US EPA ARCHIVE DOCUMENT

18 JAN 1980

PP# 9G2204. BAS 352F in or on lettuce and stone fruits (peaches, apricots, cherries, nectarines, plums). Evaluation of analytical methodology and residue data.

S. D. Davis, Ph.D, Chemist, RCB, HED (TS-769)

PM# 21 (H. Jacoby) and TOX, HED (TS-769)

THRU: Richard D. Schmitt, Acting Chief, Residue Chemistry Branch (TS-769)

BASF Wyandotte Corporation proposes that the following tolerances be established for residues of the fungicide 3-(3,5-dichlorophenyl)-5-ethenyl-5-methyl-2,4-oxazolidinedione [BAS 352F, vinclozolin (ISO prop.), Ronilan] and its dichloroaniline - containing metabolites:

peaches	25 ppm
apricots	25 ppm
lettuce	10 ppm
cherries	5 ppm
nectarines	2.5 ppm
plums	1.0 ppm

No permanent tolerances exist for BAS 352F, although a petition proposing a tolerance of 10 ppm in or on strawberries is pending (PP# 9F2205). A temporary tolerance has been established previously at 5 ppm for residues in or on strawberries.

The petitioner requests an experimental use permit for the testing of 4,050 lb Ronilan (2025 lb ai) on 7,700 acres of lettuce in 11 states and 14,616 lb Ronilan (7.308 lb ai) on 8,400 acres of stone fruit in 25 states.

Conclusions

1. The inert [redacted] does not appear to be cleared under §180.1001. The petitioner will need to obtain clearance for this inert or substitute a suitable alternate.

2a. The label restrictions for lettuce which state, "Do not apply more than 6 lb. of Ronilan in one season" are inappropriate and should be deleted or revised to specify the maximum amount applied per acre in one season.

2b. The label restrictions for stone fruit which state, "Do not apply more than 14 lb. of Ronilan in one season" are inappropriate and should be deleted or revised to indicate the maximum number of applications permitted per season.

3a. We consider the metabolism studies adequate to demonstrate that the parent compound and its 3,5-dichloroaniline - containing metabolites are the residues of concern in lettuce and stone fruit.

INERT INGREDIENT INFORMATION IS NOT INCLUDED

3b. For the purposes of this petition in which no animal feed item is involved, we consider the nature of the residue in animals to be adequately delineated. For any future proposed tolerances involving animal feed uses, a large animal (lactating ruminant) metabolism study will be required.

4. No gas chromatograms were included to support the petitioner's claim that BAS 352F and its metabolites (determined as acylated 3,5-dichloroaniline) could be distinguished by GC analysis from the pesticides registered for use on stone fruits and lettuce. We will require raw data, including chromatograms, in order to determine whether the analytical method is adequate for enforcement purposes.

5a. We judge the proposed tolerance of 10 ppm inadequate to cover residues in or on lettuce which may result from this use. We will require additional residue data reflecting the proposed use in order to determine an appropriate tolerance level.

5b. The available residue data for stone fruits do not specify the application rates in terms of lb ai/100 gal or indicate the concentration or spray volume per acre for most samples. We are therefore unable to determine the adequacy of the proposed tolerances for stone fruits. Additional data reflecting the proposed application rates in terms of lb ai/100 gal will be required. The petitioner should also be asked to consider expressing the tolerance for nectarines in whole numbers.

6. Because no animal or poultry feed items are involved in this petition, there is no reasonable likelihood of secondary residues in meat, milk, poultry, or eggs, and Category 3 of Section 180.6(a) applies for this proposed use.

Recommendation

We recommend against establishment of these tolerances because of conclusions 1, 2a, 2b, 4, 5a, and 5b.

Note to PM: If and when these tolerances are established, they should be expressed in the more specific terms of parent and its 3,5-dichloroaniline metabolites rather than the broader term dichloroaniline metabolites.

Detailed Considerations

Manufacturing Process

The manufacturing process has been described in our previous review (memo of M. Nelson, 7/23/79, PP# 9F2205). BAS 352F is prepared by the [redacted]

Formulation

Ronilan fungicide (50W) is formulated in Germany as a 50% wettable powder. All of the inerts are cleared for use under 40 CFR 180.1001(c) except [redacted] We are

(MEET INGREDIENT INFORMATION IS NOT INCLUDED
MANUFACTURING PROCESS INFORMATION IS NOT INCLUDED)
(MANUFACTURING PROCESS INFORMATION IS NOT INCLUDED
(MEET INGREDIENT INFORMATION IS NOT INCLUDED)

advised by J. A. Shaughnessy, RD (telecon, 11/14/79) that RD records do not indicate this to be an exempted inert. [redacted] The petitioner will need to obtain clearance for this inert from this Agency or substitute a suitable alternate.

The technical material is 93% pure. Impurities include a maximum [redacted]

We do not expect a residue problem from the low levels of these impurities.

Proposed Use

Lettuce

Up to 3 applications per season may be made with ground equipment at rates of 0.5 - 1 lb act/A. Initial application is recommended within 2 days after thinning or 7-10 days after transplanting lettuce, with subsequent applications 14 days apart. No limitation on treatment to harvest interval is specified.

The label restrictions which state, "Do not apply more than 6 lb. of Ronilan in one season" are inappropriate and should be deleted or revised to specify the maximum amount applied per acre in one season.

Stone Fruits

For control of brown rot blossom and twig blight on stone fruits, the petitioner proposes a minimum of 2 applications at 0.75-1 lb act/100 gal of spray with 14 days between applications and up to 3 additional blossom sprays at 7-10 day intervals. For fruit brown rot, 2 applications at 0.75-1 lb act/100 gal of spray are recommended, the first 21 days before harvest and the second 10-14 days before harvest.

The label restrictions which state, "Do not apply more than 14 lb of Ronilan in one season" are inappropriate and should be deleted or revised to indicate the maximum number of applications permitted per season.

Nature of Residue

Studies of the metabolism of ^{14}C - uniformly ring labeled BAS 352F in strawberries, grapes, rats, and soil have been detailed in our evaluation of PP# 8G2068 (memo of G. Makhijani, 1/19/79). Summaries of metabolic pathways and designation of structures are attached (Attachments 1 and 2). In strawberries, the principal metabolites are B and T; which degrade to form D, 3,5-dichloroaniline, which is conjugated.

Data submitted with this petition indicate decarboxylation, dealkylation, and conjugation in lettuce and peaches treated with BAS 352F-phenyl-U-^{14}C (see Attachment 3). Lettuce was treated twice at 1 lb/a (1.12 Kg ai/ha) at the two - true leaf stage and 19 days later. Autoradiography suggests uniform trans-

location within 1 day from the foliar application site thoughout the plant. The half-life of the parent compound was 4.3 days in the radioactive dissipation study and 5 days in nonradioactive field studies.

Lettuce samples were homoganized with methanol, filtered, extracted with methanol, concentrated, dissolved in water, and partitioned with ethyl acetate or with butanol following acidification. After further partitions, samples were analyzed by TLC, HPLC, and GC - MS. Aliquots of the butanol partition phase were acid hydrolyzed or digested with B-glucosidase or pectinase enzymes and counted. Total residues were quantitated by the proposed analytical enforcement method which measures 3,5-dichloroaniline-containing moieties. The major metabolites were B, E, and S, and a small amount of A was also formed. Metabolite B was conjugated to pectin, while S formed T prior to rapid conjugation. Metabolite E was degraded F.

Close agreement was observed between samples measured by the radioassay-combustion method and those quantified by the analytical GC-EC method. In a 12-day lettuce sample, 0.91 ppm or 92% of the total radioactive residues were found by radioassay after processing through the residue method, and 1.14 ppm were measured by GC-EC.

After 21 days virtually all of the parent material had been oxidized to a polar material most of which contained the dichloroaniline moiety and pectin. The radioactive polar residues were also quantified according to the analytical method using GC-EC and the identity of the dichloroaniline moiety confirmed by GC-MS and two-dimensional TLC. Over 85% of the polar residues contained the intact dichloroaniline moiety which could be released by alkaline hydrolysis from a larger structure. Of the 0.22 ppm total radioactive residues found by radioassay, 0.19 ppm were measured by the analytical GC-EC method.

A similar fractionation scheme was employed to identify and quantitate the metabolites of BAS 352F in peaches. Approximately 90 peaches of 1-3 inches diameter were painted evenly with a 0.1% aqueous solution of ^{14}C-uniformly ring-labeled parent compound as a 50% WP at 0.75 kg ai/ha. Samples of flesh plus peel were separated from stones and fractionation continued, with characterization of metabolites by TLC, silica gel column chromatography, HPLC, and GC-MS. The following metabolites were observed: B, 12.7%; E, 4.6%; S, 4.8%; D, 9.6%; and 51% as a very polar material, 82% of which contained components with molecular weights > 500 (53% > 10,000) and partially labile to glycolytic enzymes. The polar material also contained the 3,5 dichloroaniline moiety. The half-life of the parent compound was 9-10 days, and the half-life of the total radioactive residues was about 16 days according to one dissipation study. The 3,5-dichloroaniline moiety comprises nearly 85% of total radioactive residues.

In one peach stone, nutmeat and shell were analyzed separately. In the shell, a new metabolite, 3-chloroaniline, was detected by HPLC and confirmed by GC-MS. We consider it unnecessary to include this metabolite in the proposed tolerances, since shells are not used as food.

We consider the metabolism studies adequate to demonstrate that the parent compound and metabolites containing the 3,5-dichloroaniline moiety are the residues of concern in lettuce and stone fruits.

Earlier studies suggest that metabolism in rats is similar to that in plants, except Metabolite F is the major metabolite. Metabolite F, a dihydroxybutanoic acid, degrades further to produce D. For the purposes of this petition in which no animal feed item is involved, we consider the nature of the residue in animals to be adequately delineated. For any future proposed tolerances involving animal feed uses, a large animal (lactating ruminant) metabolism study will be required.

Analytical Methodology

Residues were analyzed by an adaptation of the method previously used for strawberries (BWC Analytical Method No. 25 for strawberries, 25A for lettuce, 25B for stone fruits), which determines residues of BAS 352F and its 3,5-dichloroaniline-containing metabolites. The method involves release of 3,5-dichloroaniline from BAS 352F and its metabolites which contain this moiety by alkaline hydrolysis and simultaneous steam distillation to achieve quantitative isolation, chloroform partition for clean-up, and analysis by GC-EC of the acylated derivative of 3,5-dichloroaniline (DCAD).

A confirmatory method submitted in PP# 9F2205 includes use of an alternate GC-EC column and/or use of N-specific electrolytic conductivity detector.

The method has undergone a successful method trial on strawberries fortified at 10 and 20 ppm (PP# 9F2205, memo of S. P. Nakhjiani, 9/7/79). Recoveries ranged from 74.0% - 99.6%. The controls were 0.05 ppm.

Lettuce samples were fortified prior to alkaline hydrolysis at 0.05 - 100 ppm with BAS 352F and at 0.05 - 10 ppm with metabolites B, D, E, or S. Metabolite B has not been identified in lettuce but was included in the recovery experiments. Recoveries averaged 97% for BAS 352F (ranged 68% - 129%), 95% for B (75 - 123%), 86% for D (61 - 115%), 89% for E (65 - 125%), 100% for S (71 - 130%). The method was sensitive to at least 0.05 ppm with controls 0.05 ppm.

Stone fruit samples were fortified at levels ranging from 0.05 - 20 ppm BAS 352F and metabolites B, D, E, and S. Recovery averaged 94% for BAS 352F (70 - 103%), 90% for B (71 - 120%), 95% for D (69 - 120%), 101% for E (64 - 123%), 98% for S (71 - 120%). The method was sensitive to 0.05 ppm, and controls were 0.05 ppm.

No gas chromatograms were included to support the petitioner's claim that BAS 352F and its metabolites (determined as DCAD) could be distinguished on the basis of GC analysis from 49 pesticides registered for use on lettuce and 91 registered for use on stone fruits. We will require raw data, including chromatograms, in order to determine whether the analytical methodology is adequate for enforcement purposes.

Residue Data
Storage Stability

Lettuce

Data for the first 5 months of a 2-year storage study were submitted. Samples were fortified at 2 ppm and frozen at - 15 C. Duplicate samples were analyzed monthly. Recoveries for BAS 352F averaged 99% (89-

110%), for metabolite B 107% (100 - 115%), for metabolite E 101% (84-124%), metabolite S 103% (90 - 121%). We consider the data adequate to demonstrate that BAS 352F and three of its metabolites in lettuce are stable over 5 months of freezing.

Stone Fruits

A similiar two-year study was initiated for stone fruits and data submitted for the first six months of storage. In samples fortified at 2 ppm, recoveries were 94% from BAS 352F (90 - 101%), 89% for metabolite B (80 - 102%), 94% for metabolite E (91 - 96%), and 102% for metabolite S (8% - 111%), demonstrative that the parent compound and three of its metabolites are stable for 6 months under these storage conditions.

Field Studies

Lettuce

Residue data were obtained from lettuce without wrapper leaves removed. Harvest samples reflected 1-3 applications at 0.5 or 1 lb ai/a and 24 - 56 days PHI. Because there is no built-in PHI inherent in the proposed use and no limitation on treatment to harvest interval specified, we have evaluated residue data collected at 0 or 1 day PHI following 2 applications at 1 lb ai/a in dissipation studies. We have assumed a 55 - 80 day maturity period for head lettuce and 45 - 60 day period for leaf lettuce with thinning 2-4 weeks after seeding or transplanting 3 weeks after planting.

Of the 4 samples available, all contained residues exceeding the proposed tolerance, even with fewer applications than the maximum permitted by the proposed use. Residues ranged from 12.3 - 60 ppm. In one dissipation study, residues exceeding the tolerance were observed evan after 5 days. We judge the proposed tolerance of 10 ppm inadequate to cover residues which may result from this use. We will require additional residue data reflecting the proposed use in order to determine an appropriate tolerance level.

Stone Fruits

For most of the stone fruit samples, treatment rates are not expressed in terms of lb ai/100 gal. In the absence of residue data reflecting the proposed use, we are unable to determine the adequacy of the proposed tolerances.

Peaches

Peaches were treated 1-12 times at 0.5 - 3 lb ai/a and harvested at 0 - 132 days after treatment. Spray volumes were specified for only a few samples. Residues ranged from 0.89 - 4.3 ppm in 22 of 26 samples harvested at 0 - 10 days PHI and in all 8 samples harvested after 10 days PHI. In 4 other samples harvested at 0 or 1 day PHI, however, values were 21, 27.5, 16.4 and 18.9 ppm. The last sample received an additional treatment by postharvest dip at 1 lb ai/100 gal. Because the petitioner does not indicate the concentration of spray volume for most of the samples, we are unable to determine the level of residues which may result from this use. Additional data reflecting application rates in terms of lb ai/100 gal will be required.

Apricots

Residues in 7 apricot samples from one tree ranged from 7.9 - 14.2 ppm following 2 or 3 applications at 1 lb ai/a in 200 gal/a with a 0-7 day PHI. Additional residue data will be required to allow determination of the adequacy of tolerances.

Plums

Four samples of plums collected at 0-8 days PHI were analyzed. Residues measured 0.34-0.87 ppm following 2 or 3 treatments at 1 lb ai/a in 200 gal/a. A single prune plum sample exhibited 0.87 ppm after four applications of 1 lb ai/a at 7 days PHI, but no spray volume was specified. We will require additional residue data to support the proposed tolerance of 1 ppm.

Cherries

For cherries, the only data submitted were for three samples harvested at 6 and 7 days PHI. Residues ranged from 1.4-3.3 ppm after 3 or 4 applications at 1 lb ai/a in 100 gal/a. We will require additional residue data reflecting the proposed use in order to determine the adequacy of the 5 ppm proposed tolerance.

Nectarines

Residues of 1.8 and 1.5 ppm were found in two nectarine samples collected 1 day and 7 days after treatment. No spray volume was specified. Additional residue data are needed to support the tolerance. The petitioner should be advised that tolerances above 1 ppm ordinarily are expressed in whole numbers and revision of the 2.5 ppm proposed tolerance should be considered.

The petitioner has not expressed the application rates in terms of lb ai/100 gal or indicated the concentration or spray volume per acre for most samples. We are therefore unable to determine the adequacy of the proposed tolerances for stone fruits. Additional data reflecting the proposed application rates in terms of lb ai/100 gal will be required. The petitioner should also be asked to consider expressing the tolerance for nectarines in whole numbers.

Meat, Milk, Poultry, and Eggs

No feeding studies have been performed. Because no animal or poultry feed items are involved in this petition, there is no reasonable likelihood of secondary residues in meat, milk, poultry, or eggs. Category 3 of Section 180.6(a) applies for this proposed use. For any future proposed tolerances involving feed items, feeding studies will be required.

Attachments (3)

cc: Reading file
Circu
Reviewer
FDA
PP# NO.
TOX
EEB

EFB
Glasgow
TS-769:RCB:Review:RDI:Section Head: