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

NOV 8 1993

OFFICE OF
PREVENTION PESTICIDES AND
TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#8F3654. Propiconazole (Tilt®) in/on Peanuts.
Amendment Dated 12/23/92. (Received CBTS 10/1/93.)
DP Barcodes: D186202, D186203, D186205, D186206,
D195499. CBTS # 12638.
MRID # 426058-01.

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This submission is a response to our review dated 11/22/88 (H. Fonouni). Ciba-Geigy Corporation is proposing tolerances of 20, 1 and 0.2 ppm for residues of propiconazole in/on peanut hay, peanut hulls, and peanuts, respectively.

Permanent tolerances have been established under 40 CFR 180.434 for residues of propiconazole and its metabolites determined as 2,4-dichlorobenzoic acid (expressed as parent compound) on a number of raw agricultural commodities (racs), ranging from milk (0.05 ppm) to rice, straw (3.0 ppm). Tolerances of 2.0 have been proposed in conjunction with PP#8F3674 for the kidney and liver of cattle, goats, hogs, horses and sheep; and these tolerances have been established with an expiration date. Permanent tolerances are pending on corn grain, forage, fodder, sweet corn (K+CWHR) and pineapples (PP#8F3674); grass seed screenings, grass hay (straw) and grass forage (PP#1F3974); mint (PP#2E4037); and oat grain and straw (PP#2F4086). CBTS had no objection to establishment of tolerances with expiration dates for corn and grass racs (PP#8F3674, memo of 9/20/93; PP#1F3974, memo of 5/17/93).

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Summary of Deficiencies Remaining to Be Resolved

A storage stability study on peanuts is necessary. Additional residue data may be necessary.

Conclusions

1. The nature of the residue in plants and animals (ruminants) is adequately understood. The residue to be regulated is parent propiconazole and its metabolites determined as 2,4-dichlorobenzoic acid.

2. Adequate enforcement methodology exists to quantify propiconazole and its metabolites in crops and animal commodities. (PP#4F3074, PP#4F3007, PP#4E3026, memo of S. Malak, 5/28/87; PP#1F3974, memo of S. Willett, 6/11/91)

   Recovery data on peanut nutmeat, hulls and hay are acceptable. Data on peanut vines will be needed if the requested grazing restriction is ever removed.

3. The storage stability study on peanuts is unacceptable and must be redone for nutmeat, hulls and hay. We are reluctant to translate preliminary data on grasses grown for seed to any other rac at this time. Recoveries from grass forage at 25-months were unacceptably high.

4. Residue data support the proposed tolerances of 20, 1 and 0.2 ppm for residues of propiconazole and metabolites in/on peanut hay, peanut hulls and peanuts, respectively. However the storage stability study on peanuts also casts doubt on the validity of these analyses. This issue will be reexamined when an acceptable storage stability study is received. Additional residue data may be required.

5. Reexamination of results of processing peanuts to soapstock and presscake leads CBTS to conclude that Section 409 tolerances (FFDCA) for these commodities are not necessary. Processing studies gave variable results, and the apparent average net increase in residues may not be analytically significant.

6. Tolerances proposed for ruminant commodities in PP#8F3674 (for corn and pineapple) are appropriate and were discussed in our memo of 5/6/93.

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Recommendation

CBTS recommends against the proposed tolerances for reasons given in Conclusions 3 (storage stability) and 4 (residue data).

Detailed Considerations

Deficiencies listed in our 11/22/88 memo are given with Ciba-Geigy's response and our comments.

CBTS Deficiency #2 (Conclusion #2 from our 11/22/88 memo)

The petitioner should revise the label to include statements prohibiting aerial application and grazing of livestock in the treated areas.

Ciba-Geigy Response

A revised Section B has been submitted with the following restriction: Do not feed green vines to livestock or graze livestock in treated area.

EPA's requirement of a restriction against aerial application has been superseded by R.S. Quick's memo to R.F. Holt, NACA, in which the requirement has been removed for uses where the recommended application water volume is greater than 2 gallons/acre. Ciba-Geigy's minimum water volume for aerial application to peanuts is 5 gallons/A.

CBTS Comment

This deficiency is resolved.

CBTS Deficiency #3b

Although the previously submitted metabolism data were found to be adequate in conjunction with previous petitions which led to a negligible dietary exposure of livestock to residues of the fungicide and its metabolites, the currently proposed applications would result in considerably higher exposure levels. The petitioner should, therefore, conduct a metabolism study in lactating cows or goats using phenyl labelled ^{14}C-CGA-64250 to determine the nature of metabolites present, and provide an adequate material balance.

Ciba-Geigy Response

The company has submitted a goat metabolism study (MRID Number 41823301). This study was conditionally accepted by EPA in reference to our petition for tolerances in grasses grown for seed. The expected levels of propiconazole in peanut commodities that lead to transfer to animal diets should be adequately covered by these goat metabolism data.

CBTS Comment

The goat metabolism study was accepted by CBTS. The study

was reviewed by S. Willett in her memo of 6/11/91 for PP#1F3974. See also our comments in our 5/6/93 and 9/20/93 memos for PP#8F3674 (M. Flood).

This deficiency is resolved.

CBTS Deficiency #4a

Analytical methodologies provided are adequate for determination of known residues of 1-([2-(2,4-dichlorophenyl)-4-propyl-1,3-dioxolan-2-yl]methyl)-1H-1,2,4-triazole and its metabolites in the subject commodities. However, recovery data need to be submitted for peanut hay.

Ciba-Geigy Response

Recovery data for peanut hay were provided in the original report, ABR-88068, in Table IX. The title of the table inaccurately described the samples as peanut foliage, but in fact the samples were peanut hay, as reported in the individual analytical reports (AG-A Reports). The mean recovery for the 16 samples was 99% with a range of 80-133% and the standard deviation of ±14%.

CBTS Comment

This deficiency is resolved. Note, however, that should residue data on peanut vines be required, acceptable recoveries on this commodity would be necessary.

CBTS Deficiency #4b

We can not presently address the adequacy of previously submitted methodology for livestock products, until results from the study requested in 3b is evaluated. Should the livestock metabolism study lead to the detection of any new metabolite(s) of toxicological concern, additional enforcement method(s) may be required.

Ciba-Geigy Response

EPA has since determined that the analytical methodology for ruminants and poultry is adequate for enforcement purposes as described in EPA's review of PP No. 1F3974 [dated June 11, 1991]...

CBTS Comment

Our review of 6/11/91 (S. Willett) concluded that adequate enforcement methodology was available for both ruminants and poultry. Ruminant and poultry metabolism studies were also reviewed in that memo. This deficiency is resolved.

CBTS Deficiency #5b

Storage stability data should be provided for peanut hay. In addition, the petitioner should provide adequate explanation for the reported increase in residues of the fungicide/metabolites on nut meat which occurs as a result of storage. [Not listed in the Conclusions section of the memo but in the text: "Since the maximum lapse period between extraction and analysis of some samples is about four months, the

petitioner should provide information on conditions under which the extracted samples were stored".]

Ciba-Geigy Response

The data were previously reported under the name of peanut fodder, which is peanut hay.

"In the same study, the residues in peanut nutmeat samples were observed to increase by 249 to 333% over their initial value during the 25-month storage stability study. While this is a large relative increase in residues, the absolute increase was not as dramatic. In the worst case example, residues in peanut nutmeat samples receiving a 2.8X exaggerated rate treatment apparently increased from 0.15 ppm to 0.5 ppm. This increase was attributed in part to desiccation of samples in the freezer during the 25-month storage period and variability in the analytical method at the relatively low residue level measured. Further, this study was not a true storage stability study in that initial residue levels were unknown and were therefore determined by analysis."

Ciba-Geigy has shown elsewhere that "At refrigerator temperatures (4°C), field-incurred residues of propiconazole are stable for minimum periods of three and eight months in extracts of soybeans and corn silage-stage forage, respectively. We conclude that these data are sufficient to address the question of extract stability in the peanut study, since all extracts were stored at refrigerator temperature and analyzed within four months of extraction."

CBTS Comment

We agree that peanut fodder is peanut hay. Ciba-Geigy's explanation for the apparent increase in residues is plausible, but we observe that any analytical method giving residue levels of 0.15 ppm and 0.5 ppm for the same sample would be unacceptable. Desiccation is a more likely explanation, although error in analysis is also a possibility. The fact remains, however, that a major uncertainty exists in the residue analyses because of the uncertainty in storage stability.

The Phase 4 review of propiconazole, dated 6/30/92, concluded that the storage stability data for peanut fodder, shells and nutmeat were "completely inadequate". "No initial analysis was performed, control samples showed high residues, and recoveries were extremely excessive bringing into doubt the integrity of the study." A new storage stability study on peanuts is required. This deficiency remains.

Interim stability results for propiconazole residues in grasses grown for seed have been submitted as Table I. Five weathered forage, straw and seed samples were analyzed at 0, 5-

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months, 8-months, 17-months and 25-months. Average results for 0- and 25-months are give in the following table:

Table 1

Interim Stability Data for Grasses Grown for Seed Substrates
Average of Five Residue Values

Substrate	0-Day (ppm)	25-Month ppm%	Init.
Forage	0.79±0.17	1.15±0.18	147±16
Straw	33±26	32±19	105±19
Seeds	32±13	33±13	106±8

Recoveries for straw and seeds are slightly high but acceptable. Recoveries from forage are too high. This may indicate unreliability in the method at levels lower than about 1 ppm. We will not translate these storage stability results to other racs in which propiconazole residues are lower.

The only additional storage stability study currently available for propiconazole is a six-month study on soybeans. Grain and fodder control samples were fortified with 0.40 ppm propiconazole. Levels of propiconazole recovered at six months were 75% of the original level in forage and 62% of the original level in grain. In this study residues declined. Whether this decline is related to the fact that weathered residues were not used -- in contrast to the studies on peanuts and grass -- or there is some species specific action remains to be determined.

We agree that the issue of stability in extracts is resolved.

CBTS Deficiency #5c

Although residue data on livestock products have been provided in conjunction with other petitions, until the results from the requested metabolism study, 3b, are evaluated DEB can not comment on the adequacy of available data.

Ciba-Geigy Response

The previously submitted goat metabolism study along with the validation data for Method AG-517 (for determination of residues in animal substrates), demonstrate that the residues of toxicological concern containing the 2,4-dichlorophenyl moiety are adequately characterized and accounted for.

CBTS Comment

This deficiency is resolved.

CBTS Deficiency #6a

The petition has proposed tolerances of 0.20, 1.0, and 20.0 ppm for residues ....in or on peanuts, peanut hulls, and hay, respectively. The proposed tolerances adequately cover the expected residues in or on the subject commodities...However, the acceptability of the proposed tolerance in or on peanut hay is contingent upon submission of adequate recovery and storage stability data on the subject feed as requested in 4a and 5b, respectively. Since the maximum residues in or on peanut soapstock and presscake exceed the residues in comparable nut meat, DEB recommends feed additive tolerances of 0.40 ppm (each) be proposed for these processed commodities.

Ciba-Geigy Response

Ciba-Geigy believes that the proposed tolerances for peanut hay are adequate and are supported by the existing data and the responses provided for Conclusions 4a and 5b, above.

Ciba-Geigy believes that [peanut processing studies] support a tolerance of 0.2 ppm in peanut nutmeat and that feed additive tolerances are not required for soapstock nor presscake processed peanut commodities. Ciba-Geigy does agree with the reviewer that in selected samples there was an apparent increase in propiconazole residues in either soapstock or presscake processed commodities compared to the unprocessed nutmeat. However, on closer examination of the data it is apparent that the small increases in residues in these fractions are inconsistent between samples...

Soapstock residue data are summarized in the following table:

Applic. Rate (g ai/A)	Nutmeat Residue (ppm)	Soapstock Residue (ppm)	Ave. Soapstock Residue (ppm)	Concentration Factor
200	<0.05	0.06, 0.10, 0.05	0.07	>1.40
400	0.10	0.15, 0.13, 0.06	0.11	1.10
563	0.06	<0.05	<0.05	<0.83
563 + 340	0.11	<0.05	<0.05	<0.45
1126 + 680	0.19	0.12	0.12	0.63

Average Concentration Factor: ca. 0.88

Solvent-extracted presscake residue data are summarized in the following table:

Application Rate (g. ai/A)	Nutmeat Residue (ppm)	Presscake Residue (ppm)	Ave. Presscake Residue (ppm)	Concentration Factor
200	<0.05	0.08, 0.07	0.075	>1.5
400	0.10	0.16, 0.10	0.13	1.3
563	0.06	<0.05	<0.05	<0.83
563 + 340	0.11	0.10	0.10	0.91
1126 + 680	0.19	0.25	0.25	1.32

Average Concentration Factor: ca. 1.17

According to Ciba-Geigy, it is more appropriate to evaluate the potential for residue concentration in soapstock or presscake processed fractions based on the average concentration factor. However, even considering the maximum observed concentration factor in soapstock, >1.4X, or presscake, >1.5X, and the maximum residue found in a 1X nutmeat sample (0.10 ppm), residues in the corresponding processed fraction would still be below the proposed tolerance for nutmeat of 0.2 ppm. Further, both soapstock and presscake are used only as animal feed supplements....

CBTS Comment

The data for soapstock show no clear evidence of concentration of residues. Concentration in presscake is more likely, but even here the results are variable -- two out of five studies showed no concentration -- and we cannot say with a reasonable degree of certainty that residues in presscake would ever exceed the proposed tolerance of 0.2 ppm. (The tolerance of 0.2 ppm was originally proposed because residues in nutmeat from one field trial were 0.12 ppm.) An average concentration factor of 1.17 applied to the proposed tolerance would only produce a concentration of 0.23 ppm, indistinguishable analytically from 0.20 ppm. Even if the maximum observed factor were applied, the concentration would be 0.30 ppm and it is doubtful whether a definite regulatory conclusion could be drawn were such a level measured, given inherent uncertainties in the analytical method. We note that the two procedural recoveries from solvent extracted presscake were 107% and 66% at the 0.1 ppm fortification level.

CBTS will therefore not require 409 tolerances for soapstock and peanut meal. This deficiency is resolved.

Additional Comment -- Residue Data

The proposed tolerances were based on results of eight field trials. The storage stability data are a cause for concern over the validity of these residue data. For this reason it is possible that additional residue data will be required, depending on the resolution of the storage stability issue.

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CBTS Deficiency #6b

We cannot presently address the adequacy of established tolerances on meat, fat, liver, kidney, meat byproducts and milk until the issues raised in 3b, 4b and 5c are resolved.

CBTS Comment

All deficiencies are resolved except for storage stability and the possible need for additional residue data. Permanent tolerances for milk, fat and meat of ruminants have been established under 40 CFR 180.434 at 0.05, 0.1 and 0.1 ppm, respectively. Tolerances with expiration date have been established at 2.0 ppm for kidney and liver. These tolerances were deemed appropriate in our 5/6/93 memo for PP#8F3674. In that memo potential residues in cattle were estimated based on a diet of grass seed screenings, corn forage and corn grain. Such a diet would still represent a "maximum" likely source of propiconazole in the diet of ruminants.

cc: RF, Circu., PP#8F3654, List C Rereg. File, Mike Flood, E. Haeberer, J. Fleuchaus (LE-132P).

H7509C:CBTS:Reviewer(MTF):CM#2:Rm804P:703-305-7990:typist(mtf):11/8/93.
RDI:SectionHead:ETHaeberer:11/8/93.