



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

AUG 12 1987

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Subject: PP#7G3547: 45639-EUP-GL; MITAC EC (Amitraz)
for use on cotton. Accession Nos. 402593-01,
-02, -03. RCB Nos. 2571 and 2572.

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NOR-AM Chemical Company, Wilmington Delaware, has requested establishment of a temporary tolerance for residues of amitraz and its metabolites containing the 2,4-dimethylaniline moiety in cottonseed at 0.3 ppm. This temporary tolerance is required to support the experimental use (45639-EUP-27) of MITAC[®] EC on cotton during the period 1-1-88 through 12-31-88. 45639-EUP-27 calls for application of 4,750 gallons (7,100 lbs. ai) of MITAC 1.5 EC to 7,100 acres of cotton in 10 states, as follows: AK(200); AZ(1,200); CA(4,200); LA(200); MS(300); TX(200); AL(200); GA(300); SC(200); and NC(100). These states accounted for ca 63% of the cottonseed harvested in the United States during 1984 (Agricultural Statistics, 1985).

Two similar request for temporary tolerances for amitraz/ metabolite residues in or on cottonseed were previously rejected by RCB (see, PP#8G2101, G.P. Makhijani, memo of 1-15-79; and PP#5G3185, C. Deyrup, memo of 2-27-85).

Tolerances are established (40 CFR 180.287) for residues of the insecticide amitraz and its 2,4-dimethylaniline metabolites (calculated as the parent compound) in and on: apples at 0 ppm; cattle fat at 0.1 ppm; cattle mbyp at 0.3 ppm; cattle meat at 0.05 ppm; meat, fat, and mbyp of goats, hogs, horses, and sheep at 0 ppm; milk at 0.03 ppm; milk fat at 0.3 ppm; and pears at 3.0 ppm.

Temporary tolerances for amitraz/metabolites in citrus and animal commodities have been issued in the past (all currently expired). In addition, several tolerance petitions (temporary and permanent) are pending.

Conclusions

1a. The metabolic nature of amitraz in cottonseed is not adequately understood. A metabolism study on cottonseed has not been submitted. In past reviews, we have similarly concluded that the metabolic fate of amitraz in lemons, pears, and cottonseed is not adequately understood (PP#2F2705, M. Firestone, memo of 1-16-87; PP#8G2120, G. Makhijani, memo of 1-15-79; PP#5G3185, C. Deyrup, memo of 2-27-85).

1b. For the purposes of this temporary tolerance request and considering the low dietary burden, we conclude that the metabolic nature of amitraz in animals is adequately understood; the residues of concern are the parent compound and its N'-(2,4 dimethylphenyl)-N-methylmethanimidamide and N-(2,4-dimethylphenyl)formamide metabolites.

2. We can draw no conclusions concerning the adequacy of the analytical method (Accession 263864, PP#4F3081) used for determining combined amitraz/metabolite residues in cottonseed. The petitioner must provide additional information with respect to the metabolic nature of amitraz in cottonseed before this deficiency can be resolved (see, conclusion 1a).

3. No storage stability data on cottonseed samples were submitted. These data will be required for a permanent tolerance.

4a. We can draw no conclusions, from the limited residue data submitted, concerning the adequacy of the proposed 0.3 ppm combined tolerance for amitraz/metabolite residues on cottonseed. The petitioner must provide additional information with respect to the metabolic nature of amitraz in cottonseed before this deficiency can be resolved (see, conclusion 1a.). Additional residue data may be required.

4b. Residue data indicate that the proposed tolerances for combined residues of amitraz in cattle fat at 0.1 ppm; cattle mbyp at 0.3 ppm; cattle meat at 0.05 ppm; milk at 0.03 ppm; and milk fat at 0.3 ppm, will not be exceeded as a result of this proposed experimental use (45639-EUP-27).

5. A processing study submitted in connection with PP#5G3185 (see, C. Deyrup, memo of 2-27-85) indicates that amitraz/metabolites do not concentrate in processed fractions derived from cottonseed. Therefore, no temporary food additive tolerance is required.

Recommendation

For the reasons cited in conclusions 1a., 2 and 4a. above, we recommend against the establishment of a temporary tolerance for combined residues of amitraz and its 2,4-dimethylaniline metabolites in or on cottonseed at 0.3 ppm.

Detailed Considerations

Manufacture and Formulation

The Product Chemistry of amitraz has been reviewed numerous times. Please refer to the Product Chemistry Chapter of the Amitraz Registration Standard (10-5-84) for a detailed discussion. In summary, Amitraz is the common name for N'-(2,4 dimethylphenyl)N[[(2,4 dimethylphenyl)imino]methyl]-N-methylmetanimidamide. Amitraz is manufactured by NOR-AM Chemical Company of Wilmington, Delaware; the technical product is ca 93% pure. Based on the available data, we do not anticipate any residue problems from the reported impurities in the TGA1. MITAC™ EC, EPA Reg. No. 45639-49, is an insecticide/miticide formulated as an emulsifiable concentrate containing 20.4% amitraz (1.5 lbs. a.i. per gallon) as its active ingredient. All inert ingredients are cleared for use under 40 CFR 180.1001.

Proposed Use

45639-EUP-27 calls for the use of MITAC™ to control mites, bollworm and tobacco budworm on cotton, as follows:

Mite control: Apply MITAC 1.5 EC as a single treatment at 2-2/3 to 4 pints (0.5 to 0.75 lbs. ai) per acre, or as two sequential applications of 2-2/3 pints per acre. Apply the product any time after cotton plants are 4 to 6 inches tall. For best results apply when mite population begins to build but before infestation reaches a high level. Do not exceed 5-1/3 pints (1.0 lbs. ai) per acre per season, and do not apply within 21 days of harvest.

Insect control: Apply MITAC 1.5 EC at 2/3 to 1-1/3 pints (0.12 to 0.25 lbs. ai) per acre as needed. Do not apply more than 5-1/3 pints (1.0 lb. ai) per acre per season, and do not apply within 21 days of harvest. When used as an insecticide, MITAC 1.5 EC should be tank-mixed with a pyrethroid insecticide.

MITAC 1.5 EC is applied utilizing either air or ground spray equipment. For aerial treatment, do not apply in less than 1 gallon of water per acre. For ground treatment do not apply in less than 10 gallon of water per acre.

Nature of the Residue

Plant metabolism: No new plant metabolism studies were submitted with this petition. Amitraz metabolism studies in apples, pears, and lemons have been submitted in conjunction with previous petition request (PP#6F1817 and PP#2F2707). In past reviews we have concluded that the metabolic fate of amitraz in lemons, pears, and cottonseed is not adequately understood. In the case of lemons and pears, a high percentage of ^{14}C -labeled residues were not chemically elucidated (PP#2F2705/ 2H5353, M. Firestone memos of 8-1-84, 9-28-84 and 1-16-85; and Amitraz Reg. Standard). In the case of cottonseed, metabolism studies have not been submitted (PP#8G2101, G.P. Makhijani, memo of 1-15-79; and PP#5G3185, C. Deyrup, memo of 2-27-85). With respect to PP#5G3185, RCB waived the requirement for a cottonseed metabolism study because of the limited acreage (300) involved; at that time we advised the registrant, as follows:

" RCB will forgo the need for a cottonseed metabolism study at this time. The petitioner should be advised that if he has any intent to greatly enlarge this EUP or make a submission for permanent amitraz tolerances on cotton products, he must submit a ^{14}C -amitraz metabolism study on cotton plants."

Since 45639-EUP-27 calls for treatment of 7,100 acres in 10 states, we conclude that a cottonseed metabolism study is required to support this temporary tolerance request.

Animal metabolism: Tracer studies on the dog, rat, calf (oral feeding) and a lactating cow (dermal exposure) were previously submitted and discussed in connection with PP#5G1558 and PP#6F1817. Based on these studies RCB continues to conclude that the residues of concern in animals are the parent compound and its N'-(2,4-dimethylphenyl)-N-methylmethanimidamide and N-(2,4-dimethylphenyl)formamide metabolites.

Note to PM: As stated in previous reviews (PP#2F2705/2H5353, M. Firestone, memos. dated 8-1-84, 9-28-84, and 1-16-85). a radiolabeled tracer study on a lactating ruminant will be required for issuance of permanent tolerances.

Analytical Method

The residue data submitted with this petition were generated using a method (with minor modifications) entitled, "Analytical Method for the Determination of Total Residues of Amitraz and its Major Metabolites, BTS 27271 and BTS 27919 in Select Hog Tissue," Nor-Am Report 12002 by L. Castro (July 86). This method was recently reviewed, in detail, by F. Griffith in connection with PP#4F3081 (see, memo dated 10-15-86). In summary, a 30 gram subsample of finely milled cottonseed is

fortified with an internal standard (BTS 28035, N'-(2,4,5-trimethylphenyl)N[[(2,4,5-trimethylphenyl)imino]methyl]N-methyl-metanimidamide) and acid hydrolyzed. Following acid hydrolysis the sample workup is made basic and the analytes of interest (anilines) are steam distilled into hexane, partitioned into water under acid conditions, then partitioned back into hexane under basic conditions and derivitized using heptafluorobutyric anhydride. The derivitized analytes are then subjected to further clean up utilizing a silica gel column. The determinative step of the assay is based on gas chromatography with electron capture detection.

Residue values were corrected for the recovery of the internal standard and were reported as amitraz equivalents. Recovery of amitraz and its major metabolites from fortified cottonseed samples are summarized in table 1:

Table 1: Amitraz/metabolites recovery data

Fortification Level(ppm)	Percent Recovery ^a		
	Amitraz	BTS 27271	BTS 27919
0.05	122, 112	112, 128	129, 133
0.1	113, 127	-	-
0.2	102	-	-
0.3	128	125, 112	126, 103

a. Recovery values are expressed as a ratio of analyte recovery to internal standard recovery. The absolute recovery of the internal standard was 63 % with a standard deviation of 13 % for 36 analyses.

b. Chemical structures are provided in attachment # 1

The method's limits of detection for all residues (amitraz, BTS 27271, and BTS 27919) is 0.05 ppm.

Residue Data

No storage stability data, for treated cottonseed samples, were provided with this petition.

Two residue studies were provided with this submission:

1. R231-Total Residues of Amitraz and Metabolites in Cottonseed Following Early and Mid-season Application

of MITAC EC in Trials Run in the US in 1985 and 1986.
(Accession No. 402593-02); and

2. R232-Total Residues of Amitraz and Metabolites in Cottonseed
Following Late season Application of MITAC EC in Trials Run
in the US in 1985 and 1986 (Accession No. 402593-03).

Study 1 (R-231) reflects 10 field trials conducted during
1985 and 1986 in AZ(1), and CA (9); study 2 (R-232) reflects
7 field trials conducted during 1985 and 1986 in AZ(1),
AR(1), CA(1), FL(1), LA(1), MS(1), and TX(1). Residue
data from these studies are summarized in tables 2 and
3 below:

Table 2: Residue levels in cottonseed from plants receiving
early and/or mid-season treatments

Site	Application ozs. ai.(dates)	PHI	Total Residue (ppm)
CA	8+8(6-1-85,7-12-85)	86	0.07
	12(6-1-85)	127	<0.05
	12(7/12/85)	86	0.12
CA	8+8(6-6-85,7-12-85)	79	0.15
	12(6-1-85)	115	<0.05
	12(7/12/85)	79	0.09
CA	8+8(6-8-85,7-12-85)	104	<0.05
	12(6-8-85)	138	0.07
	12(7/12/85)	104	<0.05
CA	8+8(6-19-85,7-12-85)	75	0.17
	12(6-19-85)	98	0.08
CA	8+8(6-28-85,7-17-85)	74	0.14
	12(6-88-85)	93	<0.05
AZ	8+8(4-15-86,7-18-86)	75	0.18
	12(7-18-86)	75	0.27
CA	8+8(6-7-86,7-10-86)	78	<0.05
	12(7-10-86)	78	<0.05
CA	12(7-10-86)	72	0.12
CA	12(6-27-86)	80	<0.05
CA	8+8(6-5-86,7-1-86)	78	<0.05
	12(7-1-86)	78	<0.05

Table 3: Residue levels in cottonseed from plants receiving late season treatments

Site	Application ozs. ai.(dates)	PHI	Total Residue (ppm)
CA	8+8(6-13-85,9-13-85)	49	<0.05
	8(9-13-85)	49	0.06
FL	8+8(6-3-85,8-29-85)	50	<0.05
	12(8-29-85)	50	0.05
AZ	8+8(7-16-85,8-21-85)	50	0.20 (Mean, n=2)
	12(7-16-85)	50	0.18 (Mean, n=2)
AR	8+8(8-8-86,8-13-86)	23	0.08
	8(8-13-86)	23	0.05
	12(8-13-86)	23	0.06
MS	8+8(7-23-86,7-28-86)	23	0.09
	12(7-23-86)	28	<0.05
TX	8+8(6-2-86,7-3-86)	21	0.08
	12(7-3-86)	21	0.07
LA	8+8(5-23-86,8-22-86)	24	0.10
	12(8-22-86)	24	<0.05

Of the 36 data points provided only 1 reflects the maximum proposed application rate (1.0 lb. ai per acre per season) and a 21 day PHI. Three other samples reflect the same application rate with PHIs of 23 or 24 days. Amitraz/metabolite residues for these 4 samples ranged from 0.08 to 0.10 ppm. The remaining 32 samples either did not reflect the maximum application rate or had PHIs far greater than 21 days.

Based on the limited data provided (4 samples), it appears that residues of amitraz plus metabolites (BTS 27271 and BTS 27919) will not exceed the proposed temporary tolerance (0.3 ppm), as a result of the proposed use stated in 45639-EUP-27. However, since the metabolic nature of amitraz in cottonseed is not adequately understood, we can draw no conclusions concerning the adequacy of these data with respect to the tolerance expression. The tolerance expression identifies amitraz, per se, and its metabolites containing the 2,4 dimethylaniline moiety, as the residue of concern.

Processing Studies

No new processing studies were provided with this petition. A cottonseed processing study, conducted by the Food Protein Research & Development Center at Texas A & M University, was previously submitted in connection with PP#5G3185. Data from that study indicate that amitraz/metabolites do not concentrate in processed fractions derived from cottonseed (PP#5G3185, C. Deyrup, memo of 2-27-85). Since no concentration of amitraz residues occurred, we do not require temporary food additive tolerances for processed cotton commodities.

Meat, Milk, poultry, and Eggs

A calf feeding study, lactating cow feeding study, and lactating cow dermal exposure study were submitted and discussed in connection with PP#OG2344 (see, L. Propst memo of 9-8-80).

In the calf feeding study, 12 animals were split into 4 groups of 3 animals; each group was dosed with amitraz at 0, 4, 12, or 40 ppm in their diet for 21 days. The animals were sacrificed 24 hours after the last dose; and liver, kidney, muscle, and fat samples were collected for analysis. No residues (ND<0.01 ppm) were found in fat and muscle tissue taken from the calves receiving 40 ppm in their diet. Similarly, residues of amitraz in the liver and kidney for the same group of animals ranged from 0.01 to 0.055 ppm; and 0.013 to 0.828 ppm, respectively. No residues were found in the liver or kidney samples of calves fed 12 ppm amitraz in their diet.

In a separate study 3 milking cows were dosed daily immediately after their morning milking for a 3 week period. One cow was used as a control while the others were dosed with either 3 or 10 ppm N'-(2,4-dimethylphenyl)N-methylmethanimidamide (a major plant metabolite) in their feed. No residues were found in the milk of these cows.

Cottonseed may account for up to 25 and 20% of the diet of beef and dairy cattle, respectively. Based on the residue data submitted, the daily dietary burden of amitraz/metabolite to cattle would be 0.025 ppm; based on the proposed temporary tolerance (0.3 ppm) the daily dietary burden to cattle would be 0.075 ppm. Since no amitraz residues were found in liver and kidney samples of calves fed 12 ppm amitraz in their diet; and no amitraz residues (ND<0.01 ppm) were found in fat and muscle tissue taken from the calves receiving 40 ppm in their diet, we conclude that the existing tolerances for cattle fat at 0.1 ppm; cattle mbyp at 0.3 ppm; cattle meat at 0.05 ppm; milk at 0.03 ppm; and milk fat at 0.3 ppm, will not be exceeded as a result of this proposed EUP.

Cottonseed is not a poultry feed item.

cc:R.F.,Circu.,F.Suhre,S.F.,PP#7G3547, PMSD/ISB
RDI:EZ:8/10/87:RDS:8/11/87
TS-769:RCB:FBS:fbs;557-1883:CM#2:RM#814:8/12/87