

Residue Chemistry Review

8/29/1995

Comments:

Subject: Fipronil in or on Corn and Animal RACs. Amendment of 6/27/95. MRID# 437396-01. CBTS# 15943.

Document

Class:

Product

Chem:

Residue 860.1200 Directions for use

Chem: 860.1300 Nature of the residue - plants, livestock

860.1380 Storage stability data

860.1550 Proposed tolerances

Biochemicals:

DP Barcode: D217612

MRIDs: 43739601

PC Codes: 129121 1H-Pyrazole-3-carbonitrile, 5-amino-1-(2,6-dichloro-4-(trifluoromethyl)phenyl)-4-((trifluoromethyl)sulfi

Actives/Inerts

CAS #: 120068-37-3

Commodities: Corn; Corn, Field; Cattle, Fat; Cattle, Kidney; Cattle, Liver; Cattle, Meat; Poultry, fat; Poultry, Kidney; Poultry, Liver; Poultry, Meat; Milk; Egg

Administrative 5F04426

#:

Reviewers: G. F. Kramer

Review Bart Suhre

Approved on: August 29, 1995

Approver:

WP Document:  - Fipronil_021.wpd

8/29/1995

MEMORANDUM

SUBJECT: PP# 5F04426. Fipronil in or on Corn and Animal RACs. Amendment of 6/27/95. MRID# 437396-01. Barcode D217612. CBTS# 15943.

FROM: G.F. Kramer, Ph.D., Chemist
Tolerance Petition Section III
Chemistry Branch I, Tolerance Support
Health Effects Division (7509C)

THRU: F.B. Suhre, Acting Section Head
Chemistry Branch I, Tolerance Support
Health Effects Division (7509C)

TO: Rick Keigwin, Product Manager
Ann Sibold, Team 10 Reviewer
Registration Division (7505C)

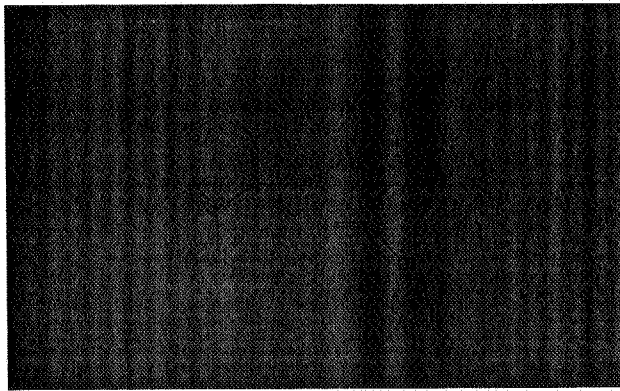
Rhône-Poulenc has submitted an application for permanent tolerances for the insecticide fipronil (5-amino-1-[2,6-dichloro-4-(trifluoromethyl)phenyl]-4-[(1R,S)-(trifluoromethyl)sulfinyl]-1H-pyrazole-3-carbonitrile) or its metabolites MB46136 (5-amino-1-[2,6-dichloro-4-(trifluoromethyl)phenyl]-4-[(trifluoromethyl)sulfonyl]-1H-pyrazole-3-carbonitrile) or MB45950 (5-amino-1-[2,6-dichloro-4-(trifluoromethyl)phenyl]-4-[(trifluoromethyl)thio]-1H-pyrazole-3-carbonitrile) on/in corn. The petitioner has proposed the following tolerances for corn and animal RACs (expressed as parent or metabolites MB45950 or MB46136):

Corn Grain	--	0.02 ppm	Corn Fodder	--	0.15 ppm
Corn Forage	--	0.15 ppm	Liver*	--	0.02 ppm
Milk*	--	0.02 ppm	Eggs	--	0.02 ppm
Fat*	--	0.08 ppm	Poultry Skin/Fat	--	0.03 ppm
Muscle*	--	0.02 ppm	Poultry Muscle	--	0.02 ppm
Kidney*	--	0.02 ppm	Poultry Liver	--	0.02 ppm

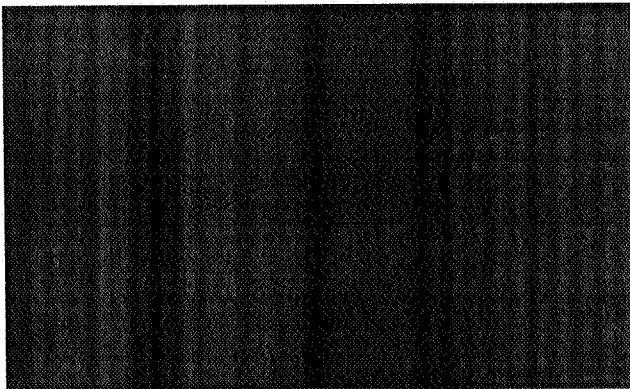
*of Dairy Cows

The current amendment addresses deficiencies pertaining to the nature of the residue in corn identified in CBTS's previous review (Memo, G. Kramer 7/25/95). Specifically, the registrant is asking for a waiver for the requested corn metabolism study using pyrazole-labelled fipronil. Even though the phenyl study found no evidence of ring cleavage, CBTS was concerned with the possibility of preferential uptake of pyrazole-derived metabolites from the soil which would not be detected using the phenyl-labelled material.

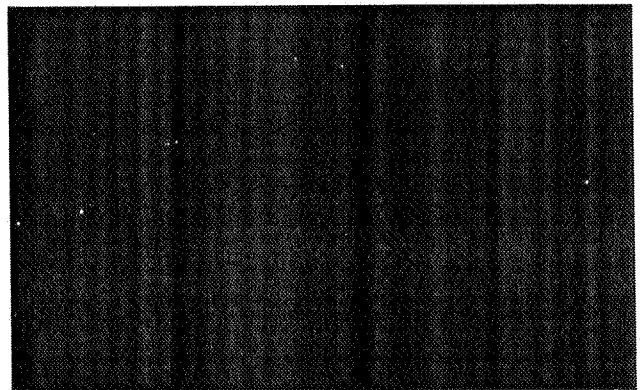
The structures of fipronil and its metabolites MB45950 and MB46136 are shown below:



Fipronil



MB46136



MB45950

RECOMMENDATIONS

CBTS continues to recommend against the proposed tolerances for fipronil in/on corn and animal RACs for reasons detailed in conclusions 1a, 2a, 2b, 3, 5b, 5c, 6e, 7b, 7d, 7e, 8b, 10c, 10d, 11b, 12b, 12c and 13b of the Memo of G. Kramer (7/25/95) and in conclusion 3 below.

CONCLUSIONS

1. CBTS has reviewed EFED's evaluation of an aerobic soil metabolism study for

fipronil (Memo, G. Maske 6/13/94). The major metabolites produced in sandy loam soil were RPA 200766 and MB 46136. No evidence of ring cleavage was observed. CBTS thus concurs with the registrant that a corn metabolism study using pyrazole-labelled fipronil is not required.

2. However, questions concerning the stability of the phenyl-labelled samples remain unanswered (conclusion 4b of Memo, G. Kramer 7/25/95). The results of the pyrazole study were to have been used to address this deficiency.

3. The registrant reports that metabolism studies using phenyl-labelled fipronil have been completed in cotton and rice. CBTS will not require the registrant to repeat the phenyl-labelled study for corn if the results of the cotton and rice metabolism studies are qualitatively the same as those of corn. CBTS requests that the registrant submit these metabolism studies for our review.

DETAILED CONSIDERATIONS

Deficiency - Conclusion 4c (from Memo, G. Kramer 7/25/95)

4c. Fipronil contains two rings but the registrant has performed metabolism studies using only [¹⁴C]phenyl-labelled fipronil. In order to fully characterize the nature of the residue in corn, the registrant should perform a metabolism study in corn using [¹⁴C]pyrazole-labelled fipronil.

Petitioner's Response: An aerobic soil metabolism study reviewed by EFED (MRID# 429186-63) demonstrates that there is no ring cleavage during soil metabolism of fipronil. There was also no evidence of ring cleavage in the corn metabolism study conducted with phenyl-labelled fipronil. Repeating the corn metabolism with pyrazole-labelled fipronil would thus not be expected to reveal the presence of any metabolites not identified in the phenyl study.

CBTS's Conclusion: CBTS has reviewed EFED's evaluation of the soil metabolism study (Memo, G. Maske 6/13/94). The major metabolites produced in sandy loam soil were RPA200766 and MB46136. No evidence of ring cleavage was observed. CBTS thus concurs with the registrant that a corn metabolism study using pyrazole-labelled fipronil is not required. However, questions concerning the stability of the phenyl-labelled samples remain unanswered (conclusion 4b of Memo, G. Kramer 7/25/95):

"Based on the data submitted, storage stability can not be demonstrated for the samples of this study. It appears that MB46136 and RPA200766 are the major metabolites of fipronil in corn, but conclusions on the relative amounts of the parent and metabolites and on the presence of RPA105048 can not be reached.

However, CBTS will not require the registrant to repeat the phenyl-labelled study if the results of the required corn metabolism study using pyrazole-labelled fipronil (see below) are qualitatively the same as the results with the phenyl label."

The registrant reports that metabolism studies using phenyl-labelled fipronil have been completed in cotton and rice. CBTS will not require the registrant to repeat the phenyl-labelled study for corn if the results of the cotton and rice metabolism studies are qualitatively the same as those of corn. CBTS requests that the registrant submit these metabolism studies for our review.

cc: PP#5F04426, Kramer, Circ., R.F., S.F.

RDI: F.B. Suhre (8/28/95), R.A. Loranger (8/28/95), M.S. Metzger (8/29/95)

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