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Metolachlor Reg. Stu
File



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

AUG 6 1992
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MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

SUBJECT: Reregistration of Metolachlor. Storage Stability of
Metolachlor Metabolites in Animal Commodities. DP
Barcode D173437. MRID No. 41506401 CBRS No. 9261.

FROM: Stephen Funk, Ph. D., Chemist *S. Funk*
Special Review Section I
Chemistry Branch II - Reregistration Support
Health Effects Division (H7509C)

THRU: Edward Zager, Chief *Edward Zager*
Chemistry Branch II - Reregistration Support
Health Effects Division (H7509C)

TO: Connie Childress
Reregistration Section I
Reregistration Branch
Special Review and Reregistration Division (H7508C)

Attached is a review of residue chemistry data for storage stability of metolachlor metabolites in animal products (tissues, milk, eggs). This information was submitted in response to requirements of the Metolachlor Registration Standard Update (06/14/89) and was reviewed by Acurex Environmental Corporation under supervision of CBRS, HED. The data assessment has undergone secondary review in the Branch and has been revised to reflect Branch policies.

The due date for this review was 06/10/92.

The storage conditions and time intervals for animal commodity samples used in support of tolerances must be fully described and correlated with the storage stability data presented. The storage stability study will be acceptable if the conditions and intervals of storage are comparable to those of samples used in support of tolerances.

If you need additional information, please advise.

Attachment: Metolachlor: Registrant's Response to Residue Chemistry Data Requirements.

cc: Circ., Metolachlor Registration Standard File, S. Funk, Acurex Environmental Corp. (0692.9b)



METOLACHLOR
(Chemical Code 108801)
(CBRS No. 9261; DP Barcode D173437)

TASK 3

**Registrant's Response
to Residue Chemistry Data
Requirements**

June 3, 1992

Contract No. 68-DO-0142

Submitted to:

U.S. Environmental Protection Agency
Arlington, VA 22202

Submitted by:

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METOLACHLOR

(Chemical Code 108801)

(CBRS No. 9261; DP Barcode D173437)

REGISTRANT'S RESPONSE TO RESIDUE CHEMISTRY REQUIREMENTS

Task 3

BACKGROUND

The Metolachlor Guidance Document dated 1/87 required data on the storage stability of metolachlor residues in animal products (tissues, milk, and eggs). In response to the Guidance Document, CIBA-GEIGY Corporation submitted interim data (1989; MRID 40980703) pertaining to the frozen storage stability of two metolachlor metabolites, 2-[(2-ethyl-6-methylphenyl)amino]-1-propanol (CGA-37913) and 4-(2-ethyl-6-methylphenyl)-2-hydroxy-5-methyl-3-morpholinane (CGA-49751), in fortified animal tissues, milk, and eggs. These data were reviewed in the Metolachlor Registration Standard Follow-Up (R. Quick; CBRS No. 4931; 6/14/89). The review concluded that CGA-37913 is stable in storage at -15 °C for up to 1 year in beef liver, milk and eggs, but declined to < 10-36% of fortification levels in beef muscle after 109 days. The review also concluded that CGA-49751 is stable at -15 °C for up to 1 year in beef muscle, liver, milk, and eggs.

CIBA-GEIGY Corp. submitted the final 2-year data (1990; MRID 41506401) pertaining to the frozen storage stability of CGA-37913 and CGA-49751 in animal tissues, milk, and eggs. This submission is reviewed here to determine its adequacy in fulfilling outstanding storage stability data requirements. The Conclusions and Recommendations stated in this review pertain only to storage stability requirements.

The nature of the residue in plants is not adequately understood. Data on the metabolism of metolachlor in potatoes is required. The nature of the residue in animals is adequately understood. Tolerances for residues of metolachlor in or on feed or food commodities are currently expressed in terms of the combined residues (free and bound) of metolachlor and its metabolites, determined as the derivatives, CGA-37913 and CGA-49751, each expressed as metolachlor [40 CFR §180.368(a), (b), and (c)].

Adequate analytical methods are available for enforcing tolerances of metolachlor and its free and bound metabolites in or on plant and animal commodities. The currently preferred method for plant matrices is listed as Method I in PAM, Vol. II and the preferred method for animal matrices is listed as Method II in PAM, Vol. II.

CONCLUSIONS/RECOMMENDATIONS

1. The data adequately depict the storage stability of metolachlor residue hydrolysates, CGA-37913 and CGA-49751, in animal tissues, milk, and eggs. The metabolite CGA-37913 is stable in frozen storage at -15 °C in milk and eggs for up to 25 months, in beef muscle for up to 2 months, and in beef liver for up to 12 months. The metabolite CGA-49751 is stable in beef muscle, beef liver, milk, and eggs stored at -15 °C for up to 25 months.
2. The registrant must submit information concerning the storage intervals and storage conditions of samples used in support of all established tolerances for residues of metolachlor.

DETAILED CONSIDERATIONS

Storage Stability Data

CIBA-GEIGY Corp. submitted the final 2-year data (1990; MRID 41506401) pertaining to the frozen storage stability of CGA-37913 and CGA-49751, metolachlor residue hydrolysates, in beef muscle, liver, milk, and eggs. Data from the 1-year interim report (1989; MRID 40980703), which has been previously reviewed (R. Quick, CB No. 4931; 6/14/89), are also presented here for completeness.

Samples of beef muscle, beef liver, milk, and eggs were each homogenized and separated into 10-gram subsamples. Each time-interval sample set consisted of five subsamples of each animal matrix. Two subsamples of each matrix were fortified with CGA-37913 and CGA-49751, each at 0.5 ppm, while the three remaining subsamples served as controls. Samples were analyzed on day 0 prior to storage, and after approximately 2, 3, 7, 12 and 25 months of frozen storage at -15 °C. At each sampling interval, a frozen control sample, two frozen control samples freshly fortified with CGA-37913 and CGA-49751 at 0.5 ppm each, and two aged fortified samples were analyzed. Data were collected using CIBA-GEIGY Method AG-388 (1979; MRID 00015543), which was previously described in the Metolachlor FRSTR (6/86) and is a modification of Method I in PAM, Vol. II. For the current study, the method was modified by replacing the silica column clean-up with a silica Sep-Pak clean-up. Residues of CGA-37913 and CGA-49751 for the current study were analyzed by a GC equipped with a capillary column and a nitrogen-phosphorous detector. The limits of detection for CGA-37913 and CGA-49751 were 0.03 and 0.05 ppm, respectively.

None of the control samples (n=24) contained detectable levels of CGA-37913 (<0.03 ppm). Apparent residues of CGA-49751 were detected in control samples of muscle (n=2; 0.11 and 0.08 ppm), liver (n=3; 0.07, 0.09, and 0.07 ppm), milk (n=1; 0.08 ppm), and eggs (n=3; 0.1, 0.05, 0.08 ppm), but were not detected in the remaining control samples (n=15). Method recoveries for CGA-37913 and CGA-49751 from the freshly

fortified samples are presented in Table 1. Recovery data for the aged fortified samples were corrected for residues detected in control samples and for method recoveries. Recoveries of CGA-37913 and CGA-49751 from fortified samples following frozen storage at -15 °C are presented in Table 2. The data indicate that CGA-37913 was stable at -15 °C in milk and eggs for up to 25 months, in beef muscle for up to 2 months, and in beef liver for up to 12 months. After 3 months of storage, residues of CGA-37913 had declined to <10-36% in beef muscle; however, subsequent analyses of beef muscle showed no further decline in levels of CGA-37913. In beef liver, residues of CGA-37913 declined to 28-34% after 25 months of storage. The metabolite CGA-49751 was stable in beef muscle, beef liver, milk, and eggs stored at -15 °C for up to 25 months.

Table 1. Method recoveries of CGA-37913 and CGA-49751 from freshly fortified^a control samples of animal tissues, milk, and eggs.

Matrix	CGA-37913		CGA-49751	
	# of Samples	Percent Recovery	# of Samples	Percent Recovery
Beef muscle	14	51-118	12	68-109
Beef liver	12	59-115	12	65-142
Milk	12	62-107	12	68-111
Eggs	12	68-146	12	62-122

^aCGA-37913 and CGA-49751 were each fortified at 0.5 ppm.

Table 2. Percent recovery of CGA-37913 and CGA-49751 from fortified^a samples of animal tissues, milk, and eggs following frozen storage at -15 °C.

Matrix	Storage Interval (months)	Percent Recovery ^b	
		CGA-37913	CGA-49751
Beef muscle	0	114, 106	94, 94
	2	114, 122	90, 96
	3	18, 16, <10, 36	96, 82
	7	16, 32, 18, 18	96, 68
	12	16, 32	112, 90
	25	26, 18	138, 126
	Beef liver	0	96, 78
2		108, 92	102, 102
3		120, 112	80, 84
7		88, 72	102, 110
12		90, 54	110, 66
25		34, 28	88, 88
Dairy milk		0	96, 88
	2	92, 68 ^c	82, 90
	3	104, 102	120, 92
	7	84, 58	90, 94
	12	110, 100	120, 104
	25	102, 90	106, 118
	Poultry eggs	0	112, 122
2		104, 84	92, 98
4		122, 112	116, 88
7		96, 92	74, 78
12		102, 172	72, 98
25		92, 66	102, 110

^aSamples were fortified with CGA-37913 and CGA-49751 at 0.5 ppm each.

^bCorrected for residues in control samples and method recoveries.

^cSamples analyzed after one month of storage.

The FRSTR (06/13/86) requested that data be supplied on the storage length and conditions of storage for samples used in support of tolerances. These data should be correlated with the storage stability study conditions for each crop and animal commodity. The requirement was reiterated in a 04/16/92 Memorandum (B. Cropp-Kolligian, CBRS No. 8317) on storage stability data for several crops.

References

Citations for the MRID documents referenced in this review are presented below. Submissions reviewed in this document are indicated by shaded type.

- 00015543 Cargile, N.L.; Ross, J.A. (1979) Analytical Method for Residues of Metolachlor Plant Metabolites Determined as CGA-37913 and CGA-49751 after Acid Hydrolysis: Method No. AG-388. Unpublished study prepared by CIBA-GEIGY Corp.
- 40980703 Cheung, M.W. (1989) Residue Stability Study of CGA-37913 and CGA-49751 (Metolachlor Residues Hydrolysates) in Beef Muscle, Beef Liver, Dairy Milk, and Poultry Eggs under Freezer Storage Conditions (One-year Interim Report): Laboratory Project ID. ABR-88165. Unpublished study prepared by CIBA-GEIGY Corp. 35 p.
- 41506401 Cheung, M.W. (1990) Residue Stability Study of CGA-37913 and CGA-49751 (Metolachlor Residues Hydrolysates) in Beef Muscle, Beef Liver, Dairy Milk, and Poultry Eggs under Freezer Storage Conditions (Final Report): Laboratory Project ID. ABR-89089. Unpublished study prepared by CIBA-GEIGY Corp. 86 p.

Agency Memoranda

CB No.: 4931
Subject: Metolachlor Registration Standard Follow-up.
From: R. Quick
To: L. Schnaubelt
Date 6/14/89
MRID(s): 40980702 to 40980708 and 40766601 and 40766602