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PP#0F2401: Pendimethalin in rice. Evalnation of analytical methods and residue data.

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The American Cyanamid Company proposes tolerances for residues of the herbicide pendimethalin, [N-(1-ethylpropyl)-3,4-dimethyl-2, 6-dinitrobenzenamine], in or on rice grain at 0.05 ppm.

Tolerances are established for combined residues of pendimethalin and its benzyl alcohol metabolite at 0.1 ppm in or on corn grain, corn fodder and forage, soybeans, soybean forage, and soybean hay (§180.361).

Tolerances for pendimethalin are pending for peanuts at 0.1 ppm (PP#6F1741), potatoes at 0.1 ppm (PP#9F2134), sorghum at 0.1 ppm (PP#9F2246), and sunflower seed at 0.1 ppm (PP#0F2373).

Conclusions

1. The petitioner should submit a definite application rate instead of a statement on the most effective rate.

2. Technical pendimethalin and the pendimethalin formulation contain a [redacted]

3. The nature of the residue in plants and animals is adequately understood. The parent compound, pendimethalin, is the significant component in rice grain. Pendimethalin and its 4-acid metabolite, 4-[(1-ethylpropyl)amino]-3,5-dinitro-o-toluic acid, are the significant components in the plant (this would include straw.)

4a. Adequate analytical methods are available for enforcement purposes for rice grain.

4b. A validated analytical method should be submitted for the 4-acid metabolite if it appears in field samples of rice straw.

5a. Residues of pendimethalin in rice grain or its processing fractions (hulls, bran, polishings) are not likely to exceed the proposed tolerance.

Additionally, residues of propanil in rice grain and straw will be adequately covered by the existing propanil tolerances.

5b. No residue data are submitted for rice straw, a livestock feed item. Such data are necessary in order to determine the level of pendimethalin and its 4-acid metabolite which is likely to be ingested by livestock. Also, a tolerance proposal will be needed to cover residues noted.

6. No residues are likely to occur in eggs and milk of livestock [§180.6(a)(3)]. The absence of rice straw residue data precludes valid conclusions as to whether such residues are likely to occur in meat, fat, and meat byproducts of livestock due to the feed use of rice straw.

7. There are no foreign tolerances to compare with U.S. tolerances.

Recommendation

We recommend against the proposed tolerance. A favorable recommendation is contingent upon the resolution of questions raised in Conclusions 1, 4(b), and 5(b).

Residues of the nitrosoamine, if any, in rice grain would be a maximum of 0.06 ppm. However, this level is an exaggerated estimate and should be viewed as merely an upper limit.

Detailed Considerations

Proposed Use

Pendimethalin is formulated as PROWL®, an emulsifiable concentrate containing 44% active ingredient (4 lb a.i./gal), for postemergence application to direct seeded rice prior to flooding as a tank-mix with propanil, (3',4'-dichloropropionanilide; Stam).

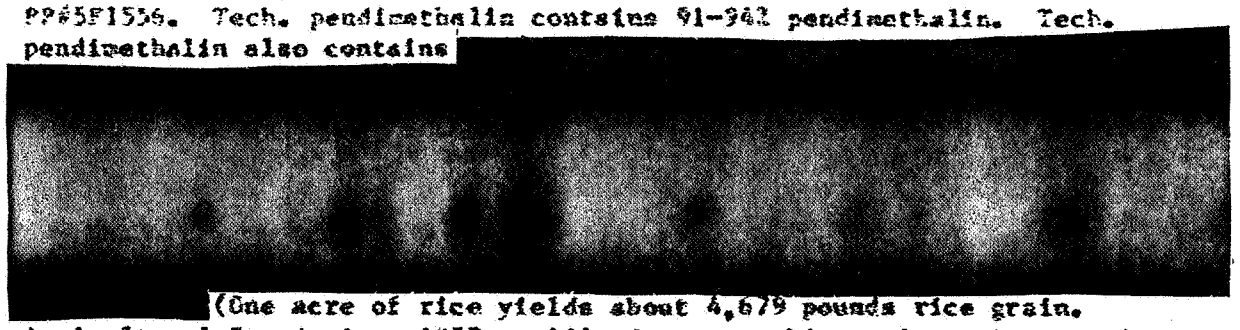
Apply 0.75-1.0 lb pendimethalin + 3.6-4.0 lb propanil per acre prior to flooding.

The petitioner merely states the above rates as most effective. A definite application rate should be submitted.

Propanil is registered for use on rice at a maximum rate of 6.0 lb act/A. Application is to occur postemergence before rice is in the late tiller stage (45-60 days after planting). No more than 3 pounds total per crop season is permitted. No application to second rice crop is permitted where double cropping is permitted. Propanil has established tolerances of 2 ppm on rice grain and 75 ppm on rice straw (§180.274).

The formulation's inert ingredients are cleared for use unde §120.1001.

The manufacturing process for technical pendimethalin is included in PP#5F1556. Tech. pendimethalin contains 91-94% pendimethalin. Tech. pendimethalin also contains



(One acre of rice yields about 4,679 pounds rice grain. Agricultural Statistics, 1977, p.19) However, this estimate is grossly exaggerated and should be viewed as merely an upper limit.

Nature of the Residue

Pendimethalin is absorbed by rice plants, translocated, and metabolized. The residues in the plant consist primarily of the parent compound, pendimethalin (CL 92,553), and its 4-acid metabolite 4-[(1-ethylpropyl) amino]-3,5-dinitro-o-toluic acid (CL 99,900) in a 1:1 ratio. In a greenhouse study, radiolabeled C^{14}-pendimethalin (as a granular formulation) was applied to flooded soils which contained seedling rice plants. The containers of flooded plants were kept in the greenhouse under artificial light. The treatment rate was equivalent to 3.0 lb act/A. (The proposed use is a postemergence application before flooding at a maximum of 1.0 lb act/A.)

The plants were sampled at 4, 8, and 20 weeks (harvest period) and analyzed for radioactivity. Radioactivity in plants increased with time. Residues were 0.20-0.24 ppm at four weeks, 0.24-0.28 ppm at 8 weeks, and 0.46-0.49 ppm at 20 weeks. The parent and its 4-acid metabolite represented 60% of the extracted plant residues. The remaining 40% was unknown, more polar components which was not further characterized. (Treatment of this material with diazomethane produced no apparent change.) Such material possibly represents natural plant constituents containing reincorporated C^{14} radioactivity.

In previous plant studies, the parent compound (CL 92,553) and its benzyl alcohol metabolite (CL 202,347) represented the major portion of the residue and, therefore, the significant components of concern. The 4-acid metabolite (an oxidation product of CL 202,347) is generally found, along with other detoxification products, but at very low levels (usually <10% of the residue). With the passage of time, an increase in the 4-acid metabolite is not unreasonable (i.e., the benzyl alcohol metabolite is converted to the 4-acid metabolite.). In this particular case of rice plants, there is a build up of the 4-acid metabolite. As a result, the parent compound and the 4-acid are the significant components of plant (which includes straw) residues.

The unknown more polar components did not respond to treatment with diazomethane. The metabolites of pendimethalin (which contain hydroxy and/or carboxylic acid groups) would be expected to show some response to this reagent when present. The absence of any response indicates that the unknown portion of the residue contained no metabolites of pendimethalin. This supports the conclusion that the C^{14}-radiolabeled material is C^{14}-activity which has been reincorporated into naturally-occurring plant constituents.

The rice seed were collected from the 20-week plants. Analyses were performed on rough rice (whole seed), hulled rice, and the hulls. The whole seed had 0.07 ppm radioactivity (expressed as parent), the rice without hulls had 0.05 ppm, and the hulls had 0.03 ppm. Thus, there is no apparent concentration of residues in the rice or hulls. (The radioactivity levels were too low for characterization.)

Analyses were preformed by methanol extraction of homogenized samples, and evaporation of the solvent. The radioactivity in the residue is determined by combustion analysis using a scintillation spectrometer. Characterization and identification of the residues were performed by radiometric techniques using two-dimensional thin layer chromatography.

We have considered the plant and animal metabolism of pendimethalin in previous reviews (PP#6G1739, PP#5F1556, PP#6G1740). Pendimethalin is absorbed, metabolized, and translocated by bean, potato, corn, cotton, and peanut plants. The metabolism of pendimethalin in rice plants is similar to that in the above plants. The significant components in plant residues are the parent compound, pendimethalin, and its benzyl alcohol metabolite. (The 4-acid metabolite is an oxidation product of the benzyl alcohol metabolite.)

The significant components in <u>rice plants</u> are pendimethalin and its 4-acid metabolite. The significant components in the <u>rice grain</u> are pendimethalin and its benzyl alcohol metabolite.

Feeding studies with animals show that ingested pendimethalin is extensively metabolized and excreted by cows, goats, and rats. Some deposition of residues occur in tissues, but no tendency toward storage or concentration is noted.

The nature of the residue in plants and animals is adequately delineated.

Analytical Method

A ground sample of rice straw is extracted by blending with methanol and filtering. An aliquot of the filtrate is acidified with hydrochloric acid, and residues are extracted into hexane which is evaporated. The residue is held for florisil column cleanup.

A ground rice grain sample is extracted by blending with a methanol/chloroform solvent system and filtering. An aliquot of the filtrate is evaporated to dryness, and the residue is taken up in hexane. The residues are extracted into acetonitrile which is evaporated to dryness. The residue is saved for florisil column cleanup.

The residues from the rice straw and the rice grain are separately cleaned up on a florisil column and eluted with a mixture of benzene and hexane. The eluate is evaporated to dryness, and the residue is taken up with benzene.

Residues in the benzene solution are determined by gas-liquid chromatography using an electron capture detection system (ECGC).

Untreated (control) samples of rice grain and rice straw had no detectable residues of pendimethalin (<0.01 ppm). Control samples of grain and straw were fortified with pendimethalin at levels of 0.05-1.0 ppm. Recoveries averaged 87-112%.

The method has been successfully tested with pendimethalin on cottonseed at levels of 0.05 ppm and 0.1 ppm (PP#5F1556).

A method for the benzyl alcohol metabolite has also been successfully tested on cottonseed at the same levels.

We believe that results of the method trials can be extended to include rice grain. A validated analytical method is needed for the 4-acid method. The method is necessary to show the absence or presence of the 4-acid component in rice straw.

A confirmatory procedure for pendimethalin and its metabolites is available (PP#5F1556).

Adequate analytical methods are available for enforcement of the tolerance for rice grain.

Propanil

Validated analytical methods are available (PAM II, methods I and II) for residue determinations in rice grain and straw and for enforcement purposes. The method II (Rohm & Haas) was used to determine propanil residues in rice grain and rice straw.

Residue Data

Samples were obtained from crops in Texas, Louisiana, and Arkansas which had single applications of Prowl alone at rates of 1.0 lb act/A and 3.0 act/A and harvested at 99 and 104 days after treatment (PHI). The proposed tank-mix treatments were single postemergence applications of 0.75-1.0 lb pendimethalin plus 1.5-3.0 lb propanil/A with PHIs of 112 and 113 days.

Residues of pendimethalin in rice grain were less than 0.05 ppm (no detectable residues). The absence of detectable residues in the grain precludes residue levels greater than 0.05 ppm in the grain byproducts (bran, polishings). Moreover, the rice metabolism study showed that residues in the hull are not likely to exceed those in the grain.

Residues of pendimethalin in rice grain or its processing fractions (hulls, bran, polishings) are not likely to exceed the proposed rice grain tolerance of 0.05 ppm. (The metabolism study indicated that the benzyl alcohol metabolite is not present in rice grain.)

No residue data are submitted for rice straw. The straw is occasionally used as a feed for livestock. Thus, residue data which show the level of residues likely to be ingested are necessary. The metabolism study indicates that the residue level and the residue components are different from those of the grain. (The plant components are pendimethalin and its 4-acid metabolite (1:1), 4-[(1-ethylpropyl)amino]-3,5-dinitro-o-toluic acid. Generally, the significant components of plants have been shown to be pendimethalin and its metabolite, 4-[(1-ethylpropyl)amino]-2-methyl-3, 5-dinitro benzyl alcohol. The 4-acid metabolite is an oxidation product of the benzyl alcohol metabolite.)

The tolerance proposals should be revised to include rice straw. A validated analytical method which determined pendimethalin and its 4-acid metabolite should also be submitted.

Residues of propanil in rice grain (<0.05 ppm) and rice straw (<0.05-0.42 ppm) will be adequately covered by the established tolerances for rice grain (2 ppm) and rice straw (75 ppm).

Meat, Milk, and Eggs

Livestock feeding studies were submitted in PP#5F1556. Lactating cows and lactating goats were fed pendimethalin daily at dietary levels of 0.5, 1.5, and 30 ppm (gozet) for periods of 10-21 days. No residues were noted in the milk of cows or goats due to feeding levels of 0.5-1.5 ppm.

Tissue analyses were performed only on the goats. Low levels of total radioactivity were noted. The liver had activity equivalent to 0.03, 0.04, and 0.25 ppm corresponding to the 0.5, 1.5, and 20 ppm feeding levels. The kidney had respective residue levels of 0.01, 0.04, and 0.09 ppm. The fat had residue levels of 0.01, 0.01, and 0.03 ppm from respective feedings levels of 0.5, 1.5, and 20 ppm. All other tissues had no detectable radioactivity (<0.01 ppm, method detection limit) from all feeding levels. Characterization of the urine and feces showed pendimethalin to be extensively metabolized and rapidly excreted. It is therefore probable that pendimethalin and its metabolite represent only a small portion of the total radioactivity noted in some tissues.

Rough rice grain, rice byproducts (bran, polishing), and rice straw are used as livestock (except pigs) feed items. (Straw is not fed to dairy cattle or poultry.) We have concluded that residues in rice grain, rice bran, and polishings would be <0.05 ppm. If we consider the exaggerated case in which cattle, poultry, horses, goats, and sheep ingested a diet consisting wholly of grain, bran, or polishings, then the maximum level of pendimethalin likely to be ingested would be 0.02 ppm. As a result, no residues of pendimethalin would be expected in eggs, milk, meat, fat, and meat byproducts of livestock from these feed items [§180.6(a)(3)].

No residue data are submitted which indicate the level of residues expected in rice straw. Without such data, we are unable to determine if pendimethalin residues are likely to result in meat, fat, and meat byproducts of beef cattle, goats, horses, and sheep.

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cc:RF, CIRC., SMITH, WATTS, FDA, TOX, EEB, EFB, PP#0F2401
RDI: QUICK, 1/23/81: SCHMITT, 1/26/81

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Pendimethalin

PETITION NO. OF2401 (A. Smith)

Codex States

☐ No Codex Proposal Step 6 or above

Residue (if Step 9): NONE

Crop(s)	Limit (mg/kg)
NONE	

Proposed U.S. Tolerances

N-(1-ethylpropyl)-3,4-dimethyl-2,6-dinitrobenzenamine

Residue:

Crop(s)	Tol. (ppm)
Rice grain	0.05

CANADIAN LIMIT

Residue: NONE

Crop	Limit (ppm)
NONE	

MEXICAN TOLERANCIA

Residue: NONE

Crop	Tolerancia (ppm)
NONE	

Note: