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

NOV 4 1987

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Memorandum

Subject: Thiophanate-methyl (Topsin® M 70W, EPA Reg. No. 4581-322; Topsin® M 4.5F, EPA Reg. No. 4581-352) on Wheat. Amended Registration Allowing Application in an Increased Geographical Area and an Additional Application.
No Acc. Number / No MRID Number
RCB Nos. 2779, 2780

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Thru: Edward Zager, Section Head, SRS 2
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Registration Division (TS-767C)

The Pennwalt Corporation, Agricultural Chemicals Division, requests Amended Registration for 2 formulations of Thiophanate-methyl, Topsin® M 70W (70% a.i. wettable powder) and Topsin® M 4.5F (4.5 lbs.a.i./gallon flowable). These formulations are currently registered for a single application to fall-seeded wheat in ID, OR and WA only. The proposed use would allow an additional application, decrease the PHI from approximately 90 to 30 days, and remove the geographical restriction currently on the label.

Tolerances are established for residues of the fungicide thiophanate-methyl [dimethyl((1,2-phenylene)bis(iminocarbonothioyl)) bis(carbamate)], its oxygen analog dimethyl-4,4'-o-phenylene bis(allophanate)(allophanate) and its benzimidazole-containing metabolites (calculated as thiophanate-methyl) on various commodities ranging from 0.05 ppm on wheat and potatoes to 50 ppm on the forage and hay of beans. Numerous tolerances are pending (40 CFR 180.371; 21 CFR 561.386). A Registration Standard has been completed for thiophanate-methyl (Residue Chemistry Chapter, 2/6/85).

Topsin® M 70W is currently registered for application to fall-seeded wheat only, in ID, OR and WA only, at 1 lb. product

(0.7 lbs.a.i.)/A after wheat is tillered but before stem elongation has begun. This corresponds to approximately a 90-day PHI. A single application could be made using either ground or aerial equipment. The following restrictions are imposed:

Do not make more than 1 application per season.

Do not cut hay within 90 days of application.

Do not allow livestock to graze in treated areas before harvest.

The Topsin® M 4.5F label reflects the same usage although 0.7 lbs.a.i./A corresponds to 20 fl. oz./A for this product.

The proposed use of Topsin® M 70W includes the use decribed above except that the 3 restrictions described above are deleted. Additionally, applications could be made at 0.5-0.7 lbs.a.i./A prior to disease formation of the flag leaf at the late boot stage prior to heading of the wheat. Two applications could be made at a 14-day interval, and the PHI would be reduced from 90 to 30 days. The following restriction is included for this new use:

Do not allow livestock to graze in treated areas before harvest.

The proposed use for Topsin® M 4.5F is identical.

Residue data were submitted with this amendment. The method used to generate these data is similar to PAM II, Method I. The wheat grain is extracted with acetone, water is added to the extract, and the acetone is removed by flash evaporation. After adjusting the pH to 6.8, extracting X3 with chloroform, and evaporating to dryness, the thiophanate-methyl (T-M) in the sample is converted to methyl-2-benzimidazolecarbamate (MBC) using acetic acid and cupric acetate. Further clean-up is accomplished by liquid-liquid partitioning, and the final sample is analyzed by scanning UV spectrophotometry recording the spectrum between 240 and 300 nm, and measuring the peak height at 281 nm. Recoveries of T-M ranged from 70-102% (average = 79%) at fortification levels of 0.05 - 0.2 ppm. Recoveries of MBC cannot be determined since, in each recovery experiment performed in which the sample was spiked with MBC, it was also spiked with T-M. Recoveries for samples spiked with both MBC and T-M ranged from 70-105% (average = 82%) at combined fortification levels of 0.04-0.28 ppm. All check samples were non-detectable (<0.05 ppm).

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Samples were not analyzed for residues of allophanate since the available plant metabolism studies indicate that allophanate accounts for no more than approximately 10% of the total residue resulting from applications of thiophanate-methyl.

Storage stability studies are not available for residues of thiophanate-methyl on wheat. However, studies for apples, bean pods and foliage, onions, cherries and other commodities indicate that residues of thiophanate-methyl and MBC are stable in frozen plant commodities stored up to 38 months. Samples obtained in this study were frozen after sampling, shipped frozen and stored frozen for less than 24 months. Storage stability data are not available for allophanate. This is an outstanding data gap identified in the Residue Chemistry Chapter of the Registration Standard (p. 51).

Residue data supplied with this submission are summarized in Table 1. Samples were collected from MS (15 samples), NE (3 samples), KS (3 samples), PA (3 samples), LA (5 samples), SD (3 samples), MI (3 samples), KY (2 samples), VA (2 samples), NY (2 samples) and GA (2 samples). Both the 70W and 4.5F formulations were used in these studies. A single study (2 samples from GA) utilized aerial applications (70W formulation). Residue data were supplied for wheat grain only. Residue data were not provided for forage or hay, and a processing study was not performed.

Table 1: Residue Data for Thiophanate-Methyl Applications to Wheat

Application Rate (lbs.a.i./A)	Number of Applications	Interval Between Apps. (Days)	PHI (days)	Residue Range (ppm)[1]
0.7	1	-	15	<0.05 - 0.09
			29,30	<0.05
			44	<0.05
	2	14 - 16	14,15	<0.05 - 0.10
			30	<0.05
			45	<0.05
	1[2]	-	15	<0.05
			30	<0.05

[1]T-M and MBC residues only. Allophanate residues were not determined.
[2]Aerial application.

Residue data were also submitted with PP#0E2289, PP#3F2908 and PP#1E2463 and reviewed by K. Arne (10/4/83). These data were for winter wheat and were obtained from CA, WA and OR. These data are summarized in Table 2 below taken from K. Arne's review.

Table 2: Previously Submitted Residue Data for Thiophanate-Methyl Applications to Wheat

Application Rate (lbs.a.i./A)	PHI (days)	Residue (ppm) Grain	Straw
2	105	<0.05	0.20
1	132	-	<0.10
0.7	92-104	<0.05	<0.10
0.35 - 0.7	147-153	<0.05	<0.10
0.7	97	<0.05	<0.10
0.52 - 1.05	133-134	<0.05	<0.10

Residue data were also submitted in response to deficiencies cited in the reviews of PP#3F2908. Samples were collected from CA (4 samples), PA (4 samples), WA (29 samples), ID (13 samples), OR (1 sample), IL (5 samples), KY (2 samples), NE (1 sample), KS (2 samples), SD (1 sample), MI (4 samples), OH (4 samples) and IN (2 samples). All data were for ground applications except for 4 samples from WA (104-149 day PHIs) and 1 from ID (87-day PHI). Both the 70W and 4.5F formulations were used. All data reflected 1 application of the pesticide. Residues were all non-detectable (<0.05 ppm for grain, <0.10 ppm for straw) at PHIs ranging from 55-143 days.

Conclusions

(1) The UV method used to generate residue data submitted with this amendment is adequate for data collection but is not adequate for enforcement because of the potential for interference. Therefore, the registrant should submit the following additional data as stated in the Residue Chemistry Chapter of the Registration Standard:

> The registrant must submit either (i)validation data regarding the specificity of the UV method (PAM, Vol. II, Method I), or (ii) validation data regarding the accuracy and sensitivity of the HPLC method (MRID 00036809) for detection of residues of concern in plants.

(2) Information from Agricultural Statistics (1985) indicate that the major winter wheat-growing states are KS (21% of total), OK (9%), TX (7%), WA (7%), CO (5%), MO (4%), NE (4%), IL (3%) and MI (3%). Other states make up 3% or less of the total winter wheat production in the U.S. The total number of samples collected from these major production

states was 7 (6 at a 30-day PHI and 1 at a 45-day PHI). The data reflecting the minimum PHI and the maximum application rate are not sufficiently representative of the major winter wheat growing areas. Additional residue data should be submitted for these areas (particularly TX, KS, OK and NE) which show maximum residues likely to result from the proposed use. These should also include aerial applications for both formulations at the maximum application rates and minimum PHIs. These data are required before RCB can determine the adequacy of the current tolerances to cover the proposed uses.

Additionally, no residue data are available for wheat forage or hay reflecting the proposed maximum application rate and PHI. These data should be submitted utilizing both the 70W and 4.5F formulations and utilizing both aerial and ground applications of the pesticides. These data are required for RCB to determine the adequacy of the established tolerances to cover the proposed uses.

(3) Residues of allophanate were not determined for the samples described in this submission because in plant metabolism studies, allophanate never accounted for more than 10% of the total residue. RCB previously did not consider this to be a deficiency because no detectable residues of allophanate would be expected at the long PHIs (90 days) prevously proposed (see K. H. Arne, 10/4/83; S. V. Hummel, 1/15/85). If additional residue data submitted from the major winter wheat producing states show no detectable residues for combined residues of T-M and MBC at the maximum application rate and minimum PHI currently proposed (30 days), then residue data for allophanate will not be needed. If detectable residues are found, the samples should also be analyzed for residues of allophanate which would also be potentially found in these samples.

(3a) The Residue Chemistry Chapter of the Registration Standard identifies the need for storage stability data for residues of allophanate in raw agricultural commodities. If residues of allophanate must be determined in wheat, then storage stability data should also be submitted for residues of allophanate in wheat.

(4) Since detectable residues were found in wheat grain (15-day PHI), and statistical analysis of the available residue data indicate that residues in wheat grain could be near the tolerance (0.05 ppm) at a 30-day PHI, a wheat processing study must be performed to show concentration of residues in processed fractions.

(4a) Allophanate residues could account for up to 10% of the total residues found in plant commodities. Since these

residues could concentrate in a particular processed fraction, the wheat fractionation study should also include determination of allophanate concentration in processed fractions.

(5) Wheat grain, forage, hay and milled products are important animal feed items. Additionally, the proposed use would increase the geographical area in which thiophanate-methyl could be used and potentially increase the residues in wheat. Therefore, exposure of T-M and its metabolites to animals could increase as a result of the proposed use. Therefore, the following deficiency related to animal metabolism identified in the Registration Standard (Residue Chemistry Chapter) should be addressed:

> ^{14}C-residues of ring-labelled [^{14}C]thiophanate-methyl must be fully characterized in the fat, muscle, liver and kidney of ruminants and poultry. Animals must be dosed for at least 3 days at a concentration sufficient to permit complete characterization of residues (free and conjugated) in tissues and organs. Animals must be sacrificed within 24 hours of the final dose. Tissues must also be analyzed with enforcement methodology to determine whether the method(s) will adequately determine all residues of toxicological concern.

(6) The following restriction should be included on the Topsin® labels in such a manner that it is clear that the restriction applies to all applications of Topsin to wheat:

> Do not allow livestock to graze in treated areas before harvest.

Recommendations

RCB recommends against this Amended Registration for the reasons discussed in (1), (2), (3), (3a), (4), (4a), (5) and (6) above.

cc: Thiophanate-methyl S.F., R.F., Amended Use S.F., PP#3F2908, Circu, M. Metzger, PMSD/ISB
RDI:E.Zager:11/3/87:RDS:11/3/87
TS-769C:RCB:M.Metzger:MM:Rm803a:CM#2:11/3/87