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HEALTH EFFECTS DIVISION
SCIENTIFIC DATA REVIEWS
EPA SERIES 361

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

July 27, 2001

MEMORANDUM

SUBJECT: Mepiquat Chloride (109101), Analytical Method for Residues of Mepiquat Chloride in Plant and Animal Commodities; DP Barcode D244052; (MRID Nos. 44498301 and 44498302); Case No. 2375.

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Executive Summary

BASF Corporation has submitted method validation (1998; MRID 44498301) and an Independent Method Validation (ILV) study (1997; MRID 4498302) for an ion chromatography method used to quantitate residues of mepiquat chloride *per se* in plant and animal commodities.

The submission was reviewed under contract by Dynamac Corporation. The review has undergone secondary review by HED and the following recommendations and conclusions were made:

1. The registrant has proposed an ion chromatography method (BASF Method D9610) for the determination of residues of mepiquat chloride *per se* in/on plant and animal commodities. The validated method LOQ for the method is 0.1 ppm for cotton commodities and 0.05 ppm for animal tissues, milk, and eggs.

2. Independent method validation has been submitted using cottonseed and cow liver. However, that study was not performed by an independent laboratory (both studies performed by Centre Analytical Laboratories [State College, PA]). An acceptable independent laboratory validation (ILV) of method D9610 is required using an independent laboratory. It is recommended that the ILV be performed for **mepiquat pentaborate** as the registrant has stated that mepiquat pentaborate will eventually replace mepiquat chloride use on cotton. Once an acceptable ILV is submitted, the method will be submitted to EPA's analytical laboratory for method tryout. Once acceptable Agency validation of the proposed ion chromatography enforcement method (D9610) has been conducted, the method can be forwarded to FDA for inclusion in PAM Vol. II as a numbered method for enforcement of residues of mepiquat in/on cotton and animal tissues, milk, and eggs.

cc: RF: List B File; D.Drew , CP Moran (RD); C. Giles-Parker (RD)
RDI: C. Eiden (7/27/01)
D.Drew:CM-2, rm 821E, 305-6028

**MEPIQUAT CHLORIDE
PC Code 109101; Case 2375
(DP Barcode D244052)**

Registrant's Response to Residue Chemistry Data Requirements

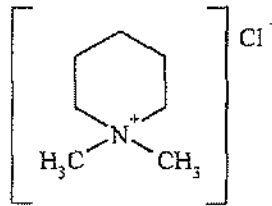
July 16, 2001

Contract No. 68-W-99-053

**Submitted to:
U.S. Environmental Protection Agency
Arlington, VA**

**Submitted by:
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MEPIQUAT CHLORIDE



REGISTRANT'S RESPONSE TO RESIDUE CHEMISTRY DATA REQUIREMENTS

PC Code 109101; Case 2375

(DP Barcode D244052)

BACKGROUND

BASF Corporation has submitted method validation (1998; MRID 44498301) and an Independent Method Validation (ILV) study (1997; MRID 4498302) for an ion chromatography method used to quantitate residues of mepiquat chloride *per se* in plant and animal commodities. The submitted method validation and ILV data for the current revision of this method (BASF Method D9106) are evaluated in this document for adequacy in fulfilling residue chemistry data requirements under OPPTS GLN 860.1340.

Mepiquat chloride is a List B chemical registered for use on cotton and grapes as a plant growth regulator. The Residue Chemistry Chapter for the Mepiquat Chloride Reregistration Eligibility Decision (RED, DP Barcode D222340) was issued 5/6/96. The qualitative nature of the residue in plants and animals is adequately understood based on acceptable metabolism studies with cotton, grapes, ruminants, and poultry. The parent, mepiquat chloride, is the residue of concern in plant and animal commodities.

Tolerances are currently established under 40 CFR §180.384 for residues of mepiquat chloride [N,N-dimethylpiperidinium chloride] in/on cottonseed (2.0 ppm), grapes (1.0 ppm), raisins (5.0 ppm), and for the fat, meat, and meat byproducts of cattle, goats, hogs, horses, and sheep (each at 0.1 ppm).

HED has recommended that the tolerance expression be modified to read "tolerances are established for the residues of the plant growth regulator mepiquat [N,N-dimethylpiperidinium]" as it has been determined that the active component is the mepiquat cation. BASF is seeking registration of mepiquat pentaborate for use on cotton and has requested for a waiver from cotton field trial requirements based on the dissociative properties of the pentaborate salt being identical to those of mepiquat chloride for which cotton field trial data are available. The HED Chemistry

Science Advisory Council (ChemSAC; minutes dated 5/16/01) has recommended for a conditional registration based on available field trial data for the chloride salt. Full registration will be contingent on submission of additional field trial data (side-by-side trials for dilute spray applications and oil-based ULV applications).

Adequate methods are available for tolerance enforcement and data collection. The Pesticide Analytical Manual (PAM Volume II) lists Method I, a GLC Method, as available for the determination of residues of mepiquat chloride *per se* in/on plant and animal commodities. The stated limit of quantitation is 0.1 ppm for cotton and 0.05 ppm for animal products.

No maximum residue limits (MRLs) for mepiquat chloride have been established by Codex for any agricultural commodity. Therefore no compatibility issues exist with respect to U.S. tolerances.

CONCLUSIONS AND RECOMMENDATIONS

1. The registrant has proposed an ion chromatography method (BASF Method D9610) for the determination of residues of mepiquat chloride *per se* in/on plant and animal commodities. The validated method LOQ for the method is 0.1 ppm for cotton commodities and 0.05 ppm for animal tissues, milk, and eggs.
2. Independent method validation has been submitted using cottonseed and cow liver. However, that study was not performed by an independent laboratory (both studies performed by Centre Analytical Laboratories [State College, PA]). An acceptable independent laboratory validation (ILV) of method D9610 is required using an independent laboratory. It is recommended that the ILV be performed for mepiquat pentaborate as the registrant has stated that mepiquat pentaborate will eventually replace mepiquat chloride use on cotton. Once an acceptable ILV is submitted, the method will be submitted to EPA's analytical laboratory for method tryout. Once acceptable Agency validation of the proposed ion chromatography enforcement method (D9610) has been conducted, the method can be forwarded to FDA for inclusion in PAM Vol. II as a numbered method for enforcement of residues of mepiquat in/on cotton and animal tissues, milk, and eggs.

DETAILED CONSIDERATIONS

OPPTS GLN 860.1340: Residue Analytical Methods

Samples of cotton and grape commodities from previously submitted field trials and processing studies and animal commodities from previously submitted feeding studies were analyzed by ion chromatography (BASF Method A9106 for plants or draft BASF Method D9610 for gin byproducts and BASF Method A9104 for animals). BASF Method A9106 (plants) was initially

accepted as an adequate data collection method and forwarded to FDA to be included in PAM Vol. II as a letter method (DP Barcodes D183140, 183187, and D183197, 10/12/93, J. Stokes). In addition, the Agency review stated that if the registrant wanted the ion chromatography method to replace the current PAM Vol. II method for enforcement purposes, validation of the method from an independent laboratory and by the Agency laboratory was required. An acceptable ILV study was previously submitted for BASF Method A9104 for raw milk and liver.

BASF has combined and modified methods A9104 and A9106 under BASF Method D9610. The original methods used dipicrylamine, a class A explosive, as a complexing agent; dipicrylamine has been replaced with a commercial complexing agent (sodium tetraphenyl borate) in the revised method. A complete method description with method validation data (MRID 44498301) and an ILV study (MRID 44498302) are submitted for the ion chromatography method D9610. Both the method validation and ILV studies were conducted by Centre Analytical Laboratories (State College, PA).

Briefly, homogenized cotton matrices (except cottonseed oil) are extracted (2x) with 25% 0.5 N HCl in methanol and homogenized animal tissues and milk are extracted with an acidic aqueous acetone solution (water:2 N HCl:acetone; 100:1:200, v:v:v) for at least 8 hours in a refrigerator. The extracts are filtered through Celite, diluted with methanol and water (cotton matrices) or acetone and water (animal commodities) and cleaned up by cation exchange chromatography; residues are eluted with 2 N HCl. The acidic eluate is adjusted to \geq pH 10 with 12 N NaOH. A solution of sodium tetraphenyl borate (2 g in 100 mL water) is added to the now basic eluate to form a tetraphenyl borate complex with mepiquat chloride residues. The eluate is then partitioned (2x) with dichloromethane. The dichloromethane phase is collected and filtered. Residues are then decomplexed by extracting (2x) with 2 N HCl. Water is added to the acidic aqueous extract which is then evaporated to dryness. The dry residue is transferred to an alumina column with acetonitrile:methanol (95:5, v:v) and eluted with acetonitrile:methanol (95:5, v:v). The eluate is evaporated to dryness and redissolved in water for ion pair chromatographic analysis. Ion chromatography with conductivity detection and a suppressor system (cation micro membrane) is used with a Hamilton PRP-1 column and a mobile phase of hexane sulfonic acid, water, and acetonitrile.

Cottonseed oil is extracted (2x) with 0.5 N HCl and the extract adjusted to \geq pH 10 with 12 N NaOH. The now basic extract is subjected to the procedures described above starting with the addition of sodium tetraphenyl borate.

The reported limit of quantification (LOQ) was 0.10 ppm for cotton matrices and 0.05 ppm for animal tissues and milk.

Method validation data were submitted for cotton matrices, animal tissues, and milk. Homogenized untreated cottonseed, gin byproduct, and refined oil samples were fortified with mepiquat chloride at 0.10 or 2.0 ppm and homogenized untreated cow liver, muscle, kidney, and fat, milk, and chicken egg samples were fortified with mepiquat chloride at 0.05 or 1.0 ppm.

Fortified samples were analyzed using the ion chromatography method D9610 described above. The results of method validation analyses are presented in Table 1.

Table 1. Method validation recoveries of mepiquat chloride from fortified untreated samples of cotton matrices and animal tissues, milk, and eggs.

Crop Substrate	Fortification Levels, ppm	% Recovery ^a	Mean ± s.d.
Cottonseed	0.10, 2.0	65, 66; 72-92 (10)	77 ± 8.1%
Cotton, gin byproducts	0.10, 2.0	75-96 (11)	83 ± 7.8%
Cotton, refined oil	0.10, 2.0	57, 66; 70-88 (10)	74 ± 8.5%
Cow, liver	0.05, 1.0	73-97 (12)	87 ± 7.4%
Cow, muscle	0.05, 1.0	74-95 (12)	86 ± 6.3%
Cow, kidney	0.05, 1.0	74-94 (12)	84 ± 5.4%
Cow, fat	0.05, 1.0	64-66 (3); 71-92 (9)	77 ± 9.0%
Cow, milk	0.05, 1.0	50; 70-93 (11)	77 ± 11%
Chicken, eggs	0.05, 1.0	70-91 (12)	80 ± 7.5%

^a Recovery values outside the acceptable 70-120% range are listed separately; each value represents a single sample unless otherwise noted in parentheses.

Independent laboratory validation

The ILV (MRID 44498302) of the ion chromatography BASF Method D9610 was performed by Centre Analytical Laboratories (State College, PA). Homogenized samples of cottonseed and cow liver were provided by BASF; cottonseed was chosen as the representative cotton commodity and liver was chosen as the most difficult animal commodity to validate. Duplicate samples of untreated cottonseed were fortified with mepiquat chloride at the LOQ (0.1 ppm) and the tolerance level (2.0 ppm). Duplicate samples of untreated cow liver were fortified with mepiquat chloride at the LOQ (0.05 ppm) and the tolerance level (0.1 ppm). Fortified and unfortified samples were analyzed using the ion chromatography BASF Method D9610 for residues of mepiquat chloride *per se*.

Successful recoveries were obtained with the first attempt for cottonseed and cow liver at both fortification levels. The results of the ILV study are shown in Table 2. Apparent residues of mepiquat chloride were less than the method LOQ in control samples of cottonseed and cow liver.

The laboratory reported that for the analysis of a set of 7 samples, approximately 16 person-hours is required for sample extraction and an additional 4 hours is required for IC analysis totaling 2 days (including data analysis). Representative sample calculations and chromatograms were provided.

Table 2. Independent method validation recoveries of mepiquat chloride from fortified cottonseed and cow liver samples analyzed using the proposed tolerance enforcement method (BASF Method D9610).

Matrix	Fortification Level, ppm	% Recovery
Cottonseed	0.1	87, 90
	2	76, 87
	Mean \pm s.d.	85 \pm 6.2
Cow, liver	0.05	77, 87
	0.1	92, 97
	Mean \pm s.d.	88 \pm 8.5

Conclusions:

The petitioner has proposed an ion chromatography method (BASF Method D9610) for the determination of residues of mepiquat chloride *per se* in/on plant and animal commodities. The validated method LOQ for the method is 0.1 ppm for cotton commodities and 0.05 ppm for animal tissues, milk, and eggs. Independent method validation have been submitted using cottonseed and cow liver. However, that study was not performed by an independent laboratory (both studies performed by Centre Analytical Laboratories [State College, PA]). An acceptable independent laboratory validation (ILV) of method D9610 is required using an independent laboratory. It is recommended that the ILV be performed for mepiquat pentaborate as the registrant has stated that mepiquat pentaborate will eventually replace mepiquat chloride use on cotton. Once an acceptable ILV is submitted, the method will be submitted to EPA's analytical laboratory for method tryout. Once acceptable Agency validation of the proposed ion chromatography enforcement method (D9610) has been conducted, the method can be forwarded to FDA for inclusion in PAM Vol. II as a numbered method for enforcement of residues of mepiquat in/on cotton and animal tissues, milk, and eggs.

EPA MEMORANDA CITED IN THIS REVIEW

DP Barcode: D162763
Subject: PP# 1F3955/1H5610 Mepiquat Chloride (N,N-dimethylpiperidinium chloride),
PONNAX Plant Regulator in or on Grapes. Evaluation of Analytical
Methodology and Residue Data. CBTS Nos. 7806, 7807, and 7808.
From: S. Koepke
To: R. Taylor/V. Walters and Toxicology Branch
Dated: 5/22/91
MRID(s): None

DP Barcode: D186624
Subject: Mepiquat Chloride. Guideline 171-4(d) Analytical Method for Milk.
Reregistration Case No. 2375. Chemical No. 109101. CBRS No. 11202.
From: S. Knizner
To: R. Whifers
Dated: 8/16/93
MRID(s): 42546201 and 42546202

DP Barcode: D183140, D183187, and D183197
Subject: Mepiquat chloride on Cotton. Proposed Increases in the Maximum Seasonal
Rate. CBTS Nos. 10671, 10689, and 10690.
From: J. Stokes
To: C. Giles-Parker/D. Wilson and R. Whifers
Dated: 10/12/93
MRID(s): 42426801 through 42426803

DP Barcode: D218492
Subject: Mepiquat Chloride. Magnitude of Residue in Milk, Meat, Poultry, and Eggs.
CBRS No. 16080.
From: F. Fort
To: P. Dobak/K. Depukat
Dated: 1/29/96
MRID(s): 43738601 through 43738603

DP Barcode: D222340
Subject: Mepiquat Chloride. List B. Case No. 2375, Chemical No. 109101. Product and Residue Chemistry Chapters for the Reregistration Eligibility Decision Document (RED). CBRS No. 16830.
From: F. Fort
To: M. Clock/P. Deschamp
Dated: 5/6/96
MRID(s): None

DP Barcode: D239446
Subject: Magnitude of the Residue in/on Cotton gin byproducts.
From: D.Drew
To: CP Moran
Dated: 7/27/01
MRID(s): 44379701

MASTER RECORD IDENTIFICATION NUMBERS

The citations for the MRID documents referred to in this review are presented below.

44498301 Malinsky, D. (1998) Method for Determination of Mepiquat Chloride Residues in Cottonseed, Cottonseed Process Fractions, Animal Tissues and Milk by Ion Chromatography. Study No. 96158 012-05; BASF Registration Document No. 96/5264. Unpublished study submitted by BASF Corporation. 112 p.

44498302 Burton, J. (1997) Independent Method Validation of BASF Analytical Method D9610, for Mepiquat Chloride in Cottonseed and Cow Liver. CAL Study No. 012-05; BASF Registration Document No. 97/5158. Unpublished study submitted by BASF Corporation. 87 p.



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Accession Number: 412-02-0010

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