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

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

This DER was originally prepared under contract by Dynamac Corporation (1910 Sedwick Rd., Building 100, Suite B; Durham, NC 27713; submitted 06/12/2006). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

45275801 Lin, K. (2000) Propiconazole-Magnitude of the Residue in or on Grain Sorghum: Final Report: Lab Project Number: 145-98: MW-FR-503-98: 0S-FR-103-98. Unpublished study prepared by Novartis Crop Protection, Inc. 222 p.

EXECUTIVE SUMMARY:

In two field trials conducted in KS and TX in 1998, propiconazole (3.6 lb/gal EC) was applied to two plots of sorghum at each site as four broadcast foliar applications during grain development at 0.11 or 0.55 lb ai/A/application, for totals of 0.44 or 2.2 lb ai/A/season (1x and 5x rates). All applications were made using ground equipment in volumes of 12-13 gal/A, and included the use of a surfactant at 0.1-0.25% of the spray volume. Single control and treated bulk samples of grain were harvested from each test at normal crop maturity, 18 or 20 days after the final treatment (DAT). The grain was cleaned to generate aspirated grain fractions (AGF) and then processed using simulated commercial procedures into flour. Prior to analysis, the grain and processed fractions were stored frozen for up to 15 months, an interval supported by the available stability data.

Combined residues of propiconazole and its 2,4-dichlorobenzoic acid (DCBA) containing metabolites in/on sorghum grain, AGF and flour were determined using an adequate GC/ECD method (Method AG-626, modified). 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 partitioned into hexane. Methylated DBCA 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) was not reported.

Total propiconazole residues in/on bulk samples of grain harvested at 18-20 DAT were 0.43 or 1.2 ppm following applications at the 1x rate and 2.2 and 6.9 ppm following applications at the 5x rate. For the 1x rate, residues in AGF were 3.39 and 6.5 ppm and residues in flour were 0.06 and 0.48 ppm. For the 5x rates, residues in AGF were 9.2 and 21.3 ppm and residues in flour were 0.22 and 2.6 ppm. The processing factors for AGF range from 3.1x-7.9x and averaged 5.1x, and the processing factors for flour range from 0.1x-0.4x and averaged at 0.3x.

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the sorghum processing study is 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, maintenance chemicals, irrigation application, and weight documentation. 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-DCBA (expressed as parent) in/on a variety of plant and animal commodities, including time-limited tolerances of 0.2 and 1.5 ppm on sorghum grain and stover [40 CFR §180.434(b)].

Syngenta has previously proposed tolerances (PP# 5F4498) for inadvertent residues on sorghum planted in rotation with propiconazole-treated wheat. This petition has been superseded by PP#2F6371, in which tolerances are being requested on sorghum commodities resulting from the direct use of propiconazole on sorghum (DP Barcode D279300, Y. Donovan, 8/18/2005). The current submission includes residue data on sorghum processed products.

TABLE A.1. Nomenclature of Propiconazole

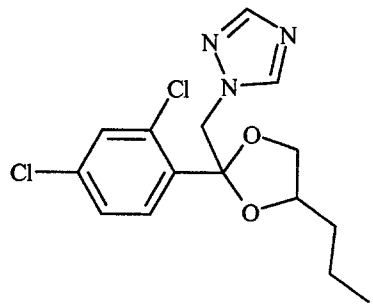
Compound	
Common name	Propiconazole
Company experimental names	CGA-64250
IUPAC name	1-[2-(2,4_dichlorophenyl)-4-propyl-1,3-dioxolan-2-ylmethyl]-1H-1,2,4-triazole
CAS name	1-[[2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]methyl]-1H-1,2,4-triazole
CAS #	60207-90-1
End-use products/EP	3.6 lb/gal EC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

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. Application and Crop Information

At two field sites in KS and TX during 1998, propiconazole (EC) was applied to two separate plots of sorghum at each site during grain development as four broadcast foliar applications at either 0.11 or 0.55 lb ai/A/application. These rates were reported to be 1x and 5x the proposed use rate (Table B.1.1).

TABLE B.1.1. Study Use Pattern							
Location (County; Year) Trial ID	End-use Product	Application Information [1]					Tank Mix/ Adjuvants
		Method; Timing	Volume (GPA) [1]	Single Rate (lb ai/A)	RTI [2] (days)	Total Rate (lb ai/A)	
Kiowa, KS 1998 MW-FR-311-98	3.6 lb/gal EC	Four broadcast foliar applications from GS 8 to GS 9 stage	12-13	0.11	11, 3, 8	0.44	Silwet 0.1%
				0.55		2.20	
Burleston, TX 1998 0S-FR-202-98	3.6 lb/gal EC	Four broadcast foliar applications from soft to hard dough stages	13	0.11	5, 5, 5	0.44	Kinetic 0.25%
				0.55		2.20	

[1] All applications were made using ground equipment.
[2] Gallons per acre
[3] RTI = Retreatment Interval.

B.2. Sample Handling and Processing Procedures

Single bulk samples (weight unspecifed) of control and treated (1x and 5x) grain were harvested from each site at normal crop maturity, 18 or 20 DAT. Samples from the TX site were shipped under ambient conditions on the day of harvest directly to the processing facility, Food and Protein Research and Development Center (FPRDC), Texas A&M University, Bryan, TX. These samples were received by FPRDC on the same day as harvest and placed in storage at ≤-12°C. Samples from the KS site were frozen immediately after harvest and then shipped on

dry ice by overnight courier to FPRDC, where samples were stored at ≤-12°C. Samples from both field sites were stored frozen for ~3 months prior to processing.

A subsample of grain from each test 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 grain was then processed into flour using simulated commercial procedures. Samples were frozen after processing and shipped on dry ice by overnight courier to Novartis Crop Protection (Greensboro, NC), where samples were prepared (homogenized) and stored at -20EC until analysis.

B.3. Analytical Methodology

Samples of sorghum grain, AGF and flour were analyzed for residues of propiconazole and its DCBA-containing metabolites using a GC/ECD method (Method AG-626, modified), 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, residues were extracted and base hydrolyzed by refluxing for 1 hour with NH_4OH/MeOH (20:80, v/v) and filtered. Residues were concentrated and oxidized to 2,4-DCBA by refluxing with $KMnO_4$ in 1N NaOH for 75 minutes. After reflux, the extract was diluted with water, sodium meta-bisulfite was added to deactivate the $KMnO_4$, and the extract was acidified by the addition of 6N HCl. Residues of DCBA were partitioned into diethyl ether:hexane (10:90, v/v), evaporated to dryness, and methylated using methyl iodide in tertabutyl ammonium hydroxide. Residues were then diluted with hexane, concentrated, and partitioned against water. Methylated residues remaining in the hexane were then analyzed by GC/ECD using external standards. The validated method LOQ is 0.05 ppm and the 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.

In conjunction with the analysis of treated samples, the above method was validated using control samples of grain, AGF and flour fortified with propiconazole at 0.05-10 ppm.

C. RESULTS AND DISCUSSION

The GC/ECD method (Method AG-626, modified) used to determine propiconazole residues in/on sorghum grain and processed products was adequately validated in conjunction with the analysis of field trial samples. Average recoveries were 79% from grain and AGF and 97% from flour. Apparent residues were <LOQ in/on all control samples of grain and flour and the control sample of AGF from the test in KS, but apparent residues were detected at 0.189 ppm in the

control sample of AGF from the test in TX. As the apparent residues in this control sample were <3% of the residues measured in the two treated samples from the same test (6.5 and 21.3 ppm), the residues in this control sample will not have an adverse impact on the processing data. The validated method LOQ for propiconazole is 0.05 ppm, and the LOD was not reported. 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 were stored at -20°C for up to 15 months prior to analysis of grain and 12.2 months prior to analysis of AGF and flour. 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). As these matrices are similar in nature to the matrices in the current processing study, these data will support the storage intervals and conditions for the sorghum grain processing study.

Total uncorrected propiconazole residues in/on bulk samples of grain harvested at 18-20 DAT were 0.43 or 1.2 ppm following applications at the 1x rate and 2.2 and 6.9 ppm following applications at the 5x rate (Table C.3). For the 1x rates, residues in AGF were 3.39 and 6.5 ppm and residues in flour were 0.06 and 0.48 ppm. For the 5x rates, residues in AGF were 9.2 and 21.3 ppm and residues in flour were 0.22 and 2.6 ppm. As residues were >LOQ in all fractions, processing factors could be calculated for each test. The processing factors were 3.1x-7.9x for AGF and 0.1x-0.4x for flour. Average processing factors were 5.1x for AGF and 0.3x for flour.

TABLE C.1. Summary of Concurrent Recoveries of Propiconazole from Sorghum and its Processed Products

Matrix	Spike level (ppm)	Sample size (n)	Recoveries (%)	Mean ∀ std dev (%)
Grain	0.05, 1.0	2	70, 88	79
AGF	0.05	2	82, 76	79
Flour	1.0, 10	2	88, 106	97

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration [1] (days)	Interval of Demonstrated Storage Stability (months) [2]
Grain	-20	10.4-15.0	36
AGF		7.8-12.2	
Flour		7.8-12.2	

[1] Interval from harvest to extraction for analysis. Extracts were stored for 3-14 days prior to analysis.
[2] DP Barcode D279300, Y. Donovan, 8/18/05.

TABLE C.3. Residue Data from Sorghum Processing Study with Propiconazole (EC).						
Location	RAC	Processed Commodity	Total Rate (lb ai/A) [1]	PHI (days)	Total Combined Residues (ppm) [2]	Processing Factor [3]
Kiowa, KS 1998 (MW-FR-311-98)	Grain	NA	0.44	20	0.43	NA
		AGF			3.39	7.9x
		Flour			0.06	0.1x
	Grain	NA	2.20		2.20	NA
		AGF			9.18	4.2x
		Flour			0.22	0.1x
Burleston, TX 1998 (0S-FR-202-98)	Grain	NA	0.44	18	1.2	NA
		AGF			6.5 [4]	5.4x
		Flour			0.48	0.4x
	Grain	NA	2.20		6.9	NA
		AGF			21.3 [4]	3.1x
		Flour			2.6	0.4x

[1] The application rates were reported to be at 1x and 5x the use rate for sorghum.
[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 sorghum grain, AGF and flour. Th LOD was not reported.
[3] Processing factors were calculated by the reviewer using uncorrected residues.
[4] The associated control sample had apparent residues of 0.189 ppm.
NA = not applicable.

D. CONCLUSION

The sorghum grain processing tests are adequate, and the results from all four tests were similar. The average processing factors for combined propiconazole residues were 5.1x in AGF and 0.3x in 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

RDI: Yan Donovan, RRB4/HED
Petition Number(s): 5F4498 (superseded by 2F6371)
DP Barcode(s): D238458
PC Code: 122101

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