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

#323EE

APR 4 1984

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: 84-LA-04. Section 18 Emergency Exemption for propiconazole (Tilt) on rice. Accession # 252458.

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The Louisiana Department of Agriculture is requesting a Section 18 emergency exemption allowing use of the fungicide propiconazole, 1-[[2-(2,4-dicholorophenyl) 4-propyl-1,3-dioxolan-2-yl]methyl]triazole, trade name: Tilt or CGA-64250, for control of various diseases on rice.

A temporary tolerance of 4 ppm for rice grain and 15 ppm for rice hulls was found to be adequate to cover residues of propiconazole, 1-[[2(2,4-dichlorophenyl) 4-propyl-1,3-dioxolan-2-yl]-triazole and its metabolites containing the 2,4-dicholorobenzoic acid (PP#1G2530, memo of J. Worthington, 1/7/82). The use involved was somewhat different from that proposed here.

The Louisiana Department of Agriculture is requesting 141,000 pounds active of propiconazole for aerial treatment of 250,000 acres of rice. The program is scheduled to begin on 5/1/84 and terminate on 9/1/84.

Propiconazole 3.6E will be applied by aerial equipment while fields are flooded as a foliar spray at 10 fld oz act/A, equivalent to 0.28 lb act/A, in 10 gallons of water at first green ring (first internode elongation). Repeat application at the same rate is recommended two weeks later.

The following restrictions are imposed: Do not apply to exposed rice heads. Do not use straw from treated rice or use straw, hulls for feed or bedding. (The restriction against feeding rice hulls is not considered practical since the hulls are not under grower's control.) Do not apply to fields where crayfish or catfish farming is practiced. Do not permit spray to drift onto catfish or minnow ponds. Water drained from treated fieldsis not to be used to irrigate crops. The pre-harvest interval will vary with variety but expected to be ca 50 days.

The metabolism of propiconazole in plants (wheat, barley, grapes and peanuts) was discussed in connection with PP#1G2530 (memo of J. Worthington, 1/7/82). It was concluded that propiconazole per se and its metabolites containing the 2,4-dicholorobenzoic acid are the principal residues of concern. We notice that the dicholorobenzoic acid metabolites are not actually part of the metabolic pathway of propicoanzole. Metabolism of propiconzale in plants involves hydroxylation of the n-propyl group of the dioxolane ring to four B-hydroxy isomers which form sugar type conjugates. Further metabolism involves deketalization of the dioxolane ring yielding the alkanol. Hydroxylation and replacement of the chlorine may occur to some degreee. A major metabolic step occurs when the alkyl bridge cleaves resulting in the formation of 1,2,4-triazole-1-alanine which readily transfers to the fruiting part of the plant. Transfer of the phenyl metabolites may also occur, however, to a lesser extent. The aniline conjugate can undergo some oxidation. Formation of 1,2,4-triazoleacetic acid is an example. We believe that the metabolites containing the 2,4-dicholorobenzoic acid might have resulted from the acid digestion of the ketone intermediate during the extraction process.

For the purpose of this Section 18 exemption we consider the residue of concern in plants to be propiconazole, its metabolites covertible to 2,4-dichlorobenzoic acid and 1,2,4-triazole and its conjutgates.

The metabolism of propiconazole in the goat was discussed in connection with PP#1G2530 (memo of J. Worthington, 1/7/82). For the purposeof this Section 18 exemption we consider the residue of concern in milk and animal tissues to be propiconazole, its metabolites that could be converted to 2,4-dichlorobenzoic acid and 1,2,4-triazole and its conjugates.

The analytical methodology for propiconazole per se in plants, including rice, was presented under report #AG354 and discussed in conncection with PP#1G2530 (memo of J. Worthington, 1/7/82). The method is also suited for determination of propiconazole per se in animals.

A modified procedure that converts propiconazole residues to 2,4-dicholorobenzoic acid was discussed in connection with PP# 1G2530. Recovery and control values in rice are available. Method sensitivity for rice grain was 0.05 ppm and that for rice straw was 0.1 ppm. The method was found adequate to enforce tolerances for rice.

In this submission, the analytical methodlogy for residue determination of propiconazole in animals is presented in report #AG-359, acc. #252548. In this method, residues of propiconazole is converted to and determined as the 2,4-dicholoro-benzoic acid in milk, eggs and animal tissues. The limit of detection is 0.05 ppm for eggs and other tissues, except liver and kidney, and 0.1 ppm for the liver and kidney. In this method, milk, eggs and blood samples are extracted using acetonitrile; whereas, tissue samples are extracted using 80% acetonitrile/water. Aliquot of the extract is partitioned with hexane to remove fat. The samples are evaporated to a small aqueous volume, then refluxed overnight in a 12 N nitric acid solution containing sucrose. Under the acid reflux, propiconazole per se and its metabolites are converted to 2,4-dichlorobenzoic acid. After addition of water, the extract is partitioned with 10% ethyl ether/hexane. The organic phase containing 2,4-dichlorobenzoic acid is evaporated to dryness and derivatized with diazomethane in the presence of excess benzoic acid. The methyl benzoate formed acts as a keeper to reduce losses due to the volatility of the derivative in subsequent steps. The derivative is cleaned up using a silica gel column. Liver samples require an additional alumina column cleanup. The cleaned extract is analyzed by gas chromatography using an electron capture dectector. At the 0.01-2.0 ppm fortification levels in a dairy feeding study, recovery values were 61-89% for milk, 68-90% for fat and tissue, 78-79% for the liver and 61-88% for the kidney of cattle. At the 0.05-1.0 ppm fortification levels in a poultry feeding study, recovery levels were 51-91% for eggs, 62-94% for fat and tissue and 68-87% for the liver of poultry.

We conclude that the analytical methodologies determine the parent, propiconazole per se, and its phenolic metabolites which are converted to the 2,4-dicholorobenzoic acid moieties. The available methodology does not determine 1,2,4-triazole or its conjugates.

Residue Data - Rice

Data submitted reflect 5 field tests from Arkansas, Louisiana and Mississippi in which propiconazole was applied either twice: at internode elongation followed by a second application at booting to 0.169 lb act/A (0.6X) or at 0.28 lb act/A (1X); or once at internode elongation using 0.28 lb act/A (1X). One test plot received 2X dosage at internode elongation. Results showed no propiconazole residues (<0.05 ppm) were dected in the rice grain in all tests reflecting 53-80 day PHI's.

Based on these studies we estimate that residues of propicorrazole and its metabolites convertible to 2,4-dichlorobenzoic acid will not exceed 0.05 ppm in rice grain.

The available data do not permit us to estimate the levels of residues of 1,2,4-triazole and its conjugates in rice grain or its fractions.

No concentration of residues of propiconazole and its metabolites convertible to 2,4-dichlorobenzoic acid was observed in rice hulls, unpolished grain, polished grain and rice bran following treatments at internode elongation at 0.28 lb act/A (1X); at internode elongation at 0.56 lb act/A (2X); or at internode elongation at 0.14 lb act/A followed by a boot stage application at 0.14 lb act/A (1X). Concentration of residues in rice milling fractions was observed at exaggerated application rates and from applications at the heading stage.

Based on these studies we do not expect residues of propionazole and its metabolites convertible to 2,4-dichlorobenzoic acid to exceed 0.05 ppm in or on rice huls, polished rice and other milled rice products as a result of the proposed use.

Meat, Milk, Poultry and Eggs

A feeding study in dairy cows was included in this submission under acc.# 252458. In this study, four groups of 3 lactating holstein cows, each was fed diets containing propiconazole at 0, 15, 75 and 150 ppm for up to 28 days. Milk was sampled twice on test days 0, 1, 4, 7, 12, 14, 21, and 28 days. Tissues were taken from sacrificed animals four hours after last dose on test days 14, 21, and 28 days. Propiconazole per se and residues of propiconazole and its metabolites which contain the 2,4-dicholoro-benzyl moiety, determined as the methyl ester of 2,4- dicholoro-benzoic acid and reported as propiconazole equivalents were quantitated using the analytical methods described above.

Test results showed no parent (propiconazole per se) residues in milk samples (<0.01 ppm) and tissue (<0.05 ppm) at all feeding levels except liver and one fat sample. In the liver, residues of propiconazole per se were quantitated at 0.14, 0.34 and 0.66 ppm reflecting 15, 75 and 150 ppm feeding levels, respectively. In one fat sample, residues of propiconazole per se was determined at 0.08 ppm, only at the highest feeding level of 150 ppm. No residues were found in the milk (<0.01 ppm) at the 15 ppm feeding level. The maximum residues were 0.08 and 0.11 ppm, reflecting higher feeding levels of 75 and 150 ppm, respectively. No residues were found in the fat and tissue, except liver and kidney, at the lower feeding level of 15 ppm; whereas, at the higher feeding levels residues were 0.08-0.23 ppm at the 75 ppm feeding level and 0.13-0.26 ppm at the 150 ppm feeding level. In the kidney, residues were 0.63, 4.7 and 6.5 ppm, reflecting 15, 75 and 150 ppm feeding levels, respectively. Similarly, in the liver, propiconazole residues were determined at 0.81, 4.3 and 5.6 ppm, reflecting 15, 75 and 150 ppm feeding levels, respectively.

A feeding study in laying hens was included in this submission under acc.# 252456. In this study 90 mature white leghorn hens were divided into four groups and administered a diet containing propiconazole at 0, 7.5, 37.5 and 75 ppm for 28 days . Eggs were collected on test days 0, 1, 3, 7, 10, 14, 17, 21 and 28. Fat, liver and tissue were sampled after sacrifice on test days 7, 14, 21 and 28 days. Propiconazole per se and residues of propicon-azole and its metabolites which contain the 2,4-benzyl dichloro-benzyl moiety determined as the methyl ester of 2,4dicholoro-benzoic acid and reported as the propiconazole equivalents were quantitaed using the analytical methods described above.

Test results showed no parent, propiconazole per se, residues were detected in the eggs or tissues (<0.05 ppm), nor in the liver (<0.1 ppm) of poultry at all dosing levels. No propiconazole residues were detected in the eggs or tissues (<0.05 ppm), nor in the liver of poultry (<0.1 ppm) at the lower dosing level of 7.5 ppm. However, at the higher dosing levels of 37.5 and 75 ppm, propiconazole residues were quantitated at 0.18 and 0.37 ppm for eggs, 0.05 and 0.11 ppm for all tissues, except liver, and 0.16 ppm and 0.47 ppm for the liver of poultry, reflecting dosing levels of 37.5 and 75 ppm, respectively.

The feed items involved in this Section 18 are rice grain with hulls, and milled fractions of rice. Based on the above studies we estimate that secondary residues of propiconazole and its metabolites convertible to 2,4-dichlorobenzoic acid will not exceed 0.05 ppm in milk, eggs and the meat, fat and meat byproducts of cattle, goats, hogs, horses, and sheep as a result of this use.

The available data do not permit us to estimate the levels of secondary residues of 1,2,4-triazole and its conjugates in meat, milk, poultry and eggs from this use.

Conclusions

1. For the purpose of this Section 18 exemption we consider the resiudes of concern in plants and animals to be propiconazole, its metabolites convertible to 2,4-dichlorobenzoic acid and 1,2,4-triazole and its conjugates.

2a. Residues of propiconazole and its metabolites convertible to 2,4-dichlorobenzoic acid will not exceed 0.05 ppm in or on rice grain, rice hulls, polished rice and rice milled products.

2b. Secondary residues of propiconazole and its metabolites convertible to 2,4-dichlorobenzoic acid will not exceed 0.05 ppm in milk, eggs and the meat, fat and meat byproducts of cattle, goats, hogs, horses, poultry and sheep as a result of this use.

2c. The available residue data do not permit us to estimate the levels of residues of 1,2,4-triazole and its conjugates in rice grain and its fractions and in meat, milk, poultry and eggs. We defer to TOX regarding their concern over those residues.

3. The methods AG-356, PP#1G2530 for rice and its fractions and AG-359 Accession number 252548 for milk, eggs and animal tissues may be used for enforcement of this Section 18 exemption. The methods determine propiconazole and its metabolites convertible to 2,4-dichlorobenzoic acid; they do not determine 1,2,4-triazole or its conjugates.

Recommendation

TOX considerations permitting (Note Conclusion 2C) we have no objections to the issuance of this Section 18 exemption. An agreement should be made with FDA regarding the legal status of the treated rice in commerce.

cc: Propiconazole, S.F.
R.F.
Subject
Circu.
Reviewer
Section 18
TOX
RDI:E.Zager:4/3/84:RDS:3/4/84
TS-769:RCB:Reviewer:S.M.:wh:RM810:CM#2:X77324:3/26/84