Primary Evaluator Yan Donovan, Chemist, RRB4/HED Date: 06/30/06

Approved by Susan Hummel, Senior Scientist, RRB4/HED Date: 06/30/06

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Rd., Building 100, Suite B, Durham, NC 27713; submitted 6/12/2006). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

44757210 Ediger, K. (1998) Propiconazole and CGA-279202--Magnitude of the Residues in or on Almonds: Final Report: Lab Project Number: 143-98: 02-FR-001-98: 0W-FR-402-98. Unpublished study prepared by Novartis Crop Protection, Inc. 202 p.

45215806 Ediger, K. (2000) CGA-279202 and Propiconazole-Magnitude of the Residues in or on Almond: Final Report: Lab Project Number: 18-99. Unpublished study prepared by Novartis Crop Protection AG. 79 p.

EXECUTIVE SUMMARY:

In five field trials conducted during 1998 and 1999 in CA, propiconazole was applied to almonds in side-by-side tests comparing the use of 45% WP and 3.6 lb/gal EC formulations. Applications were made as dilute sprays (160-207 gal/A) at two sites, as concentrated sprays (10 gal/A) at two sites, and as both dilute (150 gal/A) and concentrated (75 gal/A) sprays at the fifth site. In each test, propiconazole (EC or WP) was applied four times to almonds as foliar applications during nut development at 0.22-0.25 lb ai/A/application, at retreatment intervals (RTIs) of 6-14 days, for a total of 0.88-0.91 lb ai/A/season. All applications were made using ground equipment and adjuvants were not added to the spray mix. Single control and duplicate treated samples of nutmeats and hulls were collected from each test at normal maturity, 53-63 days after the final application (DAT). In one test, duplicate treated samples of nutmeats and hulls were collected at 40, 49, 55, 63, and 68 DAT to examined residue decline. Samples were stored frozen from collection to analysis for up to 10 months, an interval supported by available storage stability data.

Combined residues of propiconazole and its 2,4-dichlorobenzoic acid (DCBA) containing metabolites in/on almond nutmeats and hulls were determined using adequate GC/ECD methods (Methods AG-454B and AG-626). For these methods, residues are extracted and converted to 2,4-DCBA by base hydrolysis and oxidization with $KMnO_4$. Residues of DCBA are then partitioned into diethyl ether:hexane, concentrated, methylated, and cleaned-up using an acidic alumina cartridge. Methylated DBCA is determined by GC/ECD using external standards, and

residues are expressed in parent equivalents. The validated method LOQ is 0.05 ppm for nutmeats and 0.10 ppm for hulls, and a LOD was not reported.

Although the concurrent recoveries from nutmeat and hulls were generally low (60-80%), the recoveries were relatively consistent. Therefore, the method is deemed adequate for data collection. Although the raw data (instead of corrected data) were used to report residue values, the data collection method detects parent plus all metabolites containing DCBA, and yet the Agency's tolerance expression for propiconazole will be established at parent only, there fore, tolerances will not under represent the real residue levels.

Application volume and formulation type had no apparent effect on residue levels. For samples treated with the WP, combined residues range from <0.05-0.07 ppm in/on 12 samples of nutmeats and 0.57-4.60 ppm in/on 12 samples of hulls, For samples treated with the EC formulation , combined residues range from <0.05-0.09 ppm in/on 12 samples of nutmeats and 0.85-4.20 ppm in/on 12 samples of hulls. For the WP and EC formulations, average residues were respectively 0.035 and 0.041 ppm in/on nutmeats and 1.78 and 2.06 ppm in/on hulls. When data from both formulations are pooled, average residues are 0.038 ppm in/on nutmeats and 1.92 ppm in/on hulls.

In the residue decline test, residues in/on nutmeats declined slightly from an average of 0.07 ppm at 40 DAT to <0.05 ppm by 68 DAT. However, residue levels in/on hulls were variable over time. Given the variability of residues in/on hulls at a single sampling interval (1.92 ± 1.20 ppm; 53-63 DAT), the decline data most likely represent the variability in hulls residues rather than any trend in hull residue levels.

The number of trials and the geographic representation of the trials are adequate. These data will support the use of propiconazole (EC or WP) on almonds as up four foliar applications during nut development at 0.22 lb ai/A/application, at a minimum RTI of 7 days, for a total of 0.88 lb ai/A/season, with a 60-day PHI.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the almond field trial residue data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the forthcoming U.S. EPA Residue Chemistry Summary Document DP Barcode D238458.

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance and Data Confidentiality statements were provided. The study author cited several minor deviations from GLP requirements relating to collection of weather data and characterization of the spray mix. However, none of deviations were serious enough to adversely affect the conclusions of the study.

A. BACKGROUND INFORMATION

Propiconazole is a triazole-type fungicide that provides broad spectrum disease control through inhibition of sterol biosynthesis in fungi. It is registered to Syngenta Crop Protection for the control of fungal diseases on a variety of crops. Tolerances for propiconazole are currently established for the combined residues of propiconazole and its metabolites determined as 2,4-dichlorobenzoic acid (expressed as parent) in/on a variety of plant and animal commodities [40 CFR §180.434].

Syngenta previously submitted a petition (PP#9F3740) supporting the use of propiconazole, formulated as an EC, on almonds. This petition has been superseded by a more recent petition (PP#2F6371), which includes new or amended use directions for tree nut crops, of which almond is a representative crop. The current submission includes side-by-side field trials on almonds comparing residues resulting from EC and WP formulations using both dilute and concentrate spray volumes.

TABLE A.1. Nomenclature of Propiconazole

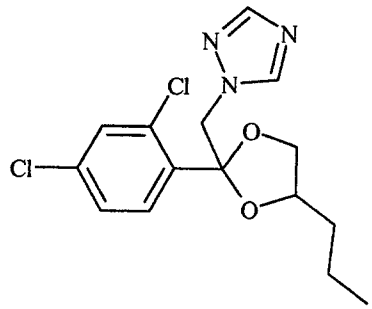
Compound	
Common name	Propiconazole
Company experimental names	CGA-64250
IUPAC name	1-[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole
CAS name	1-[[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole
CAS #	60207-90-1
End-use products/EP	3.6 lb/gal EC (Tilt Fungicide, EPA Reg. No. 100-617) 45% WP (Tilt 45W Fungicide, EPA Reg. No. 100-780)

TABLE A.2. Physicochemical Properties of Technical Grade Propiconazole.

Parameter	Value	Reference
Boiling point	120°C at 1.9 Pa, >250°C at 101.325 kPa	MRID No. 43698701
pH	4.9 at 25°C (1% aqueous dispersion)	MRID No. 43698701
Density	1.289 g/cm^3 at 20°C	MRID No. 43698701
Water solubility	0.10 g/L at 20°C	MRID No. 41720301
Solvent solubility (temperature not specified)	Completely miscible in ethanol, acetone, toluene and n-octanol. Hexane = 47 g/L	MRID No. 42030201
Vapor pressure	4.2 x 10^{-7} mm Hg at 25°C	MRID No. 41720301
Dissociation constant (pK_a)	1.09	MRID No. 43698701
Octanol/water partition coefficient Log(K_{OW})	3.72 at pH 6.6 and 25°C	MRID No. 43698701
UV/visible absorption spectrum (8max, nm)	Not available	MRID No. 40583703

B. EXPERIMENTAL DESIGN

B.1. Study Site Information

Almond trees in established orchards (7-21 years old) were maintained using typical agricultural practices for the region (Table B.1.1). Monthly rainfall and average temperature data were provided for the entire growing season from the 1999 test, but only weather data from the first half of the growing season was reported for the 1998 tests. No usual or adverse weather conditions were reported. Information was provided on maintenance chemicals and other pesticides used.

At each test site, propiconazole was applied in side-by-side tests comparing the 3.6 lb/gal EC and 45% WP formulations (Table B.1.2). Two sites used only dilute spray volumes and two sites used only concentrated spray volumes. The final site had plots comparing both dilute and concentrated spray volumes.

TABLE B.1.1. Trial Site Conditions.

Trial Identification (County, State; Year)	Soil characteristics [1]			
	Type	%OM	pH	CEC [2] (meq/g)
Fresno, CA 1998	Sandy loam	0.98	7.1	5.81
Yolo, CA 1998	Clay loam	1.63	7.2	18.24
Tulare, CA 1998	Loam	0.59	7.6	7.48
Stanislaus, CA 1998	Sand	2.18	7.3	3.46
Yolo, CA 1999	Loam	NR	NR	NR

[1] These parameters are optional except in cases where their value affects the use pattern for the chemical.
[2] Cation exchange capacity.
NR = not reported.

TABLE B.1.2. Study Use Pattern on Almonds.

Location (County, State; Year) Trial ID	End-use Product	Application Information [1]				
		Method; Timing	Volume (GPA)	Single Rate (lb ai/A)	RTI [2] (days)	Total Rate (lb ai/A)
Fresno, CA 1998 02-FR-001-98	45% WP	Four foliar applications during nut development, prior to hull split	75	0.22	7, 7, 8	0.88
			150	0.22	7, 7, 8	0.88
	3.6 lb/gal EC	Four foliar applications during nut development, prior to hull split	75	0.22	7, 7, 8	0.88
			150	0.22	7, 7, 8	0.88
Yolo, CA 1998 OW-FR-402-98	45% WP	Four foliar applications during nut development, prior to hull split	10	0.22	7, 8, 6	0.88
	3.6 lb/gal EC	Four foliar applications during nut development, prior to hull split	10	0.22	7, 8, 6	0.88
Tulare, CA 1998 OW-FR-514-98	45% WP	Four foliar applications during nut development, prior to hull split	205-207	0.22	8, 7, 7	0.88
	3.6 lb/gal EC	Four foliar applications during nut development, prior to hull split	205-207	0.22	8, 7, 7	0.88
Stanislaus, CA 1998 OW-FR-515-98	45% WP	Four foliar applications during nut development, prior to hull split	10	0.22-0.25 [3]	7, 7, 7	0.91
	3.6 lb/gal EC	Four foliar applications during nut development, prior to hull split	10	0.22	7, 7, 7	0.88
Yolo, CA 1999 0W-FR-404-99	45% WP	Four foliar applications during nut development, prior to hull split	160	0.22	14, 7, 7	0.88
	3.6 lb/gal EC	Four foliar applications during nut development, prior to hull split	160	0.22	14, 7, 7	0.88

[1] No adjuvants were included in any of the spray mixes.
[2] RTI = Retreatment Intervals between the four applications.
[3] The third application was made at 0.25 lb ai/A; all other applications were at 0.22 lb ai/A.

TABLE B.1.3. Trial Numbers and Geographical Locations.

NAFTA Growing Zones[1]	Almonds		
	Submitted	Requested	
		Canada	U.S.
1	---	---	---
2	---	---	---
3	---	---	---
4	---	---	---
5	---	---	---
6	---	---	---
7	---	---	---
8	---	---	---
9	---	---	---
10	5	---	5
11	---	---	---
12	---	---	---
Total	5	NA	5

[1] Regions 13-21 and 1A, 5A, 5B, and 7A were not included as the proposed use is for the US only.
NA = Not applicable.

B.2. Sample Handling and Preparation

Single control and duplicate treated samples of almond nutmeats and hulls (weights unspecified) were collected from each test at 53-63 DAT. In one of the tests using dilute applications of the 45% WP, single control and duplicate treated samples of nutmeats and hulls were collected also at 40, 49, 55, 63, and 68 DAT, to examine residue decline. All samples from the 1998 tests were placed into freezers after harvest and shipped frozen within ~1 month to the analytical laboratory, Central California Research Laboratories (CCRL), Fresno, CA, where samples were homogenized with dry ice and stored at <0°C until analysis. Samples from the 1999 test were frozen after harvest and shipped by freezer truck to Novartis Crop Protection (Greensboro, NC), where samples were stored at -20°C until analysis.

B.3. Analytical Methodology

Nutmeat and hull samples were analyzed for residues of propiconazole and its DCBA-containing metabolites using related GC/ECD methods (Method AG-454B or AG-626). Both methods are updated versions of the current tolerance enforcement method for propiconazole residues in plant commodities. These methods convert all residues to 2,4-DCBA through base hydrolysis and oxidation, and residues are then determined as methylated 2,4-DCBA and expressed in parent equivalents. The basic difference between the two methods is that Method AG-626 uses iodomethane for methylation of DCBA rather than diazomethane as in Method AG-454B.

For these methods, propiconazole residues are extracted by refluxing for 1 hour in NH_4OH/methanol (20:80, v/v), and filtered. Residues are concentrated and oxidized to DCBA by refluxing with $KMnO_4$ in 1N NaOH for 75 minutes. After reflux, the extract is diluted with water, the $KMnO_4$ is deactivated by the addition of sodium meta-bisulfite, and the extract is acidified by the addition of 6N HCl. Residues of DCBA are partitioned into diethyl ether:hexane (10:90, v/v), evaporated to dryness, and methylated using either diazomethane (AG-454B) or iodomethane (AG-626). Residues are then cleaned-up using an acidic alumina Sep-Pak eluted with diethyl ether:hexane (10:90, v/v), and analyzed by GC/ECD using external standards. The validated method LOQ is 0.05 ppm for nutmeats and 0.1 ppm for hulls; and a LOD was not reported.

Summary tables of the residue data were corrected by the registrant for procedural recoveries of <100%; however, spreadsheets including the uncorrected residue values were available in the raw data and were used by the reviewer to report residue values. Although the raw data (instead of corrected data) were used to report residue values, the data collection method detects parent plus all metabolites containing DCBA, and yet the Agency's tolerance expression for propiconazole will be set at parent only, there fore, tolerances will not under represent the real residue levels.

In conjunction with the analysis of field trial samples, the above methods were validated using control samples of fortified with propiconazole at 0.05-10.0 ppm for nutmeats and at 0.05-20 ppm for hulls.

C. RESULTS AND DISCUSSION

The number and geographic representation of the almond field trial data are adequate. In five field trials conducted during 1998 and 1999 in CA, propiconazole was applied to almonds in side-by-side tests comparing the use of 45% WP and 3.6 lb/gal EC formulations. Applications were made as dilute sprays (160-207 gal/A) at two sites, as concentrated sprays (10 gal/A) at two sites, and as both dilute (150 gal/A) and concentrated (75 gal/A) sprays at the fifth site. In each test, propiconazole (EC or WP) was applied four times to almonds as foliar applications during nut development at 0.22-0.25 lb ai/A/application, at RTIs of 6-14 days, for a total of 0.88-0.91 lb ai/A/season. All applications were made using ground equipment and adjuvants were not added to the spray mix. Single control and duplicate treated samples of nutmeats and hulls were collected from each test at normal maturity, 53-63 DAT. In one test, duplicate treated samples of nutmeats and hulls were collected at 40, 49, 55, 63, and 68 DAT to examined residue decline.

The GC/ECD methods (Methods AG-454B and AG-626) used to determine total propiconazole residues in/on almond nutmeats and hulls were adequately validated in conjunction with the field sample analyses. For Method AG-454B, recoveries of propiconazole were 64-76% from control samples of nutmeats fortified at 0.05-1.0 ppm, and averaged 70 ± 5% (Table C.1). Recoveries of propiconazole were 53-109% from control samples of hulls fortified at 0.1-20 ppm, and averaged 74 ± 16%. Although recoveries from nutmeat and hulls were generally low (60-80%), the recoveries were relatively consistent. Therefore, the method is deemed adequate for data collection. For Method AG-626, the average recovery of propiconazole was 79% from both nutmeats and hulls. For both methods, apparent residues of propiconazole were <LOQ in/on 9 control samples each of nutmeats and hulls. The validated method LOQ for propiconazole is 0.05 ppm in nutmeats and 0.1 ppm in hulls, and the LOD was not reported. Adequate sample calculations and example chromatograms were provided.

Samples of nutmeats and hulls were stored frozen for up to 10 months prior to extraction for analysis (Table C.2). Adequate storage stability data are available indicating that propiconazole is stable for up to 36 months in peanut nutmeats and hulls (DP Barcode D279300, Y. Donovan, 8/18/05). These data will support the frozen storage intervals for the almond trials as the peanut matrices are similar to almond nutmeats and hulls.

Application volume and formulation type had no apparent effect on residue levels (Table C.3). Following four applications of propiconazole totalling 0.88-0.91 lb ai/A, combined propiconazole residues at 53-63 DAT were <0.05-0.07 ppm in/on nutmeats and 0.57-4.60 ppm in/on hulls from trees treated with the WP formulation and <0.05-0.09 ppm in/on nutmeats and 0.85-4.20 ppm in/on hulls from trees treated with the EC formulation. For the WP and EC formulations, average residues at ~60 DAT were respectively 0.035 and 0.041 ppm in/on

nutmeats and 1.78 and 2.06 ppm in/on hulls (Table C.4). Including data from both formulations, residues in/on nutmeats were <0.05-0.09 ppm and averaged 0.038 ppm, and residues in/on hulls were 0.57-4.60 ppm and averaged 1.92 ppm.

Results from the residue decline test were variable. Residues in/on nutmeats declined slightly from an average of 0.07 ppm at 40 DAT to <0.05 ppm by 68 DAT. Residues in/on hulls initially remained relatively steadily, averaging 2.0-2.4 ppm from 40-55 DAT, before declining to an average of 0.95 ppm by 63 DAT. However, the highest hull residues were then measured at 5.1 ppm from 68 DAT. Given the variability of residues in/on hulls at a single sampling interval (1.92 ± 1.20 ppm; 53-63 DAT), the decline data most likely represent the variability in hulls residues rather than a trend in hull residue levels.

Common cultural practices were used to maintain plants, and the weather conditions and the maintenance chemicals and fertilizer used in the study did not have a notable impact on the residue data

TABLE C.1. Summary of Method Recoveries of Propiconazole from Almonds Using GC/ECD Methods (AG-454B or AG-626).

Analyte	Matrix	Spike level (ppm)	Sample size (n)	Recoveries (%)	Mean ∀ std dev (%)
Method AG-454B					
Propiconazole	Nutmeats	0.05-1.0	10	67, 76, 70, 76, 69, 65, 66, 64, 73, 74	70 ± 5
	Hulls	0.1-20.0	10	109, 72, 53, 63, 75, 79, 89, 61, 66, 77	74 ± 16
Method AG-626					
Propiconazole	Nutmeats	0.05, 5.0	2	71, 87	79
	Hulls	0.05, 10.0	2	89, 69	79

TABLE C.2 Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration[1] (months)	Interval of Demonstrated Storage Stability (months)[2]
Almond nutmeats and hulls	-20	2.4-10	36

[1] From harvest to extraction for analysis. Extracts were stored for 0-19 days prior to analysis
[2] DP Barcode D279300, Y. Donovan, 8/18/05.

TABLE C.3. Residue Data from Almond Field Trials Using Propiconazole Formulated as an EC and/or WP and Application as Dilute and/or Concentrated Sprays.

Trial ID (County, State; Year)	Zone	Variety	Total Rate (lb ai/A)	End-use Product	Appl. Volume (GPA)	PHI (days)	Propiconazole Residues (ppm)[1]
Almond Nutmeats							
Fresno, CA 1998 02-FR-001-98	10	Neplus	0.88	45% WP	150	40	0.06, 0.07
						49	0.09, 0.09
						55	<0.05, <0.05
						63	0.07, 0.07
						68	<0.05, <0.05
				45% WP	75	63	<0.05, 0.05
			0.88	3.6 lb/gal EC	150	63	0.09, 0.06
					75		0.07, 0.07
Yolo, CA 1998 OW-FR-402-98	10	Mission	0.88	45% WP	10	62	<0.05, <0.05
			0.88	3.6 lb/gal EC	10		<0.05, <0.05
Tulare, CA 1998 OW-FR-514-98	10	Mission	0.88	45% WP	205-207	63	<0.05, <0.05
			0.88	3.6 lb/gal EC	205-207		<0.05, <0.05
Stanislaus, CA 1998 OW-FR-515-98	10	Carmel	0.91	45% WP	10	62	<0.05, <0.05
			0.88	3.6 lb/gal EC	10		<0.05, <0.05
Yolo, CA 1999 0W-FR-404-99	10	Non Pariel	0.88	45% WP	160	53	<0.05, <0.05
			0.88	3.6 lb/gal EC	160		<0.05, <0.05
Almond Hulls							
Fresno, CA 1998 02-FR-001-98	10	Neplus	0.88	45% WP	150	40	2.2, 2.6
						49	2.3, 2.2
						55	2.1, 1.9
						63	0.97, 0.92
						68	5.1, 5.0
				45% WP	75	63	1.2, 1.2
			0.88	3.6 lb/gal EC	150	63	1.7, 1.8
					75		1.6, 1.9
Yolo, CA 1998 OW-FR-402-98	10	Mission	0.88	45% WP	10	62	4.6, 4.3
			0.88	3.6 lb/gal EC	10		4.2, 3.8
Tulare, CA 1998 OW-FR-514-98	10	Mission	0.88	45% WP	205-207	63	1.7, 1.0
			0.88	3.6 lb/gal EC	205-207		1.8, 1.9
Stanislaus, CA 1998 OW-FR-515-98	10	Carmel	0.91	45% WP	10	62	0.57, 0.59
			0.88	3.6 lb/gal EC	10		0.68, 0.67
Yolo, CA 1999 0W-FR-404-99	10	Non pariel	0.88	45% WP	160	53	2.3, 2.0
			0.88	3.6 lb/gal EC	160		2.6, 2.1

[1] Total propiconazole residues determined as DCBA and expressed in parent equivalents. Reported values were obtained from the raw data and are not corrected procedural recoveries. The LOQ for propiconazole residues is 0.05 ppm in/on nutmeats and 0.1 ppm in/on hulls. The LOD was not reported.

TABLE C.4. Summary of Residue Data from Almond Field Trials with Propiconazole (EC or WP).

Commodity	Total Applic. Rate (lb ai/A)	End-use Product	PHI (days)	Total Residue Levels (ppm)[1]						
				n	Min.	Max.	HAFT[2]	Median (STMdR)[3]	Mean (STMR)[3]	Std. Dev.
Nutmeats	0.88-0.91	45% WP	53-63	12	<0.05	0.07	0.07	0.025	0.035	0.018
		3.6 lb/gal EC		12	<0.05	0.09	0.08	0.025	0.041	0.024
		Both		24	<0.05	0.09	0.08	0.025	0.038	0.021
Hulls	0.88-0.91	45% WP	53-63	12	0.57	4.60	4.45	1.20	1.78	1.36
		3.6 lb/gal EC		12	0.67	4.20	4.00	1.85	2.06	1.06
		Both		24	0.57	4.60	4.45	1.75	1.92	1.20

[1] The LOQ is 0.05 ppm. Values are not corrected procedural recoveries. For calculation of the median, mean, and standard deviation, ½LOQ (0.025 ppm) was used for nutmeat samples with residues <LOQ.
[2] HAFT = Highest Average Field Trial.
[3] STMdR = Supervised Trial Median Residue; STMR = Supervised Trial Mean Residue.

D. CONCLUSION

The almond field trial data are adequate and indicate that the formulation type (WP or EC) and application volume (dilute or concentrate) do not have a notable impact on residue levels in almond nutmeat and hulls. Overall combined residues at 53-63 DAT were <0.05-0.09 ppm in/on almond nutmeats and 0.57-4.60 ppm in/on almond hulls. Average residues were 0.04 and 1.92 ppm in/on nutmeats and hulls, respectively.

E. REFERENCES

DP Barcode: D279300
Subject: Propiconazole (122101): Reregistration Eligibility Decision (RED) Document; Residue Chemistry Considerations.
From: Y. Donovan
To: S. Lewis/J. Guerry
Dated: 8/18/05
MRID: None

F. DOCUMENT TRACKING

RDI: Yan Donovan, RRB4/HED
Petition Number(s): 2F6371
DP Barcode(s): D238458
PC Code: 122101

Template Version June 2005