

US EPA ARCHIVE DOCUMENT



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

C. Failow
P/B/FOD

JUL 13 1990

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: Amended Registration for Dual® and Medal® (Metolachlor) use on Cotton; EPA Reg. Nos. 100-597, 100-673, 100-688; MRID Nos. 414255-01 through -03; DEB Nos. 6708-6710

FROM: Christine L. Olinger, Chemist
Special Registration Section I
Dietary Exposure Branch
Health Effects Division (H7509C) *Christine Olinger*

THRU: Andrew Rathman, Section Head
Special Registration Section I
Dietary Exposure Branch
Health Effects Division (H7509C) *ARR*

TO: J. Miller/R. Ikeda PM-23
Herbicide-Fungicide Branch
Registration Division (H7505C)

Ciba-Geigy Corporation requests amended registrations for products containing metolachlor for use on cotton to add post-emergence and layby applications.

Tolerances are established for residues of metolachlor in numerous commodities in 40 CFR § 180.368 ranging from 0.02 ppm for several commodities to 30 ppm for peanut hay expressed as metolachlor plus the hydrolysates 2-[(2-ethyl-6-methylphenyl) amino]-1-propanol (CGA-37913) and 4-(2-ethyl-6-methylphenyl)-2-hydroxy-5-methyl-3-morpholine (CGA-49751). A tolerance of 0.1 ppm is established for cottonseed, but none have been established for cotton forage. There are no food or feed additive tolerances.

Conclusions

1. A livestock feeding restriction is specified when metolachlor is used in combination with other chemicals, but not when used alone. Tolerances for cotton forage must be established unless the registrant lists a livestock feeding restriction.
2. For the purposes of this amended registration the nature of

the residue in plants and animals has been adequately delineated. The residue of concern is metolachlor and its hydrolysates CGA-37913 and CGA-49751.

3. The analytical methods used to collect residue data are adequate. Sufficient procedural recoveries have been conducted.
- 4a. Residues of the hydrolysates CGA-37913 and CGA-49751 are stable in corn oil for 3 months.
- 4b. Residues of the hydrolysates CGA-37913 and CGA-49751 are stable in corn forage, corn grain, peanut meats, and potato tubers for 24 months.
- 4c. Cottonseed, cottonseed oil, and cotton forage storage stability data are not available to support the magnitude of residue data.
- 5a. The residue data are adequate with regard to representation of the major growing areas for an amended registration.
- 5b. Contingent upon submission of adequate storage stability data, combined residues of metolachlor, CGA-37913, and CGA-49751 are not expected to exceed the established tolerance of 0.1 ppm in/on cottonseed.
- 5c. The limited data indicate that residues of metolachlor, CGA-37913 and CGA-49751 are not likely to exceed 5 ppm; however adequate storage stability data and addition residue data are required before a final decision can be made. A tolerance for cotton forage will have to be established before DEB can recommend for this amended registration unless a livestock feeding restriction is specified.
6. For the purposes of the proposed amended registration only, the processing data are adequate.
7. An increase of secondary residues in meat, milk, poultry, and eggs would not be expected by the amended use of metolachlor on cotton.

Recommendation

Because of the deficiencies noted in items 1, 4c, and 5c above, DEB is recommending against the amended registration of products containing metolachlor for use on cotton. Cottonseed and cotton forage storage stability data must be submitted demonstrating a storage interval of 21 months. A livestock feeding restriction must be specified whether metolachlor is used alone or in combination with other chemicals. If the registrant

does not want a feeding restriction cotton forage tolerances must be established. Additional cotton forage residue data would be required before DEB could recommend for a tolerance.

Detailed Considerations

Proposed Use

Dual® or Medal® may be applied either pre-plant incorporated, pre-emergence, or post-emergence at a rate of 1.5 lb a.i./A on sandy loams (only in NM, OK, and TX), 1.5-2 lb a.i./A on medium soils, or 2 lb a.i./A on fine soils. Layby application may be made at rates of 1.5 lb a.i./A on coarse soils, 1.5-2 lb a.i./A on medium soils, or 2 lb a.i./A on fine soils. A layby application may be made after pre-plant incorporated, pre-emergence, or post-emergence for a seasonal maximum of 3 lb a.i./A on coarse soils or 4 lb a.i./A on medium and fine soils. Pre-emergence applications may be made in AR, LA, MS, OK, TN, TX, and the bootheel of MO. Post-emergence and layby applications may be made in AR, AZ, CA, LA, MS, NM, OK, TN, TX, and the bootheel of MO.

Grazing restrictions and pre-harvest intervals have not been imposed when metolachlor is used alone. Grazing restrictions are specified when metolachlor is mixed with other chemicals prior to application. This inconsistency should be clarified. Layby and post-emergence applications will likely produce higher residues in/on forage, an animal feed item, than would be expected from the currently registered pre-plant/pre-emergence use. A tolerance on cotton forage will be required before DEB can recommend for the proposed label amendment. If a tolerance is established, a pre-harvest interval must be specified on the label. Alternatively the registrant may include a livestock feeding restriction on the label for metolachlor when used either alone or in combination with other chemicals.

Nature of the Residue

Plants

According to the FRSTR (6/13/86) the metabolism of metolachlor in corn and soybeans has been adequately described for the purposes of establishing tolerances. Very little, if any, metolachlor per se was found in the mature plant. Metabolites which upon hydrolysis produced 2-[(2-ethyl-6-methylphenyl)amino]-1-propanol (CGA-37913) and 4-(2-ethyl-6-methylphenyl)-2-hydroxy-5-methyl-3-morpholine (CGA-49751) were found to be common in plants. Data suggested that compounds present before hydrolysis are predominantly α -thioglycoside metabolites and the α -oxygen glycoside analogues. Similar metabolism has been found in soybeans as in corn. The nature of the residue in root crops has not been adequately elucidated because only 49.3% of plant radioactivity has

been characterized. For the purposes of this amended registration the nature of the residue in plants has been adequately delineated. The residue of concern is metolachlor and its hydrolysates CGA-37913 and CGA-49751.

Animals

Metolachlor is rapidly metabolized and almost totally eliminated in the urine and feces of ruminants, rats, and poultry. Metolachlor per se was not detected in any of the excreta or tissues. When ¹⁴C-labelled metabolites of metolachlor, biosynthesized in corn, was fed to goats, no parent or metabolites were found in tissue or milk. The FRSTR concluded that the metabolism is adequately delineated for the purposes of establishing tolerances. For the purposes of this amended registration the nature of the residue in animals has been adequately delineated. The residue of concern is metolachlor and its hydrolysates CGA-37913 and CGA-49751.

Analytical Method

Method AG-338 was used for collection of residue data. Although this is not the enforcement method, the FRSTR concluded that this method is adequate for developing residue data.

In the method metolachlor residues are converted to CGA-37913 and CGA-49751 by refluxing with 6N HCl overnight. For the determination of CGA-37913 an aliquot of the acidic extract is made basic with 50% NaOH and then partitioned with hexane. The hexane extract is cleaned-up on a silica gel column. The final extract is analyzed on a GC system with electrolytic conductivity detection in the nitrogen mode. For the determination of CGA-49751 an aliquot of the original extract is partitioned with dichloromethane (DCM). The DCM extract is partitioned with a 5% sodium carbonate solution and subjected to clean-up on an alumina column. CGA-49751 is converted to its chloroethanol derivative by reaction with boron trichloride and 2-chloroethanol. The derivative is partitioned into hexane and the extract is then applied to a silica gel column followed by an alumina column. The eluate is analyzed on a GC with nitrogen/phosphorus detection. The limit of detection for CGA-37913 is 0.03 ppm and for CGA-49751 is 0.05 ppm.

A modification of method AG-303, a soil method, was used to analyze for metolachlor per se residues in oil fractions. An aliquot of the oil is diluted with hexane and partitioned with acetonitrile. The acetonitrile phase is evaporated to dryness and applied to an alumina clean-up column. The hexane/ethyl ether eluate is evaporated to dryness and reconstituted in hexane. The final extract is analyzed on a GC system with an OV-17 column and an electrolytic conductivity detector in the halogen mode. The limit of detection of metolachlor is 0.05 ppm.

Storage Stability (MRID No. 414255-02)

The registrant has submitted residue storage stability data in response to the FRSTR. Storage stability data were required for all commodities for which tolerances have been established since only corn and bell pepper stability data are available.

In the study submitted corn forage, corn grain, corn oil, peanut meat, and potato tuber samples were fortified with CGA-37913 and CGA-49751 at a level of 0.5 ppm each and were placed into frozen storage. At 0, 3, 6, 9, 12, and 24 months duplicate samples were removed from storage and analyzed along with duplicate procedural recoveries for each substrate. The 0-12 month samples were analyzed by a contract lab, while the 24 month samples were sent to the sponsor after 1 year and analyzed by them at 24 months.

Samples were analyzed for CGA-37913 and CGA-49751 using method AG-338 as described. GC conditions were modified to use higher resolution capillary columns. A Sep-Pak silica cartridge was substituted for the silica gel clean-up column for the 24 month sample analysis. The procedural recoveries for CGA-37913 averaged 89.8 ± 16.4 (n=60) for all matrices while for CGA-49751 recoveries averaged 90.1 ± 14.7 (n=60). Samples placed into storage were corrected for residues found in the control and procedural recoveries. This is acceptable since the controls were placed into frozen storage at the same time as the fortified controls. Results of analysis of the storage stability samples are presented in the following table.

Interval	Commodity	Percent Recovery	
		CGA-37913*	CGA-49751*
0	Corn Forage	84, 106	134, 116
32	"	94, 104	106, 108
96	"	122, 122	102, 90
186	"	162, 70	60, 66
369	"	98, 122	110, 98
764	"	76, 82	114, 124
0	Corn Grain	70, 82	96, 108
31-32	"	82, 72	96, 94
96	"	74, 100	98, 100
188	"	72, 72	84, 118
371	"	104, 104	100, 98
767	"	66, 68	104, 104
0	Corn Oil	106, 94	116, 90
43	"	102, 106	78, 118
102	"	76, 102	116, 108
193	"	58, 54	144, 144
377	"	50, <10	90, 98
763	"	46, 64	102, 98
0	Peanut Meat	90, 98	98, 116
31-34	"	90, 82	100, 90
104	"	98, 102	106, 110
215	"	62, 66	106, 98
374	"	98, 70	74, 90
764	"	76, 86	126, 112
0	Potato Tubers	106, 116	94, 96
34	"	66, 70	84, 76
104	"	94, 82	130, 118
220	"	76, 62	106, 102
374	"	98, 106	76, 76
769	"	70, 72	96, 100

*Duplicate samples were analyzed at each interval.

Based on these data the registrant has concluded that the maximum storage interval for corn forage, corn grain, corn oil, peanut meats, and potato tubers is two years. DEB concurs with these intervals with the exception of corn oil. Good recoveries are obtained through 3 months, but there is a sharp decline at 6 months to less than 60% recovery at subsequent intervals, with the exception of one duplicate at 24 mos. (64%). DEB concludes the maximum storage interval for corn oil is 3 months.

Cottonseed, cotton forage, and cottonseed processed product storage stability data are not available. DEB has reservations translating peanut and corn stability data to cotton commodities since data have been presented for so few RAC's. DEB typically requires consistent stability data on many different RAC's before translating stability data. Before the residue data submitted in support of this amended registration can be deemed acceptable storage stability data for cottonseed and associated products must be presented.

Magnitude of Residue

Crop Field Trials

Residue trials were conducted in 1983 and 1985 in five states: CA, MS, SC, AZ, and TX. Dual® 8E was applied at 1X and 2X rates in two or three applications at varying intervals including pre-emergence, post-emergence, and layby. Pre-harvest intervals ranged from 53-111 days.

Samples were stored frozen and analyzed by method AG-338 for CGA-49751 and CGA-37913. Procedural recoveries averaged 88.3±14.3% (n=44) for CGA-37913 at spiking levels from 0.02-0.5 ppm for all commodities and processed products and 89.2±10.2% (n=36) for CGA-49751 at levels from 0.04 to 0.5 ppm. Results of analysis are presented below.

Site	Appl 1 ¹	Appl 2 ¹	Appl 3 ¹	PHI	Cottonseed		Cotton Forage	
					ppm Found	ppm Found	ppm Found	ppm Found
					CGA-37913	CGA-49751	CGA-37913	CGA-49751
CA	1; Post-E	1; Post-E	2; Layby	60,111 ²	<0.03	<0.05	0.08, 0.11	0.10, 0.11
CA	2; Post-E	2; Post-E	4; Layby	60,111 ²	<0.03	<0.05	1.1	0.88
MS	1; Post-E	1; Post-E	2; Layby	53, 54	<0.03	<0.05	0.28, 0.34	0.77, 0.82
MS	2; Pre-E	2; Layby	--	53, 54	<0.03	<0.05	0.35, 0.25	0.97, 0.20
MS	4; Pre-E	4; Layby	--	53, 54	<0.03	<0.05	0.81	1.4
SC	2; Pre-E	2; Layby	--	75, 76	<0.03	<0.05	0.62, 0.81	0.18, 0.23
SC	4; Pre-E	4; Layby	--	75, 76	<0.03	<0.05	0.76	0.28
AZ	2; PPI	2; Layby	--	78	<0.03	<0.05	0.04, 0.05	0.05, 0.07
AZ	1; Post-E	1; Post-E	2; Layby	78	<0.03	<0.05	0.91, 0.86	2.6, 1.2
AZ	2; Post-E	2; Post-E	4; Layby	78	<0.03	<0.05	2.3	4.7
TX	1; Post-E	1; Post-E	2; Layby	105	<0.03	<0.05	N/A	N/A
TX	1; Post-E	1; Post-E	2; Layby	100	<0.03	<0.05	<0.03, <0.03	0.10, 0.08
MS	1; Post-E	1; Post-E	2; Layby	90	<0.03	<0.05	<0.03, <0.03	<0.05, <0.05
MS	2; Post-E	2; Post-E	4; Layby	90	0.09, <0.03	<0.05	<0.03, <0.03	<0.05, <0.05

¹Application rate in lb a.i./A is listed first; application type is second.

²Forage harvested at 60 days; cottonseed at 111 days.

The states where the trials were conducted represent the approximately 77% of the total growing areas (Agricultural Statistics 1986). The residue data are adequate. Combined residues of CGA-37913 and CGA-49751 are not expected to exceed the established tolerance of 0.1 ppm for cottonseed. At the 1X application rate the combined residues of CGA-37913 and CGA-49751 are not expected to exceed 5.0 ppm.

Cotton forage tolerances have not been established, and most likely minimal residues were expected from the currently registered pre-plant and pre-emergence use. However greater residues are expected with the proposed post-emergence and layby applications. Therefore DEB cannot recommend for this amended registration until cotton forage tolerances have been established. Cotton forage data from additional sites will be required before DEB can recommend for a tolerance. DEB could recommend for the proposed amended registration if a livestock feeding restriction is added to the label. Cottonseed and forage storage stability data demonstrating

stability for an interval of 21 months will be required to support these residue studies.

Processing Studies

Processing studies were conducted on cottonseed from the CA and MS trials conducted at the 1X and 2X rates. Cottonseed was processed into crude oil, refined oil, refined bleached oil, refined bleached hydrogenated oil, and refined bleached hydrogenated deodorized oil. The procedure used for processing and storage condition of the processed products prior to analysis were not described. The cottonseed and processed products were analyzed for CGA-37913 and CGA-49751 by method AG-338. Procedural recoveries were described in the previous section. Results are presented in the following table.

Commodity	Rate	CA Trial		MS Trial	
		ppm Found CGA-37913*	ppm Found CGA-49751	ppm Found CGA-37913	ppm Found CGA-49751
Cottonseed	Control	<0.03	<0.05	<0.03	<0.05
"	1X	<0.03	<0.05	<0.03	<0.05
"	2X	<0.03	<0.05	<0.03	<0.05
Kernels	Control	<0.03	<0.05	<0.03	<0.05
"	1X	<0.03	<0.05	<0.03	<0.05
"	2X	<0.03	<0.05	<0.03	<0.05
Meal	Control	<0.03	<0.05	<0.03	<0.05
"	1X	<0.03	<0.05	<0.03	<0.05
"	2X	<0.03	<0.05	<0.03	<0.05
Hulls	Control	<0.03	<0.05	<0.03	<0.05
"	1X	<0.03	<0.05	<0.03	<0.05
"	2X	<0.03	<0.05	<0.03	<0.05
Soapstock	Control	0.17, 0.16, 0.17	.06	0.07, 0.06	<0.05
"	1X	0.08, 0.07, 0.08	<0.05	<0.03, 0.04	<0.05
"	2X	0.10, 0.09, 0.10	<0.05	<0.03, 0.03	<0.05
Crude Oil	Control	0.14, 0.14, 0.14	<0.05	0.16, 0.07, 0.16	<0.05
"	1X	0.11, 0.10, 0.11	<0.05	0.17, 0.05, 0.15	<0.05
"	2X	0.10, 0.12, 0.11	<0.05	0.12, 0.03, 0.08	<0.05
Refined Oil	Control	0.12, 0.14, 0.12	<0.05	0.07, <0.03, 0.04	<0.05
"	1X	0.12, 0.13, 0.13	<0.05	0.08, 0.04, 0.04	<0.05
"	2X	0.10, 0.10, 0.11	<0.05	0.09, 0.04, 0.04	<0.05
R.B. Oil	Control	<0.03	<0.05	<0.03	<0.05
"	1X	<0.03	<0.05	<0.03	<0.05
"	2X	<0.03	<0.05	<0.03	<0.05
R.B.H. Oil	Control	<0.03	<0.05	<0.03	<0.05
"	1X	<0.03	<0.05	<0.03	<0.05
"	2X	<0.03	<0.05	<0.03	<0.05
R.B.H.D. Oil	Control	<0.03	<0.05	<0.03	<0.05
"	1X	<0.03	<0.05	<0.03	<0.05
"	2X	<0.03	<0.05	<0.03	<0.05

Some of replicate CGA-37913 analyses were done on a second GC column.

CGA-37913 and CGA-49751 results reported as metolachlor equivalents.

R.B. = Refined, bleached; R.B.H = Refined, bleached, hydrogenated;

R.B.H.D. = Refined, bleached, hydrogenated, deodorized.

Because of the apparent residues found in some of the oil fractions, the refined oil from the CA trial was analyzed for the parent metolachlor by a modification of method AG-303 as described in the Analytical Methods section of this review. Procedural

recoveries averaged 71.5 (n=2). At the 1X application rate 0.35-0.39 ppm metolachlor was found and at the 2X rate 0.55-0.48 ppm was found.

The registrant has proposed that the residues are either contamination or a substrate artifact. In support of their discussion they cite a processing study (MRID No. 40980707) conducted at 3X and 5X application rates where residues of metolachlor and hydrolysates were not detected in the cottonseed or any of the processed fractions. Higher resolution capillary columns were used and no matrix interference was detected. Although the registrant's explanation for the apparent residues is plausible, DEB cannot conclude that it is due to contamination or matrix interference in the absence of confirming chromatographic or GC/MS data.

This deficiency alone will not impede DEB from recommending against the proposed label amendment since residues were not detected in the cotton seed and refined oils. Processing data deficiencies remain a FRSTR issue and the cottonseed processing studies will be addressed in the reregistration process. The registrant is advised that the processing procedures, storage intervals and conditions, and cottonseed processed product storage stability data will be required for these studies to be considered acceptable.

Meat, Milk, Poultry, and Eggs

Cotton forage is a livestock feed item, but tolerances have not been established. Based on the residue data submitted, a tolerance of 5.0 ppm should be proposed by the registrant. The maximum metolachlor and hydrolysate residues expected for livestock is for dairy cattle fed 60% peanut hay (at a tolerance of 30 ppm) and 40% soybean forage (at a tolerance of 8.0 ppm) for a dietary burden of 22.8 ppm. If cotton forage were substituted for the soybean forage, the dietary burden would be 21.6 ppm. Therefore an increase of secondary residues would not be expected by the amended use of metolachlor on cotton.

cc: CLOlinger (DEB), Circulate (7), RF, SF, Reg. Std. File,
RDSchmitt, C. Furlow (PIB/FOD)
H7509C:DEB:CLOlinger:clo:CM#2:Rm 803C:557-1406: 7/11/90
RDI: ARRathman: 7/09/90 RALoranger: 7/11/90