



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

MAY 19 1988

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#8E3616 (RCB No. 3588) - Metolachlor on Bell
Peppers - Evaluation of Analytical Method and
Residue Data (MRID Nos. 405573-00 and 405573-01)

FROM: Martin F. Kovacs, Jr., Ph.D., Chemist *Martin F. Kovacs Jr.*
Tolerance Petition Section II
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

TO: Hoyt L. Jamerson, Minor Uses Officer, PM 43
Registration Support and
Emergency Response Branch
Registration Division (TS-767C)

and

Toxicology Branch
Hazard Evaluation Division (TS-769C)

THRU: John H. Onley, Ph.D., Section Head *John H. Onley*
Tolerance Petition Section II
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

The petitioner, IR-4, on behalf of the IR-4 National Director, Dr. R.H. Kupelian, and the Agricultural Experiment Stations of Arkansas, Oklahoma, Florida (FL), Texas (TX), and the U.S. Department of Agriculture request the establishment of a tolerance for the combined residues of the herbicide metolachlor (2-chloro-N-(2-ethyl-6-methyl phenyl)-N-(2-methoxy-1-methylethyl)acetamide) and its metabolites, determined as the derivatives, 2-[(2-ethyl-6-methyl phenyl)amino]-1-propanol and 4-(2-ethyl-6-methylphenyl)-2-hydroxy-5-methyl-3-morpholinone in or on the raw agricultural commodity (RAC) bell peppers at 0.1 ppm.

Metolachlor tolerances are established for several RACs under 40 CFR 180.368(a) at levels ranging from 0.02 to 30 ppm. Tolerances for the related RACs chili peppers (0.5 ppm) and tobasco peppers (0.5 ppm) with regional registration are established under 40 CFR 180.368(c). Tolerances are pending on the following commodities: apples (0.1), flaxseed (0.2), flax hulls (0.4), flax meal (0.2 FA), sorghum fodder (10), sorghum forage (10), sunflower hulls (0.6 FA), sunflower meal (0.6 FA), sunflower seed (0.3) and nongrass animal feeds group (3.0 ppm).

The Residue and Product Chemistry Chapters of the Metolachlor Final Registration Standard and Tolerance Reassessment (FRSTR) were completed on June 13, 1986.

Ciba-Geigy Corporation has submitted a letter dated January 16, 1986 from C.F. Brinkley to H.L. Jamerson of EPA, authorizing the use of previously submitted metolachlor data available in the Agency files in support of the proposed tolerance on bell peppers.

Conclusions

1. The petitioner will need to submit a revised Section B/label to include the following statement "Do not harvest bell peppers within 60 days of DUAL application to transplanted peppers or within 90 days following application to direct seeded peppers." The revised Section B/label should also include the following restriction "Do not apply more than once per growing season."
2. RCB considers the nature of the residue in bell peppers to be adequately understood for the purposes of supporting the proposed use on bell peppers. The residues of concern in both plants and animals consist of the parent compound, metolachlor, and its metabolites, determined as the derivatives, 2-[(2-ethyl-6-methylphenyl)amino]-1-propanol (CGA-37913) and 4-(2-ethyl-6-methylphenyl)-2-hydroxy-5-methyl-3-morpholinone (CGA-49751).
- 3a. RCB concludes that adequate analytical methods are available to enforce the proposed 0.1 ppm metolachlor tolerance for bell peppers.
- 3b. RCB recommends that all of the additional bell pepper residue studies requested by RCB (see Conclusion 4c below) must be accompanied by raw analytical data to include recovery data, sample calculations, and all sample chromatograms.

- 4a. No information is currently available to RCB concerning the storage stability (i.e., sample integrity) of either CGA-49751 or CGA-37913 residues in sample extracts which were stored up to 3 months at -4 to +4 °C prior to analysis. If the petitioner has residue data to support no loss of residues after storage for up to 3 months in sample extracts, then he should provide such data. RCB recommends that sample extracts prepared in the additionally requested bell pepper residue studies be analyzed as soon as possible, i.e., within that time where there is proof of no residue degradation.
- 4b. RCB concludes that insufficient residue data are available in this petition which reflect the proposed use and consequently support the proposed tolerance.
- 4c. Residue data reflecting both preplant soil incorporated and preemergence broadcast applications to direct seeded bell peppers are needed from California (CA) and FL. Additional residue data from TX reflecting these same use patterns are also needed. Residue data reflecting both preplant soil incorporated and posttransplant broadcast applications to CA and TX transplanted bell peppers and preplant soil incorporated application to FL bell peppers are needed. Additional residue data reflecting both preplant soil incorporated and posttransplant broadcast applications to Maryland (MD) transplanted bell peppers and posttransplant broadcast applications to FL bell peppers are also needed.
- 4d. Submitted residue data must reflect the revised Section B/label recommended by RCB above under Conclusion 1.
- 4e. Submitted residue data must also be accompanied by recovery data, sample calculations and all sample chromatograms (see Conclusion 3b above) and prepared sample extracts must be analyzed as soon as possible following preparation (see Conclusion 4a above).
5. Since bell peppers are not an animal feed item, RCB considers the likelihood of secondary residues resulting in meat, milk, poultry, and eggs to fall under Category 3 of 40 CFR 180.6(a), i.e., there is no reasonable expectation of finite residues from the proposed use.

6. An International Residue Limit Status sheet is attached to this review. There are no Codex, Canadian, and Mexican tolerances for metolachlor on bell peppers. Therefore, no compatibility questions exist with respect to Codex.

Detailed Considerations

Manufacture and Formulation

The manufacturing process for metolachlor and the composition of the technical material are discussed in RCB's review of PP#8F2081 (see A. Smith memorandum of April 2, 1979). Technical metolachlor is approximately 95 percent pure. RCB does not expect the impurities to present a residue problem.

The metolachlor formulation proposed for use on bell peppers is Dual® 8E, an emulsifiable concentrate containing 8 lb ai per gallon. The inerts in this formulation are all cleared under 40 CFR 180.1001(c) or (d).

Proposed Use on Bell Peppers

Metolachlor is to be used to control yellow nutsedge and other problem annual weeds in the production of bell peppers.

DUAL 8E herbicide may be applied preplant incorporated or preemergence broadcast for direct seeded bell peppers, preplant incorporated or posttransplant broadcast for transplanted bell peppers. Apply DUAL 8E with ground application equipment at the maximum rate of 1.5 pints (1.5 lb ai) per acre in a minimum of 10 gallons. Do not harvest bell peppers within 60 days of DUAL application.

RCB's Comments/Conclusions re: Proposed Use

The proposed PHI of 60 days is inconsistent with and does not reflect cultural practices related to the proposed application to direct seeded bell peppers. This is evidenced by the submitted TX residue trial reflecting a 90-day PHI following application to a direct seeded early maturing bell pepper variety. Therefore, to reflect the latter use pattern, RCB recommends that the petitioner submit a revised Section B/label to include the following statement "Do not harvest bell peppers within 60 days of DUAL application to transplanted peppers or within 90 days following application to direct seeded peppers." The revised Section B/label should also include the following restriction "Do not apply more than once per growing season."

Nature of the Residue

No new metabolism studies were included in the subject petition; however, the nature of the residue has been discussed in RCB's previous reviews of metolachlor as well as in the Metolachlor FRSTR dated June 13, 1986.

In plants (corn, soybeans), the major metabolic pathway involves conjugation with glutathione, formation of the mercaptan, conjugation of the mercaptan with glucuronic acid, hydrolysis of the methyl ester, and conjugation of the alcohol with a neutral sugar (see K. Arne memorandum of December 15, 1983 re: PP#3F2957).

In animals (goats, rats), metolachlor is rapidly eliminated with only trace residues remaining in tissues (primarily liver). Conjugated residues in urine consist of the same bound metolachlor metabolites as those found in plants (although the natural compounds to which these metabolites are bound are different for plants and animals).

The nature of the residue is considered adequately understood for the purposes of supporting the proposed use on bell peppers. The residues of concern in both plants and animals consist of the parent compound metolachlor (free plus bound) and its metabolites (free plus bound) 2-[(2-ethyl-6-methylphenyl)amino]-1-propanol (CGA-37913) and 4-(2-ethyl-6-methylphenyl)-2-hydroxy-5-methyl-3-morpholinone (CGA-49751).

Analytical Methodology

The method used to generate the residue data submitted in this petition is Ciba-Geigy method AG-338 dated April 23, 1979 and entitled "Analytical Method for Residues of Metolachlor Plant Metabolites Determined as CGA-37913 and CGA-49751 After Acid Hydrolysis." This method is a variation of method AG-286, which has successfully undergone a method trial (see R. Watts memorandums of July 28 and 29, 1976).

In brief, metolachlor and its metabolites (free plus bound) are hydrolyzed by acid (6N HCl) refluxed to CGA-37913 and CGA-49751, which are then determined separately by gas liquid chromatography (GLC) under different column conditions.

CGA-49751 residues are partitioned into dichloromethane, washed with 5 percent sodium carbonate, then chromatographed on 16 percent moisture silica gel column. Residues of CGA-49751 are then converted to the chloroethanol derivative which is partitioned into hexane and cleaned up on a 16 percent moisture silica gel column. Quantitation is by GLC using a nitrogen-phosphorous ionization detector in the nitrogen mode.

Residues of CGA-37913 are partitioned into hexane following the addition of a sodium hydroxide solution. The residues are then cleaned up by the use of successive chromatographic columns - first on alumina (18% moisture) and then on silica gel. Quantitation is by GLC using a nitrogen-phosphorous ionization detector in the nitrogen mode.

Recoveries of CGA-49751 fortified at 0.02 to 0.08 ppm ranged from 62.7 to 110.0 percent and averaged 85.5 percent, while recoveries of CGA-37913 fortified at 0.02 to 0.04 ppm ranged from 87.2 to 100.0 percent and averaged 95.5 percent.

All control values for both CGA-49751 and CGA-37913 were reported at < 0.01 ppm. The claimed sensitivity of the method for both CGA-49751 and CGA-37913 was 0.01 ppm; submitted chromatograms from the residue trials supported these claimed sensitivity levels.

The petitioner reports that selected samples in the TX residue trial at the 2X treatment rate were checked for residues of CGA-37913, and since none was found, a report of the results was not prepared by the laboratory chemist.

In RCB's opinion, although selected samples reflecting a 2X application rate indicated no detectable residues of CGA-37913, other samples possibly at a lower 1X application rate may have resulted in detectable residues if they had been looked for and reported by the residue analyst.

RCB recommends that all of the additional bell pepper residue studies requested by RCB (see Residue Data section below) must be accompanied by raw analytical data to include recovery data, sample calculations, and all sample chromatograms.

RCB concludes that adequate analytical methodology is available for enforcement purposes.

Residue Data

Storage Stability

In conjunction with the MD residue trial, a storage fortification (stability) study was conducted using bell peppers stored frozen for 5 to 5 1/2 months. Following fortification with metolachlor at 0.04 ppm, method recoveries of CGA-49751 and CGA-37913 were 81.0 and 93.5 percent, respectively, and comparable storage stability recoveries were 72.0 and 82.0 percent, respectively. RCB notes that in this recovery study sample extracts containing CGA-49751 and CGA-37913 residues were stored at -4 °C for 24 and 9 days,

respectively, prior to analysis. Previously submitted storage stability data for metolachlor in corn fodder and grain demonstrated no appreciable loss of CGA-37913 residues for up to 13 months when stored at -15 °C [see Residue Chemistry Chapter (Storage Stability Data) Metolachlor FRSTR dated June 13, 1986].

In the current petition, treated bell pepper samples were stored frozen from 2 to 10 months at -13 to -20 °C prior to sample extraction. Sample extracts were then stored at -4 to +4 °C for 1 week to 3 months prior to sample analyses. No information is currently available to RCB concerning the storage stability of either CGA-49751 or CGA-37913 residues in sample extracts. Therefore, to alleviate any future RCB concerns regarding the stability of these residues in prepared sample extracts, RCB recommends that the sample extracts prepared in the additionally requested bell pepper residue studies be analyzed within that time where there is proof of no residue degradation.

RCB concludes that the available sample storage stability data do not support the residue data submitted due to a lack of information regarding the stability of CGA-49751 and CGA-37913 residues in sample extracts stored up to 3 months. The petitioner should submit such data.

Field Trials

Field trials were conducted in CA (1982), TX (1981), MD (1984), and FL (1986). These States are representative of the major bell pepper production areas of the United States. All trials reflected a single application of DUAL 8E at rates approximating either 1.5 (1X) or 3.0 (2X) lbs ai/A to transplanted bell peppers in the CA, MD, and FL trials and to direct seeded bell peppers in the TX trial. The reported PHIs for the (transplanted pepper) CA, MD, and FL trials of 62 to 64 days and for the (direct seeded) TX trial of 90 days are consistent with and reflect cultural practices related to bell pepper production.

The CA trial reflected a preplant broadcast treatment only, the FL trial a posttransplant broadcast treatment only and the MD trial both a preplant soil incorporated and post-transplant treatment for transplanted bell peppers. The TX trial reflected both a preplant soil incorporated and pre-emergence broadcast treatment to direct seeded bell peppers.

The residue data are presented below.

State	Application Rate (lb ai/A)	PHI (Days)	Residue Level (ppm) ^a		Total
			CGA-37913	CGA-49751	
CA	1.75	62	<0.01	<0.01	<0.02
	3.5	62	<0.01	<0.01	<0.02
TX	1.5	90	<0.01	<0.01-0.045	<0.02-0.045
	3.0	90	<0.01	<0.01	<0.02
MD	Preplant				
	1.5	64	<0.01	<0.01	<0.02
	Preplant				
	3.0	64	<0.01-0.01	<0.01-0.03	<0.02-0.041
	Posttransplant				
	1.5	62	<0.01	<0.01	<0.02
	Posttransplant				
	3.0	62	<0.01	<0.01-0.032	<0.02-0.032
FL	1.5	63	<0.01-0.013	<0.01-0.015	<0.02-0.015
	3.0	63	<0.01-0.098	<0.01-0.025	<0.014-0.108

^a Residue levels not corrected for method recovery.

RCB concludes that insufficient residue data are available in this petition which reflect the proposed use (i.e., preplant soil incorporated and preemergence broadcast application to direct seeded bell peppers and preplant soil incorporated and posttransplant broadcast application to transplanted peppers) and consequently support the proposed tolerance.

Residue data reflecting both preplant soil incorporated and preemergence broadcast applications to direct seeded bell peppers are needed from CA and FL. Additional residue data from TX reflecting these same use patterns are also needed. Residue data reflecting both preplant soil incorporated and posttransplant broadcast applications to CA and TX transplanted bell peppers and preplant soil incorporated application to FL bell peppers are needed. Additional residue data reflecting both preplant soil incorporated and posttransplant broadcast applications to MD transplanted bell peppers and posttransplant broadcast applications to FL bell peppers are also needed.

All submitted residue data must reflect the revised Section B/label recommended by RCB under Proposed Use on Bell Peppers cited above and be accompanied by raw analytical data to include recovery data, sample calculations, and all sample chromatograms. All prepared sample extracts must also be analyzed as soon as possible following preparation, i.e., within that time where there is proof of no residue degradation.

Residues in Meat, Milk, Poultry, and Eggs

Since bell peppers are not an animal feed item, RCB considers the likelihood of secondary residues resulting in meat, milk, poultry, and eggs to fall under Category 3 of 40 CFR 180.6(a), i.e., there is no reasonable expectation of finite residues from the proposed use.

Other Considerations

An International Residue Limit Status sheet is attached to this review. There are no Codex, Canadian, and Mexican tolerances for metolachlor on bell peppers. Therefore, no compatibility questions exist with respect to Codex.

Attachment

cc: R.F., Circu, Reviewer(M.Kovacs), PP#8E3616, Metolachlor
Registration Standard File, PMSD/ISB(Eldredge)
RDI: J.H. Onley: 5/11/88: R.D. Schmitt: 5/11/88
TS-769: RCB: M.Kovacs: CM#2: Rm810x7689: Typist Kendrick: 5/14/88
Edited by: mfk 5/18/88

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL METOLACHLOR

CODEX NO. _____

CODEX STATUS:

☒ No Codex Proposal
Step 6 or above

Residue(if Step 8): _____

<u>Crop(s)</u>	<u>Limit</u> <u>(mg/kg)</u>
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CANADIAN LIMITS:

☒ No Canadian limit (on bell peppers)

Residue: _____

<u>Crop(s)</u>	<u>Limit</u> <u>(mg/kg)</u>
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PROPOSED U.S. TOLERANCES:

Petition No. 8E 3616

RCB Reviewer MARTIN F. KOVACS JR.

Residue: METOLACHLOR AND ITS METABOLITE
DETERMINED AS 2-[(2-ETHYL-6-METHYL-PHENYL)
AMINO]-1-PROPANOL AND 4- (2-ETHYL-6-METHYL
PHENYL)-2-HYDROXY-5-METHYL-3-MORPHOLINONE

<u>Crop(s)</u>	<u>Limit</u> <u>(mg/kg)</u>
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<u>BELL PEPPERS</u>	<u>0.1</u>
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MEXICAN LIMITS:

☒ No Mexican limit

Residue: _____

<u>Crop(s)</u>	<u>Limit</u> <u>(mg/kg)</u>
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NOTES: _____