

BAS 510 F
Lettuce
PMRA a.i. code (CCH)

Nature of the Residue in Plants
OPPTS 860.1300
DACO 6.3

PC Code: 128008
MRID: 45405021
Submission # 2001-1027, 1036, 1043



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

Date: July 2, 2003

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DP Barcode: D278386

Petition: 1F06313

Citation: 45405021 Hamm, R. (1999) Metabolism of BASF 510 F in Lettuce: Final Report:
Lab Project Number: 1999/11240: 44875. Unpublished study prepared by BASF
Aktiengesellschaft. 49 p.

Sponsor: BASF Corporation

Background

The information contained herein was compiled by Dynamac Corporation (20440 Century Boulevard, Suite 100, Germantown MD 20874), a contractor under the supervision of RAB2/HED. This DER has undergone secondary review by PMRA/Canada, and peer review by RAB2, and reflects current HED and Office of Pesticide Programs (OPP) policies.

Executive Summary

BASF Corporation has submitted a study investigating the metabolism of [¹⁴C]BAS 510 F in lettuce. The in-life and analytical phases of the study were conducted by BASF Aktiengesellschaft (Limburgerhof, Germany). Lettuce samples were collected 18 days following

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the last of three foliar applications of [^{14}C]BAS 510 F, uniformly labeled on the phenyl rings (diphenyl label) or labeled at the 3-position of the pyridine ring (pyridine label), at 0.624 lb ai/A/application (700 g ai/ha, for a total of 2.1 kg ai/ha; ~4X the proposed label rate). Total radioactive residues (TRR; calculated by summing extractable and non-extractable residues) were 17.54 ppm and 17.62 ppm in/on lettuce treated with diphenyl-label [^{14}C]BAS 510 F and pyridine-label [^{14}C]BAS 510 F, respectively. Material balances, based on sample combustion, were 85.1% and 99.3% for the diphenyl and pyridine labels, respectively.

For both labels, 99.3% of the TRR were extracted with methanol. The extracts were analyzed by HPLC, and the results of the chromatography were confirmed by LC/MS/MS. The unchanged parent, BAS 510 F, was the only component identified in lettuce, accounting for 99.3% TRR (17.41 ppm, diphenyl label, or 17.51 ppm, pyridine label). Non-extractable residues accounted for 0.7% TRR and were not further analyzed. No other known or postulated metabolite of BAS 510 were used in these experiments.

No storage stability analyses were conducted in this study, based upon the relatively short harvest-to-analysis intervals (64-109 days) involved and the fact that the radioactivity was quantitatively extracted (>99% TRR) from lettuce samples and was positively identified as parent BAS 510F. Moreover, storage stability data from the bean (MRID 45405023) and lettuce (MRID 45405022) metabolism studies are available to validate the storage period of the lettuce samples in this study.

The submitted study is considered **acceptable** to satisfy data requirements for a plant metabolism study with lettuce.

GLP Compliance

Signed and dated GLP, Quality Assurance, and Data Confidentiality statements were provided. The petitioner stated that the study was conducted in accordance with the GLP regulations established in Germany (Appendix 1 to §19a Section 1, Chemikaliengesetz of 25-July-1994; Official Bulletin/Federal Republic of Germany I 1994, p. 1703) instead of U.S. EPA GLP regulations or Canadian GLP standards.

1. Materials and Methods

1.1. Substance

Active Ingredient

Common Name:	Nicobifen (ISO, proposed)
IUPAC Name:	2-Chloro-N-(4'-chlorobiphenyl-2-yl)nicotinamide
CAS Name:	3-Pyridinecarboxamide, 2-chloro-N-(4'chloro[1,1'-biphenyl]-2-yl)-
CAS Number:	188425-85-6

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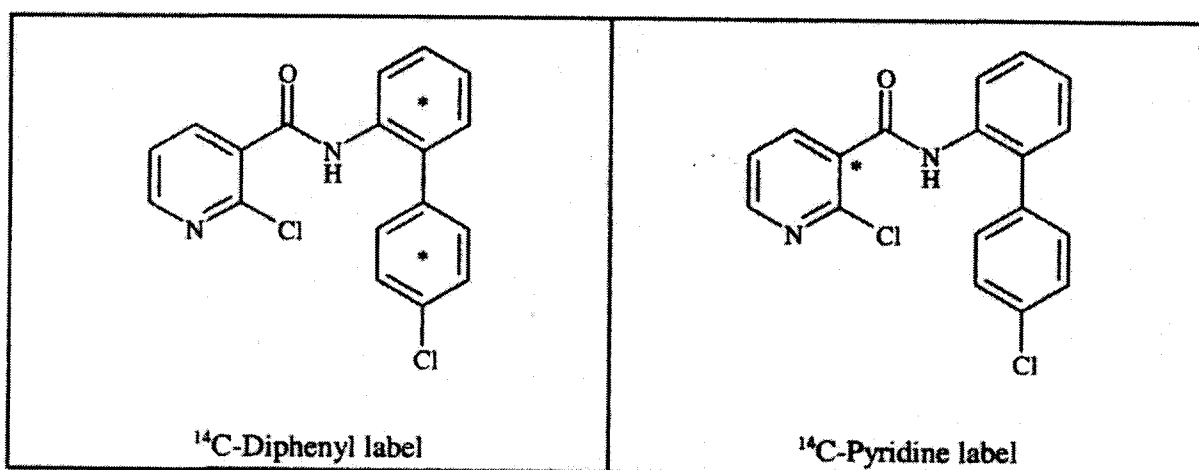
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Company Name: BAS 510 F
Other Synonyms: BASF Registry No. 300355

Location of Isotopic Label (diphenyl label): Uniformly labeled in both phenyl rings
Radiochemical Purity: >99%
Specific Activity: 314,000 dpm/ μ g (μ Ci/mmol not provided)

Location of Isotopic Label (pyridine label): Labeled at the 3-position in the pyridine ring
Radiochemical Purity: >99%
Specific Activity: 349,000 dpm/ μ g (μ Ci/mmol not provided)



1.2. Crop and Site

Type and Variety of Crop: Lettuce, *var.* Nadine
Growth Environment: 15 individual plastic pots (per label) in a greenhouse or vegetation hall (Limburgerhof, Germany)
Conditions: Pots were filled with loamy sand soil. Plants were automatically irrigated with tap water. Fertilizer was applied as necessary.

1.3. Application

Type of Application: Foliar spray application using a hand sprayer
Application Matrix: The radiolabeled test substances were dissolved in acetone and mixed with suspension concentrate formulation blank and water.
Application Rate: 0.624 lb ai/A/application (700 g ai/ha/application)
Number of Applications: Three
Timing of Applications: First application at GS 13 (8 days after planting of seedlings at 2-leaf stage); second application 14 days later; third application 14 days later

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Pre-harvest Interval(s): Mature lettuce samples were collected 18 days after final application (at growth stage BBCH 49).

1.4. Harvest/Post-harvest Procedures

All samples were frozen immediately after sampling and were stored frozen (≤ -18 C) until analysis.

Table 1.4.1. Summary of Storage Conditions			
Matrix	RAC or Extract	Storage Temperature (°C)	Total Duration (days)*
Lettuce	Leaves (RAC)	≤ -18 C	64-109

* total duration is the time from harvest-to-final analysis.

No storage stability analyses were conducted in this study. The registrant did not undertake to establish freezer storage stability, based upon the relatively short harvest-to-analysis intervals (64-109 days) involved and the fact that the radioactivity was quantitatively extracted ($>99\%$ TRR) from the lettuce samples and was positively identified as parent BAS 510F. Storage stability information are available in the bean metabolism study (MRID 45405023) to support storage of diphenyl label bean samples for up to 5 months and storage of pyridine label bean samples for up to 27 months prior to completion of analysis. Also, storage stability data in the grape metabolism study (MRID 45405022) indicate that the extraction profiles of grapes stored for approximately 16 months were very similar to those extracted within 2 months of sample collection. Collectively, these data are considered sufficient to support the lack of freezer storage stability information in the lettuce samples for the duration of this study.

1.5. Analytical Methods

Samples of lettuce leaves from both labels were homogenized and subjected to combustion/LSC for determination of total radioactive residues (TRR). The reported limits of quantitation (calculated) were 0.0004 and 0.0003 ppm for the diphenyl and pyridine label samples, respectively.

Subsamples of homogenized lettuce were extracted with methanol (MeOH) three times, and the extracts were isolated by centrifugation.

Combined MeOH extracts were subjected to analysis by HPLC. HPLC analyses were conducted using a Nucleosil C-18 column and a gradient mobile phase of water, acetonitrile, and formic acid. A radioactivity monitor was used for detection of analytes. The petitioner did not identify any reference standards used except radiolabeled BAS 510 F.

The identification of BAS 510 F in lettuce extracts was confirmed by electrospray ionization LC/MS/MS. The analyses were conducted using a Nucleosil C18 column and a mobile phase of water, acetonitrile, and formic acid.

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2. Results

Table 2.1. Total Radioactive Residues in Lettuce Leaves Following Three Foliar Applications of Isotopically Labeled BAS 510 F.

Label Location	Crop Matrix	Application Rate	PHI, days	TRR, ppm		% Mass Balance ³
				Combustion ¹	Calculation ²	
Diphenyl label	Lettuce	3 x 0.624 lb ai/A	18	20.6	17.54	85.1%
Pyridine label	Lettuce	3 x 0.624 lb ai/A	18	17.75	17.62	99.3%

¹ As determined by direct combustion/LSC.

² Calculated by summing extractable residues and non-extractable residues. The petitioner used the calculated value for all reported results because of the high water content of lettuce.

³ Based on sample combustion.

Table 2.2.1. Extraction, Characterization, and Identification of Radioactive Residues in Lettuce Leaf (TRR = 17.54 ppm) Harvested 18 Days Following Three Foliar Applications of [Diphenyl-¹⁴C]BAS 510 F at 0.624 lb ai/A/application.

Fraction ID	% TRR	ppm	Residue ID	% TRR	ppm	Comments
Methanol extract	99.3	17.41	BAS 510 F	99.3	17.41	Identification confirmed by LC/MS/MS.
Non-extractable	0.7	0.129	Not further analyzed			

Table 2.2.2. Extraction, Characterization, and Identification of Radioactive Residues in Lettuce Leaf (TRR = 17.62 ppm) Harvested 18 Days Following Three Foliar Applications of [Pyridin-3-¹⁴C]BAS 510 F at 0.624 lb ai/A/application.

Fraction ID	% TRR	ppm	Residue ID	% TRR	ppm	Comments
Methanol extract	99.3	17.51	BAS 510 F	99.3	17.51	Identification confirmed by LC/MS/MS.
Non-extractable	0.7	0.115	Not further analyzed			

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Table 2.3. Summary of Characterization and Identification of Radioactive Residues in Lettuce Leaf Following Three Foliar Applications of Isotopically Labeled BAS 510 F at 0.624 lb ai/A/application.

Metabolite or Fraction	[Diphenyl-U- ¹⁴ C]BAS 510 F		[Pyridin-3- ¹⁴ C]BAS 510 F	
	Lettuce (TRR = 17.54 ppm)		Lettuce (TRR = 17.62 ppm)	
	%TRR	ppm	%TRR	ppm
BAS 510 F	99.3	17.41	99.3	17.51
Total Identified (TI)	99.3	17.410	99.3	17.510
Total Characterized (TC)	--	--	--	--
Total Extractable (TE)	99.3	17.41	99.3	17.51
Total Bound (TB)	0.7	0.129	0.7	0.115
% Mass Balance	100		100	

TC = Sum of all unidentified, extractable residues

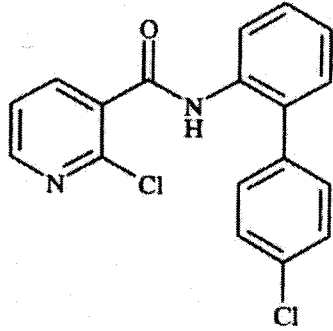
TE = Sum of TI and TC

% Mass Balance = TE %TRR + TB % TRR. Note that because of the high water content of lettuce, the petitioner calculated TRR by summing extractable and non-extractable residues; therefore, mass balance is at 100% for both matrices. See Table 2.1 for actual mass balance based on combustion of samples.

2.4 Proposed Metabolic Fate of BAS 510 F in Lettuce.

As summarized in Table 2.3 above, parent BAS 510 F accounted for >99% of the TRR. No significant metabolism of the parent compound occurred in lettuce, and no metabolites were identified in the study.

Table 2.4. Compounds Identified in Lettuce

Identifier	Chemical Name	Structure	Comments
BAS 510 F (Parent Compound)	3-Pyridinecarboxamide, 2-chloro-N-(4'chloro[1,1'- biphenyl]-2-yl)-		Sole residue identified in lettuce, at >99% TRR.

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3. Discussion

3.1. Methods

Radiolabeled [^{14}C]BAS 510 F, labeled at the 3-position of the pyridine ring or uniformly labeled on the phenyl rings, was applied three times to lettuce plants as a foliar spray application at 0.624 lb ai/A/application (700 g ai/ha/application, for a total of 2.1 kg ai/ha, -4X the proposed label rate), with 14-day retreatment intervals. Mature lettuce samples were collected 18 days following the final application and TRR were determined by combustion/LSC. The petitioner used the calculated TRR values (extractable radioactivity plus non-extractable residues) for reporting results, because of the high water content of lettuce samples. Material balances of the leaf, based on sample combustion, were 85.1% and 99.3% for the diphenyl and pyridine labels, respectively.

For both labels, 99.3% of the TRR were extracted with methanol. The extracts were analyzed by HPLC and the results were confirmed by LC/MS/MS. These methods adequately characterized/identified the majority of the residues in lettuce.

3.2. Results

Following three foliar applications of [^{14}C]BAS 510 F, labeled in the diphenyl portion or in the pyridine ring, at 0.624 lb ai/A/application (700 g ai/ha), TRR were 17.54 ppm and 17.62 ppm, respectively, in/on lettuce collected 18 days following the last application.

The unchanged parent, BAS 510 F, was the only component identified in lettuce leaf, accounting for 99.3% TRR (17.41 ppm, diphenyl label, or 17.51 ppm, pyridine label). Non-extractable residues in the leaf accounted for 0.7% TRR and were not further analyzed.

Storage stability data from the bean (MRID 45405023) and lettuce (MRID 45405022) metabolism studies were available to validate the storage period (≤ 109 days) of lettuce samples prior to analysis.

The submitted study is considered acceptable and satisfies the data requirements for a plant metabolism study with lettuce.

4. Deficiencies

No deficiencies were identified.

5. References

None.