions were not reported. The radiochemical purity of the test substance was not reported.

2. It was stated that the incubation temperature was 25°C during the study. Daily temperature measurements during the study period were not reported. Subdivision N guidelines recommend that the incubation temperature be maintained at 25 ± 1°C during hydrolysis studies.

3. Daily pH measurements during the study period were not reported.

4. Sterility data to confirm that the samples remained sterile throughout the study were not provided. Since BAS 510 F did not degrade during the study, this deviation has minimal impact on the study results.

5. Sampling intervals for the definitive study were reported as 0, 6, 10, 15, 20 and 30 days on page 14. However, sampling intervals were reported as 0, 6, 11, 15, 20 and 30 days in Table 1 of the study report (p. 18). The reviewer used the sampling intervals reported in Table 1 of the study report.

6. Storage of samples prior to analysis was inadequately described; storage temperature and length of storage prior to analysis were not provided. It was only stated that "if necessary, samples were stored in a freezer before analysis" (p. 14).

7. The limits of detection and quantitation for the LSC, HPLC, and HPTLC methods were not reported. Limits of detection and quantitation should be reported to allow the reviewer to evaluate the adequacy of the test method.

8. Physical properties of the test substance were not provided in the study report. The water solubility value of 6 mg/L at 20 °C was obtained from MRID 45405216 (p. 12), included with this submission. However, in other MRIDs included with the submission (e.g., MRID 45405210), it was reported that the water solubility at 20 °C is 4.64 mg/L (ppm; p. 13). Clarification by the registrant is necessary. It is noted that this hydrolysis study was conducted at 3 ppm, or approximately half of the water solubility reported in this study.

V. REFERENCES: No references were cited in the study.