

US EPA ARCHIVE DOCUMENT



Primary Evaluator Yan Donovan, Chemist, RRB4/HED Date: 07/03/06

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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 was reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

44548402 Vincent, T. (1998) Propiconazole--Magnitude of the Residues in or on Wheat, Including Processed Fractions, Following an Application of TILT: Lab Project Number: 46-96: ABR-97143: 411124. Unpublished study prepared by Novartis Crop Protection, Inc. 189 p.

EXECUTIVE SUMMARY:

In two wheat field trials conducted in ID and ND in 1996, propiconazole (3.6 lb/gal EC) was applied to four separate plots of wheat at each site as a single broadcast foliar application at booting (Feekes Growth Stage 10) or at heading (Feekes Growth Stage 10.5) at 0.11-0.12 lb ai/A or 0.55-0.62 lb ai/A (1x and 5x rates). All applications were made using ground equipment in volumes of 15-21 gal/A, and did not include the use of any adjuvants. Single control and treated bulk samples of grain were harvested from each test at normal crop maturity, 63-67 days following the application at booting or 55-57 days following the application at heading. The grain was cleaned to generate aspirated grain fractions (AGF) and then processed using simulated commercial procedures into wheat germ, bran, middlings, shorts and flour (low grade and patent). Prior to analysis, the grain and processed fractions were stored frozen for up to 4.9 months, an interval supported by the available stability data.

Combined residues of propiconazole and its 2,4-dichlorobenzoic acid (DCBA) containing metabolites in/on wheat grain, straw and processed fractions were determined using an adequate GC/ECD method (Method AG-454B). For this method, 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 DCBA is determined by GC/ECD using external standards, and residues are expressed in parent equivalents. The validated method limit of quantitation (LOQ) is 0.05 ppm, and the limit of detection (LOD) is 0.02 ppm.

For the tests conducted at the reported 1x rate, total propiconazole residues were <LOQ in/on all samples of grain and all processed fractions, with the exception of AGF. AGF samples from the 1x applications were <LOQ in one test and 0.08-0.14 ppm in the remaining three 1x tests, indicating the potential for concentration of residues in AGF. However, reliable processing factors could not be calculated at residues in the RAC were <LOQ.



Residues were also <LOQ in/on grain samples from two of the tests conducted at 5x rates; however, in the remaining two 5x tests, residues in/on grain were 0.16 ppm at 67 days following an application at booting and 0.24 ppm at 57 days following an application at heading. In these tests, residues were 1.3-1.4 ppm in AGF, ≤ 0.06 ppm in germ, 0.05-0.17 ppm in bran, and <LOQ in middlings, shorts and flour. Calculated processing factors for these tests were 5.8-8.1x for AGF, $\leq 0.3x$ for germ, 0.3-0.7x for bran, $\leq 0.2x$ for middlings, shorts and flour. Average processing factors were 7.0x for AGF, 0.2x for germ, 0.5x for bran and <0.1x for middlings, shorts and flour.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the wheat processing study 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 minor deviations from GLP compliance, pertaining to the collection of weather data, tank mix storage stability data and maintenance of records. None of these deviations affect the overall acceptability 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, including permanent tolerances of 0.1 and 1.5 ppm on wheat grain and straw [40 CFR §180.434(a)].

Syngenta has submitted a petition (PP#2F6371) proposing tolerances and the use of propiconazole on a variety of cereal grains, including wheat. The current submission includes residue data from several processing studies on wheat, in which propiconazole (EC) was applied to wheat at up to Feekes Growth Stage 10.5 (heading) at 1x and 5x rates.

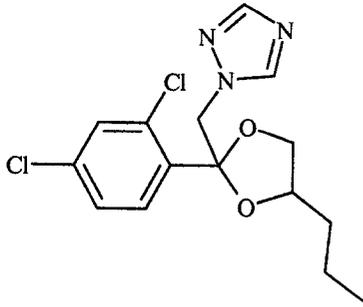
Compound	
Common name	Propiconazole
Company experimental names	CGA-64250
IUPAC name	1-[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole
CAS name	1-[[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole
CAS #	60207-90-1
End-use products/EPs	3.6 lb/gal EC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



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 (λ _{max} , nm)	Not available	MRID No. 40583703

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

Four treated plots and a control plot were established at each test site (Table B.1.1). At both sites, propiconazole (3.6 lb/gal EC) was applied to wheat as a single broadcast foliar application at either booting (Feekes Growth Stage 10) or heading (Feekes growth stage 10.5) at target rates of 0.11 lb ai/A (1x) and 0.55 lb ai/A (5x).

TABLE B.1.1. Study Use Pattern on Wheat.

Location (County, State; Year) Trial ID	End-use Product	Application Information ¹				
		Method; Timing	Volume (GPA) ²	Single Rate (lb ai/A)	RTI ³ (days)	Total Rate (lb ai/A)
Latah, ID 1996 0W-FR-672-96	3.6 lb/gal EC	Single broadcast foliar application at Feekes Growth Stage 10 (boot stage)	21	0.12	NA	0.12
			21	0.62	NA	0.62
		Single broadcast foliar application at Feekes Growth Stage 10.5 (heading)	21	0.12	NA	0.12
			21	0.62	NA	0.62
Foster, ND 1996 MW-FR-515-96	3.6 lb/gal EC	Single broadcast foliar application at Feekes Growth Stage 10 (boot stage)	15	0.11	NA	0.11
			15	0.55	NA	0.55
		Single broadcast foliar application at Feekes Growth Stage 10.5 (heading)	15	0.11	NA	0.11
			15	0.55	NA	0.55

¹ All applications were made using ground equipment, and did not include the use of any spray adjuvants.

² Gallons per acre

³ RTI = Retreatment Interval.

NA = not applicable.



B.2. Sample Handling and Processing Procedures

Single bulk samples (weight unspecified) of control and treated (1x and 5x) wheat grain were harvested at normal crop maturity, which was 63-67 days following the application at booting or 55-57 days following the application at heading. Samples were then shipped by overnight courier under ambient conditions to the processing facility, Food and Protein Research and Development Center, Texas A&M University, Bryan, TX, where samples were stored at $\leq -12^{\circ}\text{C}$ until processing. A subsample of grain was collected at the processing facility, and samples of AGF were then generated and collected using procedures that simulate the movement of grain during transport and storage. Cleaned wheat grain was then processed into flour using simulated commercial procedures, and samples of wheat germ, bran, middlings, shorts, and flour (low grade and patent) were collected during processing. Samples were frozen within ~2 hours of collection and shipped to on dry ice by overnight courier to Novartis Crop Protection (Greensboro, NC), where samples were prepared (homogenized) and stored at -20°C . Samples were later shipped frozen to the analytical laboratory, ABC Laboratories (Columbia, MO), where samples were stored at -20°C until analysis.

B.3. Analytical Methodology

Samples of wheat grain and processed fractions were analyzed for residues of propiconazole and its DCBA-containing metabolites using a GC/ECD method (Method AG-454B), which is an updated version of the current tolerance enforcement method for propiconazole residues in plant commodities. The method converts 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.

For this method, 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 diazomethane. 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 roots and processed fractions, and the LOD is 0.02 ppm.

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.

In conjunction with the analysis of field trial samples, the above method was validated using control samples fortified propiconazole at 0.05-20 ppm for grain and at 0.05 and 0.10 ppm for AGF and each processed fraction.



C. RESULTS AND DISCUSSION

The GC/ECD method (Method AG-454B) used to determine propiconazole residues in/on wheat grain and processed fractions was adequately validated in conjunction with the analysis of field trial samples. Average recoveries of propiconazole were $85 \pm 15\%$ from grain fortified at 0.05-20 ppm (Table C.1). For AGF and grain processed fractions, recoveries averaged 83-86% from samples fortified at 0.05 and 0.10 ppm, with standard deviations of $\pm 11-21\%$. Apparent residues of propiconazole were non-detectable (<0.02 ppm) in/on control samples of grain and all processed fractions, with the exception of one control sample of grain, which had apparent residues above the LOD, but $<LOQ$. The validated method LOQ for propiconazole is 0.05 ppm, and the LOD is 0.02 ppm. Adequate sample calculations and example chromatograms were provided. Although the study author reported residue values corrected for concurrent recoveries of $<100\%$, uncorrected residues values are used and reported in this review.

Samples of wheat grain, AGF and processed fractions were stored frozen for up to 4.9 months prior to extraction for analysis (Table C.2). Adequate storage stability data are available indicating that residues of propiconazole and its metabolites are stable at -20°C for up to 36 months on a wide variety of plant commodities, including wheat grain and corn meal (DP Barcode D279300, Y. Donovan, 8/18/05), which are similar in nature to the matrices in the current processing study. These data will support the storage intervals and conditions for the wheat grain processing study.

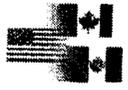
TABLE C.1. Summary of Concurrent Recoveries of Propiconazole from Wheat Grain, AGF and Processed Fractions.

Matrix	Spike level (ppm)	Sample size (n)	Recoveries (%)	Mean ∇ std dev (%)
Grain	0.05	5	101, 75, 73, 61, 77	85 ± 15
	0.10	4	72, 107, 79, 88	
	0.50	2	105, 95	
	20.0	1	86	
AGF	0.05, 0.10	4	73, 91, 78, 96	85 ± 11
Germ	0.05, 0.10	4	97, 68, 84, 102	88 ± 15
Bran	0.05, 0.10	4	78, 67, 73, 113	83 ± 21
Middlings	0.05, 0.10	4	77, 82, 83, 103	86 ± 11
Shorts	0.05, 0.10	4	77, 68, 84, 102	83 ± 14
Flour (low grade and patent)	0.05, 0.10	8	94, 95, 78, 99, 89, 105, 117, 93	96 ± 11

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature ($^\circ\text{C}$)	Actual Storage Duration ¹ (months)	Interval of Demonstrated Storage Stability (months) ²
Grain, AGF and processed fractions	-20	1.2-4.9	36

¹ From harvest to extraction for analysis. Samples were analyzed within 1-10 days of extraction.
² DP Barcode D279300, Y. Donovan, 8/18/05.



Following applications at 0.11-0.12 lb ai/A (1x rate), total uncorrected propiconazole residues were <LOQ in/on mature samples of grain harvested at either 63-67 days following an application at booting or 55-57 days following an application at heading (Table C.3). For the tests conducted at 1x, residues were also <LOQ in all wheat processed fractions, with the exception of AGF. AGF samples from the 1x applications were <LOQ in one test and 0.08-0.14 ppm in the remaining three 1x tests. As residues were <LOQ in grain, reliable processing factors could not be calculated from the tests conducted at 1x.

For the applications at 0.55-62 lb ai/A (5x rate), total propiconazole residues were also <LOQ in/on grain samples from the two tests conducted in ND. The data from these tests indicated there is the potential for concentration of residues in AGF and bran, but processing factor were not calculated for these two tests as residues in the RAC were <LOQ. For the two 5x tests conducted in ID, total propiconazole residues in/on grain were 0.16 ppm at 67 days following an application at booting and 0.24 ppm at 57 days following an application at heading. In these two tests, residues were 1.3-1.4 ppm in AGF, ≤ 0.06 ppm in germ, 0.05-0.17 ppm in bran, and <LOQ in middlings, shorts and flour. The calculated processing factors for these two tests were 5.8-8.1x for AGF, ≤ 0.3 x for germ, 0.3-0.7x for bran, ≤ 0.2 x for middlings, shorts and flour. Average processing factors were 7.0x for AGF, 0.2x for germ, 0.5x for bran and <0.1x for middlings, shorts and flour.



Table C.3. Residue Data from Wheat Processing Studies with Propiconazole (EC) Applied as a Late-season Application at Booting or Heading.

Location (County, State; Year) Trial ID	Application Timing	Total Rate (lb ai/A) ¹	RAC	Processed Commodity	PHI (days)	Total Residues (ppm) ²	Processing Factors ³
Latah, ID 1996 0W-FR-672-96	Feekes Growth stage 10 (booting)	0.12	Grain	NA	67	(0.02) ⁴	NA
				AGF		0.08	NC
				Germ		(0.03)	NC
				Bran		ND	NC
				Middlings		ND	NC
				Shorts		ND	NC
				Low grade flour		ND	NC
				Patent flour		ND	NC
	0.62	Grain	NA	67	0.16	NA	
			AGF		1.3	8.1x	
			Germ		(0.03)	<0.2x	
			Bran		0.05	0.3x	
			Middlings		(0.02)	<0.1x	
			Shorts		ND	<0.1x	
			Low grade flour		ND	<0.1x	
			Patent flour		ND	<0.1x	
	Feekes Growth stage 10.5 (heading)	0.12	Grain	NA	57	ND	NC
				AGF		0.14	NC
				Germ		ND	NC
				Bran		(0.02)	NC
				Middlings		ND	NC
				Shorts		ND	NC
				Low grade flour		ND	NC
				Patent flour		ND	NC
0.62	Grain	NA	57	0.24	NA		
		AGF		1.4	5.8x		
		Germ		0.06	0.3x		
		Bran		0.17	0.7x		
		Middlings		(0.03)	0.1x		
		Shorts		(0.04)	0.2x		
		Low grade flour		ND	<0.1x		
		Patent flour		ND	<0.1x		



Table C.3. Residue Data from Wheat Processing Studies with Propiconazole (EC) Applied as a Late-season Application at Booting or Heading.

Location (County, State; Year) Trial ID	Application Timing	Total Rate (lb ai/A) ¹	RAC	Processed Commodity	PHI (days)	Total Residues (ppm) ²	Processing Factors ³
Foster, ND 1996 MW-FR-515-96	Feekes Growth stage 10 (booting)	0.11	Grain	NA	63	ND	NA
				AGF		(0.02)	NC
				Germ		ND	NC
				Bran		(0.03)	NC
				Middlings		ND	NC
				Shorts		ND	NC
				Low grade flour		ND	NC
				Patent flour		ND	NC
		0.55	Grain	NA	63	(0.03)	NA
				AGF		0.08	NC
				Germ		(0.02)	NC
				Bran		0.09	NC
				Middlings		ND	NC
				Shorts		0.04	NC
	Low grade flour			ND		NC	
	Patent flour			ND		NC	
	Feekes Growth stage 10.5 (heading)	0.11	Grain	NA	55	ND	NA
				AGF		0.10	NC
				Germ		(0.02)	NC
				Bran		0.07	NC
				Middlings		ND	NC
				Shorts		0.03	NC
				Low grade flour		ND	NC
				Patent flour		ND	NC
0.55		Grain	NA	55	ND	NA	
			AGF		0.32	NC	
Germ	0.14	NC					
Bran	0.30	NC					
Middlings	(0.05)	NC					
Shorts	0.10	NC					
Low grade flour	ND	NC					
Patent flour	(0.02)	NC					

¹ The application rates were reported to be at 1x and 5x the use rate for wheat.
² Total propiconazole residues were 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 wheat grain and processed fractions, and the LOD is 0.02 ppm.
³ Processing factors were calculated by the reviewer using uncorrected residues.
⁴ Values in parentheses are residues reported below the LOQ, but \geq LOD.
 NA = not applicable
 ND = not detected; <0.02 ppm.
 NC = not calculated. Processing factors were not calculated for test in which grain residues were <LOQ.



D. CONCLUSION

The wheat grain processing tests are adequate. In the two 5x tests in which residues in/on grain were above the method LOQ, residues were shown to concentrate in wheat AGF by an average of 7x. However, residues were reduced by 0.2x in germ, 0.5x in bran and <0.1x in middlings, shorts and flour.

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

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

Template Version June 2005