US EPA ARCHIVE DOCUMENT

NOV 27 1973

November 23, 1973

PP# 3F1410 and FAP# 3H4033. Benomyl on citrus. Evaluation of analytical method and residue data.

Coordination Branch and Toxicology Branch

The E.I. duPont de Nemours Co. proposes establishment of a pesticide residue tolerance for combined residues of the fungicide benomyl [methyl-1-(butylcarbamoyl)-2-benzimidazolecarbamate] and its metabolites containing the benzimidazole moiety in or on the raw agricultural commodity citrus fruits at 10 ppm (from preharvest and/or postharvest application) and a food additive tolerance for residues in dried citrus pulp at 50 ppm.

Tolerances have been established for residues of benomyl (Sec. 180.294) in or on various stonefruits at 15 ppm (PP# 0F1000), in or on bananas at 1 ppm (PP# 0F0906), in or on apples and pears at 7 ppm (PP# 1F1033 and FAP# 2H5009 for 70 ppm on dried apple pomace), in or on cucumbers, summer squash, melons at 1 ppm (PP# 1F1045), in or on celery at 3 ppm (PP# 1F1145), in or on citrus fruit (PP# 2F1197), strawberries at 5 ppm (PP#2F1212), in or on grapes at 10 ppm, with 0.1 ppm on meat and meat by-products and with 125 ppm on dried grape pomace and raisin waste (PP# 2F1218 and FAP# 2H5004), and in or on nuts at 0.2 ppm (PP# 2F1240). Tolerances have also been established for benomyl in milk, meat, fat and meat by-products of poultry and livestock.

Tolerance requests are pending for residues of benomyl in or on beans at 2 ppm and bean vines at 50 ppm (PP# 4F1421) and in or on pineapples for postharvest treatment at 35 ppm(PP# 4F1427).

Conclusions:

1. The metabolism of Benomyl in plants and animals is adequately understood.
2. The data are adequate to show that there is little if any conversion of benomyl to STB or BUB during drying of citrus pulp.
3. Adequate analytical methods are available to enforce the proposed tolerance for benomyl and its metabolites containing the benzimidazole moiety.
4a. The residue data submitted for preharvest applications do not reflect the proposed usage. There is no limitation as to the number of applications a grove would normally receive. Where data are submitted on multiple applications the doses are low and the PHI is excessive. Data are needed to reflect the proposed use.
4b. There are no data to determine maximum residue levels when postharvest control of Penicillium is necessary. [There is no way to evaluate how many applications a grove has undergone before it receives treatment at postharvest, specifically for Penicillium]. Data are needed to reflect the proposed use.
4c. Since we cannot draw any conclusions as to what the maximum residues will be in the fruit we must defer judgement on an adequate food additive tolerance level until more relevant data are available.

5. We cannot make a Sec. 180.6(a) conclusion until the question of residue levels in the actual feed item is resolved.

Recommendations

We recommend that the permanent tolerances of 10 ppm for benomyl in or on citrus and 40 ppm on dried citrus pulp not be established due to conclusions 4a, 4b, 4c and 5.

## Detailed Considerations

Formulation:

Benlate Benomyl Fungicide is formulated as a 50% wettable powder. The remainder is composed of inert ingredients. All of the inerts are now contained in Sec. 180.1001 (c).

Proposed Use

The proposed use of benomyl is for the control of certain diseases of citrus such as scab, greasy spot, green mold, blue mold, stem-end rot and postharvest fruit decay caused by Penicillium sp., and Diplodia.

Preharvest Use:

The formulation is to be applied as a spray with ground equipment, using enough water to insure complete coverage of grove trees. The chemical is not to be used in conjunction with alkaline pesticides, such as basic copper sulfate or Bordeaux mixture or lime sulfur. Additionally livestock are not to be grazed in treated areas.

For Scab: Apply 0.75-1.5 lbs act/acre during mid-June to mid-July. There is no indication of how many treatments are used on the average.

For Fruit Decay: Apply 0.5-1 lb act/acre anytime from 3 weeks prior to harvest up to day of harvest. Therefore, the possibility exists of a preharvest spray on the day of harvest and a postharvest treatment on the same day.

Postharvest Use:

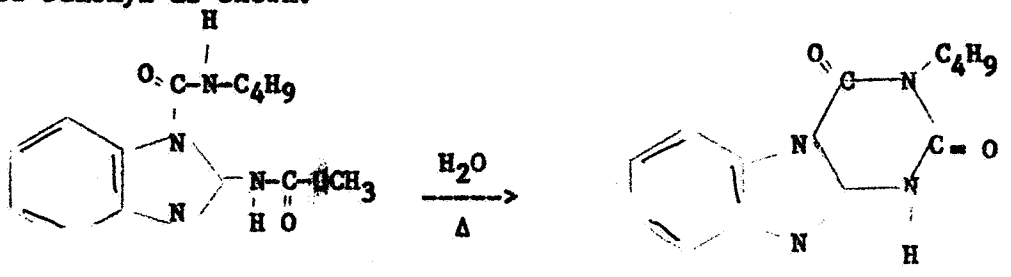
For Fruit Decay: Apply as a dip, flood or spray using 0.5-1.0 lb act/100 gal (600-1200 ppm) in water. Citrus wax may also be incorporated. A citrus wax spray using 2 lbs act/100 gal (2400 ppm) is also permitted for use in control of Penicillium.

**Nature of the Residue:**

The metabolism of benomyl in plants was adequately discussed in PP# 0F0936. Oranges were dipped in a suspension of 315 ppm of 2-$C^{14}$ labelled benomyl. TLC showed that the residues are in or on the peel. The metabolites in or on the peel after one day were 90% benomyl and 10% as methyl 2-$C^{14}$ benzimidazolecarbamate. After 61 days residues are 61% benomyl and 39% methyl 2-$C^{14}$ benzimidazolecarbamate. Residues in the pulp were <0.05 ppm. The 2-$C^{14}$ benzimidazolecarbamate further degrades slowly to 2-aminobenzimidazole, then to $CO_2$ and other fragments.

The metabolism of benomyl in animals has been discussed in PP# 0G0936 and PP# 1F1010. Two new metabolites, methyl-4 and 5 hydroxy-2-benzimidazolecarbamate are formed in animals.

Two new compounds have been found to occur from heat and alkaline conversion of benomyl as shown.

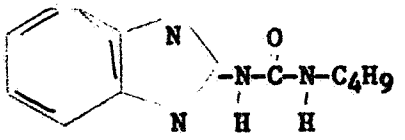



BENOMYL

STB

1,2,3,4-tetrahydro-3-butyl-2,4-dioxo-5-triazino [α] benzimidazole

↓ BASE, Δ




1-(2-benzimidazoyl)-3-N-butyl urea

BUB

Modification of the label restricting the use of benomyl in conjunction with alkaline pesticide formulations has been considered adequate to cover this problem. Analyses for STB were conducted by liming of the fruit and examination of the residue for STB. No STB (<0.1 ppm) was found.

Additionally, the question arises as to whether drying operations can convert benomyl to STB or BUB. Analyses of commercially prepared dried pulp showed no residue of STB (<0.1 ppm).

Therefore STB and BUB are not a problem. We consider the metabolism of benomyl in citrus to be understood.

Analytical Method

Residue data were obtained by fluorometric and liquid chromatographic procedures by the method of Pease and Holt JAOAC, 54,6,1971, p. 1399.

Recovery studies (fluorometric) on oranges showed recoveries averaging 82% for fresh fruit and 99% for wet pulp where 0.20 to 2.0 ppm of benomyl were added. Recoveries for press cake (before liming and with 0.40 and 1 ppm added) were 116%; for press liquor (0.40 and 1.0 ppm added) at 79%; and for molasses (0.20 and 0.40 ppm added) at 126%. Good recovery values were obtained for grapefruit also.

We estimate the sensitivity of the method to be 0.5 ppm. Control values ranged from a low of 0.08 to a high of 0.49 ppm for both fresh fruit and pressed citrus cake. We anticipate that these control values will present no problems in relation to the proposed tolerances. Additionally, we would expect the method as modified by AMS to give lower control values and improved sensitivity.

The fluorometric procedure has been successfully tested by both our Analytical Methods Section and by FDA Kansas City District on bananas in connection with PP# OF0906. Satisfactory recoveries were obtained at fortification levels of 0.2 and 0.4 ppm. A modified version of the method which can be used for confirmatory purposes was developed by AMS.

Recovery studies (LC) for oranges where 0.20 to 4 ppm were added averaged 102% and were good for grapefruit, limes, lemons and tangelos. The studies for STB reflected lower recoveries for various fractions of oranges. These ranged from 50% for press liquor fortified with 0.10 to 0.60 ppm, to 76% for fresh fruits fortified with 0.10 to 0.40 ppm.

Since the method is now described for benomyl and its metabolites containing the benzimidazole moiety and since all possible metabolites described possess the benzimidazole moiety we feel the analytical method is adequate for both enforcement purposes and for obtaining residue data.

Residue data:

The data submitted here is, for the most part, repeated from PP# 2G1197. Additionally, the use pattern has been changed from what it was and the PHI can now be as low as zero days. There are no data to support these changes. There are only two values reflecting zero days PHI preharvest spray; one for oranges was 0.3 ppm at 3.1 lbs A/acre and one for limes at 0.5 lbs A/acre at 1.2 ppm. Only the value for limes had a postharvest dip at 2#/100 gal which resulted in a residue of 5.4 ppm. Also, the maximum rate has been changed (from PP# 2G1197) for greasy spot control from 1 to 1.5 lbs A/acre. In general the data submitted do not reflect the higher uses. The data are not adequate to show that under conditions of multiple applications at maximum allowed usage as well as a zero day preharvest application followed by a dip at maximum concentrations for Penicillium the residues will not exceed the proposed tolerance. Residue data will be required to evaluate these higher rates. The data indicate that if a grove received two or three applications at 1 lb. A/acre and another application at zero days harvest conceivably a level of 5 ppm could result. Postharvest treatment normally could yield 5 ppm. Penicillium treatment could result in a level greater than the proposed tolerance.

There are no data reflecting the maximum proposed use in combination i.e. (pre and postharvest). While we agree that a concentration of 10 X will be adequate in evaluating the food additive tolerance an appropriate tolerance level cannot be determined. Therefore, we must defer any final conclusion on a food additive tolerance until additional data are made available.

Meat, Milk and Eggs

Dried citrus pulp can be utilized in cattle feed at levels of 25-35% of the diet. The available data are not adequate to determine the residues likely to be encountered in the process of obtaining the dried citrus pulp (see residue data above). Feeding studies have been submitted in PP#2F1192 and PP#2F1218. Since data are not available to support the Food additive tolerance of 50 ppm, we cannot make a decision relative to Sec. 180.6(a).

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FDRGee: 11/23/73