Primary Evaluator — Date: Oct 21, 2008
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This DER was originally prepared under contract by Dynamac Corporation (2275 Research Boulevard, Suite 300; Rockville, MD 20850; submitted 05/20/2008). The DER has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

STUDY REPORT:

46829503 Oakes, T., Ediger, K. (2005) S-Metolachlor - Magnitude of the Residues In Sorghum Aspirated Grain Fractions: Lab Project Number: T000965-03. Unpublished study prepared by Syngenta Crop Protection, Inc. 90 p.

EXECUTIVE SUMMARY:

Syngenta Crop Protection has submitted data pertaining to aspirated grain fractions (AGF) for sorghum grain. One field trial was conducted in the United States (Zone 5) during the 2003 growing season. A single broadcast foliar application of a 7.64 lb/gal emulsifiable concentrate (EC) formulation of S-metolachlor was made to sorghum (V4 plant growth stage) at a rate of 1.67 lb ai/A. Application was made using ground equipment in an 11 gal/A spray volume, without use of an adjuvant.

Control and treated subsamples and bulk samples of grain were harvested at normal crop maturity, 100 days after treatment (DAT). Within 2-4 months of harvest, the frozen bulk grain samples were processed into AGF using simulated commercial procedures. Prior to analysis, samples were stored at ≤-13 °C for up to 8.3 months for grain (RAC) and 9.6 months for AGF. These storage conditions and durations are supported by the available storage stability data.

Residues of S-metolachlor in/on sorghum grain and AGF were determined as SYN506357 and SYN508500 (S-enantiomers of CGA-37913 and CGA-49751) using a LC/MS/MS method (Syngenta Method No. 1848-01), which is derived from the current tolerance enforcement method. For this method, residues are acid hydrolyzed to CGA-37913 and CGA-49751 and cleaned up by solvent partitioning and using an alumina column. Residues are then determined by LC/MS/MS analysis, using a reverse phase chiral column to separate out the S-enantiomers. For each matrix, the limit of quantitation (LOQ) is 0.03 ppm for SYN506357 and 0.05 ppm for SYN508500, each expressed in parent equivalents. The method limit of detection was not reported. The method was adequate for data collection for sorghum grain and AGF based on acceptable concurrent method recoveries. Although concurrent method recoveries for SYN508500 were lower (62-69%) than the acceptable range of 70-120% for both commodities,

the method was adequate for data collection as the recoveries were consistent (average recovery 65% with 5% CV) for sorghum grain and AGF.

Residues of SYN508500 and SYN506357, reported as S-metolachlor equivalents, in sorghum grain were each below the method LOQ (<0.05 and <0.03 ppm, respectively), for total residues of <0.08 ppm. In two samples of sorghum AGF, residues of SYN508500 were below the LOQ (<0.05 ppm) and residues of SYN506357 were 0.06 and 0.09 ppm, for total residues of <0.11 and <0.14 ppm.

The data indicate that total S-metolachlor residues concentrate slightly in sorghum AGF, with concentration factors of 2.75-3.5x (average 3.1x).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the sorghum AGF residue data are classified as scientifically acceptable. The acceptability of this study for regulatory purposes is addressed in the U.S. EPA Residue Chemistry Summary Document, D332842 (D. McNeilly; Oct 21, 2008).

COMPLIANCE:

Signed and dated Good Laboratory Practice (GLP), Quality Assurance, and Data Confidentiality statements were provided. No deviations from regulatory requirements were reported which would have an impact on the validity of the study.

A. BACKGROUND INFORMATION

S-Metolachlor [S-2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methylethyl) acetamide] is a selective, chloroacetanilide herbicide that is applied to a variety of crops as a preplant, PPI, pre-emergence, or post-emergence-directed application, primarily for the control of grass weeds. It is currently registered to Syngenta Crop Protection for use on a wide variety of crops, including uses on sorghum as either a preplant surface, PPI, or preemergence application at 0.95-1.60 lb ai/A, with the rate depending on the soil type and amounts of organic matter.

Syngenta has submitted the current AGF study in response to deficiencies outlined in the Revised Residue Chemistry Chapter of the Metolachlor and S-Metolachlor TRED (D292881, S. Kinard, 8/15/03). The chemical structure and nomenclature of S-metolachlor and its regulated hydrolytic derivatives are presented in Table A.1, and the physicochemical properties of S-metolachlor are presented in Table A.2.

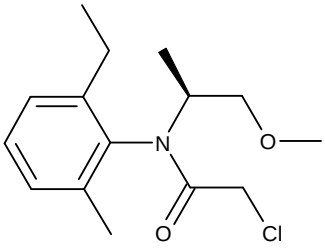
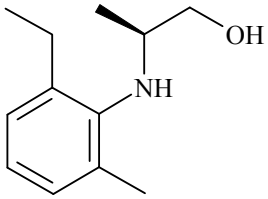
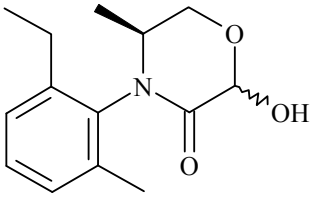
TABLE A.1. Nomenclature of S-Metolachlor and its Regulated Derivatives.	
Parent compound	
Common name	S-Metolachlor
Company experimental name	CGA-77102
IUPAC name	(S)-2-chloro-N-(2-ethyl-6-methyl-phenyl)-N-(2-methoxy-1-methyl-ethyl)-acetamide
CAS name	2-chloro-N-(2-ethyl-6-methylphenyl)-N-[(1S)2-methoxy-1-methylethyl]-acetamide
CAS registry number	87392-12-9
End-use product (EP)	7.64 lb/gal EC (Dual II Magnum Herbicide; EPA Reg. No. 100-818)
Regulated residue	
Common name	None
Company experimental names	SYN506357 (S-enantiomer of CGA 37913)
IUPAC name	(S)-2-[(2-ethyl-6-methylphenyl) amino]-1-propanol
CAS name	(S)-2-[(2-ethyl-6-methylphenyl) amino]-1-propanol
CAS #	82508-08-5
Regulated residue	
Common name	None
Company experimental names	CGA-49751 SYN508500 (S-enantiomer of CGA 49751)
IUPAC name	4-(2-ethyl-6-methylphenyl)-2-hydroxy-5-methyl-3-morpholine
CAS name	4-(2-ethyl-6-methylphenyl)-2-hydroxy-5-methyl-3-morpholine
CAS #	61520-54-5

TABLE A.2. Physicochemical Properties of S-Metolachlor.		
Parameter	Value	Reference
Melting point/range	Not applicable, liquid at room temperature	MRID 47121701
pH	7.8 at 25°C (1% aqueous dispersion)	
Density	1.117 g/cm^3 at 20°C	
Water solubility (25°C)	0.48 g/L	
Solvent solubility (mg/L at 25°C)	Completely miscible with methanol, acetone, toluene, n-octanol, n-hexane, ethyl acetate, dichloromethane	
Vapor pressure at 25°C	2.8 x 10^{-5} mm Hg	
Dissociation constant (pK$_a$)	No dissociation constant in pH range 2-12	
Octanol/water partition coefficient Log(K$_{OW}$)	3.05 at 25°C	
UV/visible absorption spectrum	Neutral: 534 l/mol•cm @ 266.4 nm 443 l/mol•cm @ 274.4 nm Acidic: 534 l/mol•cm @ 266.4 nm 444 l/mol•cm @ 274.4 nm Basic: 531 l/mol•cm @ 266.4 nm 411 l/mol•cm @ 274.4 nm	

B. EXPERIMENTAL DESIGN

B.1. Application and Crop Information

One field trial was conducted in the United States (Zone 5, KS) during the 2003 growing season, for the generation of AGF (Table B.1.1). A single broadcast foliar application of a 7.64 lb/gal EC formulation of S-metolachlor was made to sorghum at a rate of 1.67 lb ai/A at the V4 stage. The application was made using ground equipment in an 11 gal/A spray volume, without use of an adjuvant. The registrant indicated that a second field trial was initiated in TX (Zone 4); however, this field trial was lost when the grower accidently destroyed the trial as he rushed to harvest grain sorghum ahead of an expected hurricane.

TABLE B.1.1. Study Use Pattern.							
Location (City, State; Year) Trial ID	End-Use Product	Application Information					Tank Mix/ Adjuvants
		Method; Timing	Volume (gal/A)	Rate (lb ai/A) [g ai/ha]	RTI [1] (days)	Total Rate (lb ai/A) [g ai/ha]	
Hudson, KS; 2003 (NA-HR-003-03)	7.64 lb/gal EC	Broadcast foliar spray at V4 stage (four visible collars)	10.9	1.67 [1872]	--	1.67 [1872]	None

[1] RTI = Retreatment Interval.

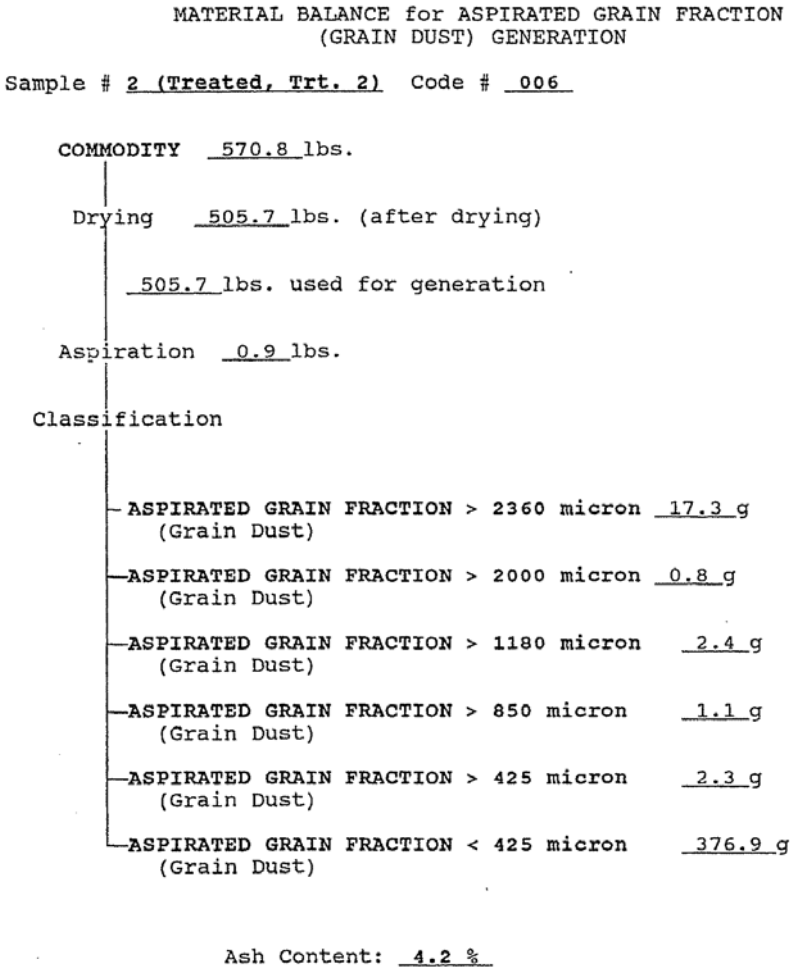
B.2. Sample Handling and Processing Procedures

Duplicate control and treated RAC samples of mature grain were collected at maturity, 100 DAT, frozen, and shipped within 13 days to Syngenta Crop Protection, Inc. (Greensboro, NC) for sample preparation. In addition, composite replicate samples of sorghum grain were shipped fresh within 1 day of collection to the processing facility, Texas A&M University, Food Protein

Research and Development Center (Bryan, TX), where they were stored frozen (≤-23 ºC) until processing. Samples were processed into aspirated grain fractions (AGF) within 77-138 days using simulated commercial procedures via drying, aspiration, and classification of aspirated material (Figure B.1).

After generation of AGF, whole grain and AGF samples were shipped frozen to Syngenta Crop Protection, Inc. (Greensboro, NC) for sample preparation. Samples were prepared by grinding with dry ice using a table top mill, and the prepared samples were shipped frozen to ADPEN Laboratories (Jacksonville, FL) for analysis.

FIGURE B.1. Processing Flowchart for Sorghum Aspirated Grain Fractions.



B.3. Analytical Methodology

Samples of sorghum grain and AGF were analyzed for residues of S-metolachlor using an LC/MS/MS method (Syngenta Method No. 1848-01). This method is an updated version of the current tolerance enforcement method (AG-338) that utilizes LC/MS/MS detection rather than

GC/NPD and uses a chiral HPLC column to separate out the S-enantiomers (SYN506357 and SYN508500) of the hydrolysis products CGA-37913 and CGA 49751. This method has been previously reviewed by HED (DP# 296904, R. Loranger, 4/17/2006).

Briefly, samples are initially refluxed in 6 N HCl for 16 hours. An aqueous aliquot is cooled, filtered, and made basic. Residues are then partitioned into dichloromethane (DCM) and cleaned up using an alumina column. The column is initially eluted with DCM followed by acetone/water. Residues of SYN506357 in the initial DCM eluate are concentrated and redissolved in water/acetonitrile for LC/MS/MS analysis. Residues of SYN508500 in the secondary acetone/water eluate are concentrated and redissolved in water/propanol/methanol for LC/MS/MS analysis. The method uses a reverse phase chiral HPLC column to separate out the two S-enantiomers, which are then detected and quantified by MS/MS. Residues of SYN506357 and SYN508500 are converted to S-metolachlor equivalents by the respective molecular weight factors of 1.47 and 1.14. The LOQ is 0.05 ppm for SYN508500 and 0.03 ppm for SYN506357, each expressed in parent equivalents. The method limit of detection was not reported.

The above method was validated in conjunction with the analysis of field trial samples, using control samples of sorghum grain and AGF fortified with SYN508500 at 0.05 ppm and 0.5 ppm (AGF only), and SYN506357 at 0.03 ppm and 0.3 ppm (AGF only).

C. RESULTS AND DISCUSSION

The LC/MS/MS method (Method No. 1848-01) used for determining residues of S-metolachlor in/on sorghum grain and AGF was validated in conjunction with the analysis of the study samples. The validated LOQ is 0.05 ppm for SYN508500 and 0.03 ppm for SYN506357, each expressed in parent equivalents, for both sorghum grain and AGF. Concurrent method recoveries of SYN506357 were within the acceptable range of 70-120% for both commodities. For SYN508500, concurrent method recoveries were consistently lower (62-69%) than the acceptable range for both commodities (Table C.1). Apparent residues of both analytes were <LOQ in/on two samples each of untreated sorghum grain and AGF. Adequate sample calculations and example chromatograms were provided, and the fortification levels used for the concurrent recoveries adequately bracket measured residue levels.

Samples of sorghum grain were stored frozen (≤-13 °C) for up to 8.3 months prior to analysis (Table C.2), and samples of AGF were stored frozen for up to 9.6 months prior to analysis. Adequate storage stability data are available indicating that metolachlor residues (CGA-37913 and CGA-49751) are stable under frozen storage conditions for at least 2 years in corn grain and soybean meal and hulls and 37 months in cottonseed (DP# 2922881, S. Kinard, 8/15/03). These storage stability data will support the storage conditions and durations of the grain and AGF samples from the current sorghum field trial.

Residue data from the sorghum AGF study are presented in Table C.3. Residues of SYN508500 and SYN506357, reported as S-metolachlor equivalents, in sorghum grain were each below the method LOQ (<0.05 and <0.03 ppm, respectively), for total residues of <0.08 ppm. In two

samples of sorghum AGF, residues of SYN508500 were below the LOQ (<0.05 ppm) and residues of SYN506357 were 0.06 and 0.09 ppm, for total residues of <0.11 and <0.14 ppm.

The data indicate that total S-metolachlor residues concentrate slightly in sorghum AGF, with concentration factors of 2.75-3.5x (average 3.1x).

TABLE C.1. Summary of Concurrent Recoveries of S-Metolachlor Residues from Sorghum Matrices.

Analyte	Sorghum Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
SYN508500	Grain	0.05	1	69	69
	Grain (prior to processing)	0.05	1	64	64
	AGF	0.05	1	62	62
		0.50	1	63	63
SYN506357	Grain	0.03	1	88	88
	Grain (prior to processing)	0.03	1	83	83
	AGF	0.03	1	103	103
		0.30	1	91	91

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration [1]	Interval of Demonstrated Storage Stability [2]
Sorghum, grain	-13 to -21	253 days (8.3 months)	24 months in corn grain, soybean meal and hulls 37 months in cottonseed
Sorghum, AGF	-13 to -21	253-291 days (8.3-9.6 months)	

[1] Actual storage duration from harvest to analysis. All samples were analyzed within 2-6 days of extraction.
[2] D292881, S. Kinard, 8/15/03.

TABLE C.3. Residue Data from Sorghum AGF Study with S-Metolachlor.

Location (City, State; Year) Trial ID	Total Rate (lb ai/A)	PHI[1] (days)	Fraction	Residues (ppm) [1]			Processing Factor [2] (Average)
				SYN508500	SYN506357	Combined	
Hudson, KS; 2003 (NA-HR-003-03)	1.67	100	Grain (RAC)	<0.05, <0.05	<0.03, <0.03	<0.08, <0.08	--
			Grain (prior to processing)	<0.05	<0.03	<0.08	--
			AGF	<0.05, <0.05	0.06, 0.09	<0.11, <0.14	2.75x, 3.5x (average = 3.1x)

[1] Residues are expressed in parent equivalents. In each commodity, the LOQs are 0.03 ppm for SYN506357 and 0.05 ppm for SYN508500, for a combined LOQ of 0.08 ppm. For calculating combined residues, the LOQ was used for values <LOQ.
[2] Processing factors calculated by dividing the residue in the processed fraction by the ½ LOQ in the sorghum grain (RAC).

D. CONCLUSION

The submitted AGF study is adequate. An acceptable method was used for quantitation for residues of SYN508500 and SYN506357 in/on sorghum samples, and the study is supported by adequate storage stability data. The data indicate that total S-metolachlor residues may concentrate slightly in sorghum AGF, with concentration factors of 2.75-3.5x (average 3.1x).

E. REFERENCES

DP#: 292881; PP#s: 7F04897, 9E06055, 7E04916, 2E06374, 4E04420, 8E05029, and 8E05030. Revised Metolachlor and S-Metolachlor Residue Chemistry Chapter for the Tolerance Reassessment Eligibility Decision (TRED) and Registration for Use on Asparagus, Carrots, Cotton, Horseradish, Green Onions, Peppers, Rhubarb, Sugar Beet, Sunflower, and Swiss Chard; S. Kinard; 8/15/03. MRIDs: 44378401, 44908701, 45544701

DP#: 96904; PP# 3E6787. S-Metolachlor. Petition for Tolerances on Various Crops, Crop Groups, and Livestock Commodities. Summary of Analytical Chemistry and Residue Data; R. Loranger; 4/17/06. MRID(s): 45499609, 45499610, and 46046501-46046506.

F. DOCUMENT TRACKING

Petition Number: None
DP#: 332848
PC Code: 108800