

US EPA ARCHIVE DOCUMENT



Primary Evaluator

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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:

46829502 Oakes, T., Ediger, K. (2004) S-Metolachlor - Magnitude of the Residues In Soybean Aspirated Grain Fractions: Lab Project Number: T000964-03. Unpublished study prepared by Syngenta Crop Protection, Inc. 118 p.

EXECUTIVE SUMMARY:

Syngenta Crop Protection submitted data pertaining to aspirated grain fractions (AGF) from soybeans. Two field trials were conducted in the United States (IL and IA; Zone 5) during the 2003 growing season. In each test, a 7.64 lb/gal emulsifiable concentrate (EC) formulation of S-metolachlor was applied to soybeans as a combination of a preplant incorporated (PPI) soil application at planting followed by a broadcast foliar application at BBCH 61-65. The application rates for the PPI and post-emergence applications were respectively 0.792-1.16 and 1.26-1.28 lb ai/A, for a total of 2.07-2.42 lb ai/A/season. The retreatment interval (RTI) for the two applications was 56-67 days. All applications were made using ground equipment at volumes of 8-17 gal/A, and none of the applications included the use of an adjuvant.

Control and treated subsamples and bulk samples of seeds were harvested from both tests at normal crop maturity, 87-93 days after treatment (DAT). Within ~2-5 months of harvest, the frozen bulk seed samples were processed into AGF using simulated commercial procedures. Prior to analysis, samples were stored at ≤ -13 °C for up to 7.5 months for seeds (RAC) and 8.8 months for AGF. These storage conditions and durations are supported by the available storage stability data.

Residues of S-metolachlor in/on soybean seed 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 soybean seed and AGF based on acceptable concurrent method recoveries.

Residues of SYN508500 and SYN506357, reported as S-metolachlor equivalents, in soybean seed were each below the method LOQ (<0.05 and <0.03 ppm, respectively), for total residues of <0.08 ppm. In the sample of soybean AGF from the IL trial, residues of SYN508500 and SYN506357 were 0.10 and 0.11 ppm, respectively, for total residues of 0.21 ppm. In the sample of soybean AGF from the IA trial, residues of SYN508500 and SYN506357 were below the LOQ (<0.05 ppm) and 0.05 ppm, respectively, for total residues of <0.10 ppm.

The data indicate that total S-metolachlor residues may concentrate in soybean AGF, with concentration factors of 2.5 or 5.3x (average 3.9x).

STUDY/WAIVER ACCEPTABILITY/DEFICIENCIES/CLARIFICATIONS:

Under the conditions and parameters used in the study, the soybean 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 soybeans. The current use on soybeans allows for use of S-metolachlor as a preplant surface, PPI, or preemergence application at 0.95-1.90 lb ai/A or a postemergence application at 0.95-1.26 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.



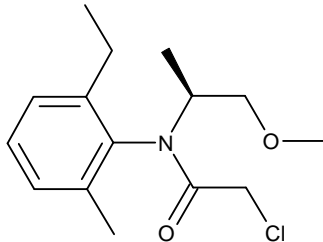
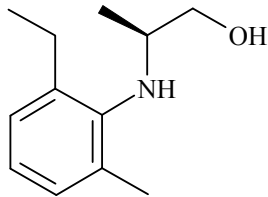
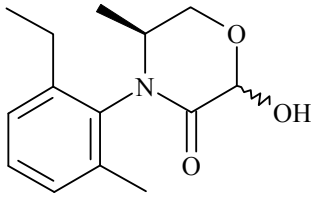
Parent compound	
Common name	S-Metolachlor
Company experimental name	CGA-77102
IUPAC name	(S)-2-chloro-N-(2-ethyl-6-methylphenyl)-N-(2-methoxy-1-methyl-ethyl)-acetamide
CAS name	2-chloro-N-(2-ethyl-6-methylphenyl)-N-[(1S)2-methoxy-1-methylethyl]-acetamide
CAS registry number	87392-12-9
End-use product (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

Two field trials were conducted in the United States (IL and IA; Zone 5) during the 2003 growing season, for the generation of AGF (Table B.1.1). In both tests, S-metolachlor (7.64 lb/gal EC) was applied to soybeans as a combination of a PPI application at planting followed by a broadcast foliar application at BBCH 61-65. The application rates for the PPI and post-emergence applications were respectively 0.792-1.16 and 1.26-1.28 lb ai/A, for a total of 2.07-2.42 lb ai/A/season. The RTI for the two applications was 56-67 days. All applications were made using ground equipment at volumes of 8-17 gal/A, and none of the applications included the use of an adjuvant.

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 ³ (days)	Total Rate (lb ai/A) [g ai/ha]	
Champaign, IL; 2003 (N4-HR-004-03)	7.64 lb/gal EC	1. Preplant incorporated soil spray at planting	8.1	1.16 [1300]	--	2.42 [2712]	None
		2. Broadcast foliar spray; BBCH 65	13.4	1.26 [1412]	67		
Richland, IA; 2003 (NE-HR-003-03)	7.64 lb/gal EC	1. Preplant incorporated soil spray at planting	9.2	0.792 [888]	--	2.07 [2320]	None
		2. Broadcast foliar spray; BBCH 61	16.9	1.28 [1435]	56		

³ RTI = Retreatment Interval.



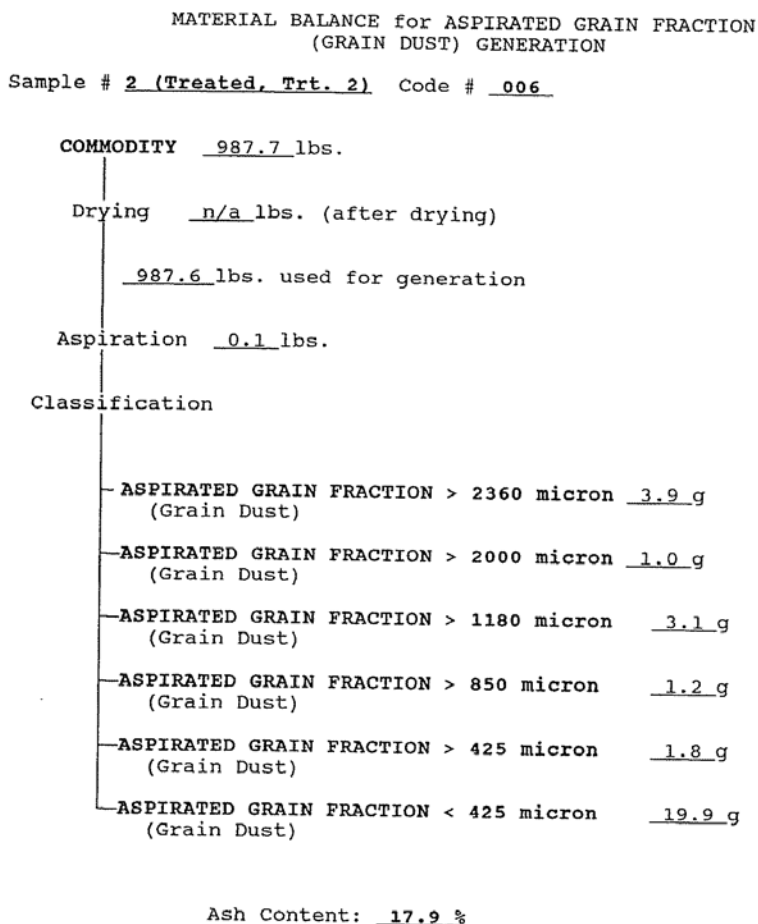
B.2. Sample Handling and Processing Procedures

Duplicate control and treated RAC samples of dried soybean seed were collected at maturity, 87-93 DAT, frozen and shipped within 0-9 days to Syngenta Crop Protection, Inc. (Greensboro, NC) for sample preparation. In addition, composite replicate samples of soybean seed were shipped fresh (from IL test site) or frozen (from IA test site) within 0-1 day of collection to the processing facility, Texas A&M University, Food Protein Research and Development Center (Bryan, TX), where they were stored frozen ($\leq -23^{\circ}\text{C}$) until processing. Samples were processed into AGF within 121-139 days (from the IL test site) and 52-55 days (from the IA test site) using simulated commercial procedures via drying, aspiration, and classification of aspirated material (Figure B.1).

After generation of AGF, whole seed 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 Soybean Aspirated Grain Fractions.



B.3. Analytical Methodology

Samples of soybean seed 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 reviewed by HED (D296904, 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 soybean seed and AGF fortified with SYN508500 at 0.05 ppm and SYN506357 at 0.03 ppm.

C. RESULTS AND DISCUSSION

The LC/MS/MS method (Method No. 1848-01) used for determining residues of S-metolachlor in/on soybean seed 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 soybean seed and AGF. Concurrent method recoveries of SYN506357 were within the acceptable range of 70-120% for both commodities. For SYN508500, concurrent method recoveries were generally within the acceptable range with the exception of two low recoveries (66 and 69%) observed in two soybean dried seed samples fortified at 0.05 ppm (Table C.1). Apparent residues of both analytes were <LOQ in/on two samples of untreated soybean seed and one sample of untreated soybean AGF from each field trial. Adequate sample calculations and example chromatograms were provided, but the fortification levels used for the concurrent recoveries did not adequately bracket measured residue levels in the AGF sample from one of the trials.

Samples of soybean seeds were stored frozen ($\leq -13^{\circ}\text{C}$) for up to 7.5 months prior to analysis (Table C.2), and samples of AGF were stored frozen for up to 8.8 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 hulls and meal and 37 months for cottonseed (D292881, S. Kinard, 8/15/03). These storage stability data will support the storage conditions and durations of seed and AGF samples from the current soybean field trials.

Residue data from the soybean AGF study are presented in Table C.3. Residues of SYN508500 and SYN506357, reported as S-metolachlor equivalents, in soybean seed were each below the method LOQ (<0.05 and <0.03 ppm, respectively), for total residues of <0.08 ppm. In the sample of soybean AGF from the IL trial, residues of SYN508500 and SYN506357 were 0.10 and 0.11 ppm, respectively, for total residues of 0.21 ppm. In the sample of soybean AGF from the IA trial, residues of SYN508500 and SYN506357 were below the LOQ (<0.05 ppm) and 0.05 ppm, respectively, for total residues of <0.10 ppm.

The data indicate that total S-metolachlor residues may concentrate in soybean AGF, with concentration factors of 2.5 or 5.3x (average 3.9x).



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

Analyte	Soybean Matrix	Spike Level (ppm)	Sample Size (n)	Recoveries (%)	Mean (%)
SYN508500	Dried seed	0.05	2	69, 78	73
	Dried seed (prior to processing)	0.05	2	66, 70	68
	AGF	0.05	2	74, 100	87
SYN506357	Dried seed	0.03	2	82, 97	90
	Dried seed (prior to processing)	0.03	2	78, 92	85
	AGF	0.03	2	80, 100	90

TABLE C.2. Summary of Storage Conditions.

Matrix	Storage Temperature (°C)	Actual Storage Duration ¹	Interval of Demonstrated Storage Stability ²
Soybean, dried seed	-13 to -21	224-228 days (7.4-7.5 months)	24 months in corn grain, soybean meal and hulls 37 months in cottonseed
Soybean, AGF	-13 to -21	224-268 days (7.4-8.8 months)	

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

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

Location (City, State; Year) Trial ID	Total Rate (lb ai/A)	PHI (days)	Fraction	Residues (ppm) ¹			Processing Factor ²
				SYN508500	SYN506357	Combined	
Champaign, IL; 2003 (N4-HR-004-03)	2.42	87	Dried Seed (RAC)	<0.05, <0.05	<0.03, <0.03	<0.08, <0.08	--
			Dried seed (prior to processing)	<0.05	<0.03	<0.08	--
			AGF	0.10	0.11	0.21	5.3x
Richland, IA; 2003 (NE-HR-003-03)	2.07	93	Dried Seed (RAC)	<0.05, <0.05	<0.03, <0.03	<0.08, <0.08	--
			Dried seed (prior to processing)	<0.05	<0.03	<0.08	--
			AGF	<0.05	0.05	<0.10	2.5x

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, ½ the LOQ was used for values <LOQ.
² Processing factors calculated by dividing the residue in the processed fraction by the average residue in the soybean seed (RAC).

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D. CONCLUSION

The soybean AGF trial is adequate. An acceptable method was used for quantitation for residues of SYN508500 and SYN506357 in/on soybean samples, and the study is supported by adequate storage stability data. The data indicate that total S-metolachlor residues may concentrate in soybean AGF, with concentration factors of 2.5 or 5.3x (average 3.9x).

E. REFERENCES

D292881; 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.

D296904; 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. MRIDs: 45499609, 45499610, and 46046501-46046506.

F. DOCUMENT TRACKING

Petition Number: None
DP#: 332847
PC Code: 108800