3-21-83

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

MAR 2 1 1983

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: PP# 3F2810. Iprodione on Stonefruit. Evaluation of analytical methods and residue data.

FROM: R. B. Perfetti, Ph.D., Chemist
Residue Chemistry Branch, HED (TS-769)

TO: Product Manager No. 21 (H. Jacoby)
Fungicide-Herbicide Branch
Registration Division (TS-767)

and

Toxicology Branch, HED (TS-769)

THRU: C. L. Trichilo, Chief
Residue Chemistry Branch

Rhone-Poulenc, Inc. requests the establishment of tolerances for combined residues of the fungicide iprodione (3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide), its isomer 3-(1-methylethyl)-N-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide and its metabolite 3-(3,5-dichlorophenyl-2,4-dioxo-1-imidazolidinecarboxamide in or on stone fruits at 20 ppm.

Tolerances for iprodione have been established previously on a variety of commodities. Those tolerances range from 0.05 ppm on almonds (temporary) to 20 ppm on cherries, nectarines and peaches.

Three other iprodione petitions are pending 2F2728, 3G2787 and 3G2801.

Conclusions

1. The metabolism of iprodione in stone fruits is adequately understood. The terminal residue of concern wil consist of iprodione its isomer and the des-isopropyl metabolite.

2. Adequate analytical methods are available for enforcement purposes.

3a. Based on data on plums, prunes and apricots submitted in conjunction with this petition as well as that of previous studies the proposed 20 ppm tolerance level for these commodities is adequate.

3b. Since, at present, crop group tolerances are not set for non-negligible residue situations a revised Section F proposing the tolerances for combined residues of iprodione, its isomer and its des-isopropyl metabolite in terms of the specific crops apricots and plums (fresh prunes) is needed.

3c. Since no concentration of residues was observed upon drying, no food-additive tolerance for dried prunes is needed.

4. There will be no problems with secondary residues in meat, milk, poultry or eggs involved with this use.

5. The International Tolerance Sheet is attached. There are Codex tolerances of 10 ppm on peaches and 7 ppm plums. These tolerances are expressed in terms of iprodione per se. Since real resdiues of the iosmer of iprodione (RP 30228) and its metabolite (RP 32490) were observed in the residue data on the subject crops we can see no pathway for making the present tolerance proposals for combined residues of parent, RP 30228 and RP 32490 compatible with the Codex tolerances.

Recommendations

We recommend that the proposed tolerances not be established for the reasons given in conclusion 3b. Requirements for resolution of this deficiency are discussed in that conclusion above.

Note to PAM Editor: Please see our recommendation regarding methodology discussed in the Analytical Methods Section.

Detailed Considerations

Formulation:

The formulation proposed for use is Rhone-Poulenc's Rovral fungicide (EPA Registration No. 359-685). Rovral is formulated as a wettable powder containing 53.16% technical iprodione. All inerts in the formulation are cleared under Section 180.1001.

The manufacturing process for iprodione as well as identities and percentages of impurities was reviewed in conjunction with PP# 8G2087 (memo of 3/2/79, A. Rathman) which see. Technical iprodione is typically 95% pure with none of the impurities comprising more [redacted] of the material. We would expect no additional residue problems with the low levels of these impurities in the formulation.

Proposed Use:

To control fungus on apricots, plums and prunes apply 0.5 to 1.0 lb active ingredient/acre (0.125 to 0.25 lb active ingredient/100 gallons of spray) as foliar treatment in 20-400 gallons of water per acre using ground equipment or in 15-20 gallons/acre if application is via aircraft. Applications can be made at early bloom, at full bloom, at petal fall or when conditions favor disease infection in the five weeks prior to harvest up to and including the day of harvest. Restrictions prohibiting the grazing of treated orchards or the feeding of cover crops grown in treated orchards to livestock are prescribed. A maximum of 5 applications per year is to be made and a minimum interval between treatments in the 5 weeks prior to harvest is prescribed. A maximum of 1.0 lb of active ingredient/acre per application is to be made.

Nature of the Residue:

No new metabolism studies were submitted in this petition. Previously submitted studies on peaches, strawberries and wheat indicated that there is little migration after foliar treatment but that uptake via the root system after ground application occurs with subsequent translocation to aerial plant parts. In all three plant species, the major portion of the radioactive residue (>90% in the case of peaches) was identified as iprodione, its isomer and its des-isopropyl metabolite.

The nature of the residue in the subject crops is adequately understood from data on other plant species. The terminal residue of concern will consist of parent, its isomer and the des-isopropyl metabolite.

Because no animal feed items are involved in this petition, the nature of the residues in livestock is not being discussed here.

Analytical Method

The method used to obtain residue data was submitted and reviewed in conjunction with PP# 2F2596 (memo of 5/13/82).

Briefly this method involved blending the sample with acetone (Note: In some analyses one ml of concentrated HCl was added to acetone before blending), filtration and evaporation of the solvent. To the remaining aqueous solution was added sodium sulfate solution and the solution was extracted with 10% ethyl acetate/methylene chloride. The ethyl acetate/methylene chloride solution was dried over sodium sulfate, evaporated to dryness and redissolved in 3:1 ethyl acetate/toluene. The sample was further cleaned-up on both a gel permeation column and a Florisil column. The samples were eluted from the Florisil column as two fractions, one containing parent and RP 30228 and the second containing the des-isopropyl metabolite RP 32490. These fractions were taken to dryness, redissolved in benzene and analyzed via glc using a ^{16}Ni electron capture detector. An optional hexane/acetonitrile partitioning is available for very dirty samples of fraction 1.

Validation data submitted reflected fortification of cherries, plums, prunes (fresh and dried), peaches, nectarines and apricots at levels of 0.05 to 10.4 ppm with iprodione; its isomer (RP 30228) or its metaboite (RP 32490). Recoveries for all 3 compounds ranged from 70 to 148% with one value for peaches spiked at 0.052 ppm with iprodione reported as 283%. Blank values for all of the materials ranged from non-detectable to 0.34 ppm. Chromatograms were submitted.

A ^{14}C-labeled method validation study on peaches as well as a limited interference study were submitted and reviewed in conjunction with PP# 2F2596.

The method described above is similar to the procedure which has undergone a successful method trial on kiwi fruit at levels of 0.01 and 7 ppm with minor modifications. A TLC procedure is also available for confirmatory purposes. We conclude that adequate analytical methods are available for enforcement purposes (Note to PAM editor: We recommend that the analytical method No. 151, this petition, tab D-4 labeled Report No. 81/008 be included as method B in the PAM. This document also contains the TLC confirmatory procedure as well as the interference study mentioned above).

Residue Data

Residue data submitted in this petition reflected eleven studies on cherries (1), prunes (3), peaches (3), nectarines (2), plums (1), and apricots (1) grown in Michigan (2), Oregon (1), New York (1), South Carolina (1), Virginia (1), and California (5). These trials involved 4 to 6 applications of iprodione to the subject crops at rates of 0.5 to 1.0 lb active ingredient per acre via ground equipment or aircraft in 4 to 80 gallons of spray/acre by air and 35 to 400 gallons

of spray/acre when ground equipment was employed. All studies utilized the Rovral 50 WP formulation and foliar treatments. Plot sizes ranged from 1.5 to 10 acres.

Residues on cherries grown in Michigan were 1.4 ppm for iprodione and <0.05 ppm each for the isomer of iprodione (RP 30228) and its des-isopropyl metabolite (RP 32490) respectively after 1 day.

Residues of parent, RP 30228 and RP 32490 on prunes grown in Oregon, New York or Michigan ranged from 0.75 to 1.5 ppm, from <0.05 to 0.06 ppm and from <0.05 to 0.06 ppm respectively at 0 to 3 day PHI's. Fresh prunes containing 1.5 pm of iprodine, 0.05 ppm of RP 30228 and <0.05 ppm of RP 32490 were sun-dried for 2 days and the resulting residues were 0.24 ppm, <0.05 ppm and <0.05 ppm for parent, RP 30228 and RB 32490 respectively indicating that no concentration of residues occurs in drying of fruit.

Zero day residues of peaches grown in South Carolina and California ranged from <0.05 to 1.4 ppm for iprodione, were <0.05 ppm for RP 30228 and ranged from <0.03 to 1.2 ppm for RP 32490.

Nectarines grown in Virginia and California showed residues of parent, RP 30228 and RP 32490 of 0.11 to 1.2, <0.05 and <0.05 ppm after 5 or 0 day PHI's respectively.

Residues of iprodione, its isomer and its metabolite were 0.17 ppm, <0.05 ppm and 0.05 ppm respectively on plums grown in California after a 0 day PHI.

Zero day residues of iprodione, RP 30228 and RP 32490 were 2.7 ppm, <0.05 ppm and 0.07 ppm respectively on apricots grown in California.

No significant difference was observed in the crops described above when iprodione was applied aerially vs using ground equipment.

Based on the data on plums, prunes and apricots submitted above as well as that of previous studies it is our judgment that the proposed 20 ppm tolerance level for these commodities is adequate. (Note: Although the residue data submitted in this petition show residues are less than 5 ppm, residue data submitted in PP# 2F2596 show residues resulting in cherries and peaches of up to 20 ppm from the same use pattern as is proposed here.) The petitioner should be informed, however, that a revised Section F proposing the tolerances in terms of apricots, plums (fresh prunes) is needed since we do not, at this point set non-negligible residue tolerances on crop groups.

No food additive tolerance for dried prunes is needed since no concentration of residues was observed upon drying of this commodity.

Finally, samples of peaches, cherries, plums, apricots, and prunes were held in frozen storage for 25 to 381 days. We are raising no question with respect to this storage time, however, since the petitioner has submitted a pseudo-storage stability study in conjunction with PP# 8G2087 which indicated that iprodione residues were stable in frozen storage for ca. 1 year.

Meat, Milk, Poultry and Eggs

Animal metabolism and feeding studies have been submitted and reviewed in conjunction with PP# 2F2728 (memo of 10/25/82, M. Kovacs). Since, however, the label contains restrictions prohibiting the grazing of treated orchards or the feeding of cover crops grown in treated orchards to livestock, no feed items are involved and there will be no problem with secondary residues of iprodione occurring in meat, milk, poultry or eggs under this present use.

Other Considerations

The International Tolerance sheet is attached. There are Codex tolerances of 10 ppm on peaches and 7 ppm on plums. these tolerances are in terms of parent iprodione per se. since real residues of isomer of iprodione (RP 30228) and its metabolite (RP 32490) were observed in the residue trials submitted to date we can see no pathway for making the present tolerance proposals for combined residues of parent, isomer and metabolite compatible with the Codex tolerances.

cc: R.F.
Circu
Reviewer
FDA
TOX
EEB
EFB
PP# No.
Robert E. Thompson (Res. Triangle Park, NC)
RDI:Section Head:RSQ:Date:3/7:RDS:Date:3/7/83
TS-769:RCB: :pad:RM:810:CM:#2x77324:03/15/83
FILE:RCB 13

INTERNATIONAL RESIDUE LIMIT STATUS

F.d. 3/1/85

CHEMICAL Iprodione
3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidine carboxamide)

PETITION NO 3F2810

CCPR NO.

Codex Status

☐ No Codex Proposal Step 6 or above

Residue (if Step 9): ★
iprodione

Crop(s)	Limit (mg/kg)
peaches	10
plums	7

Proposed U. S. Tolerances

Iprodione, its isomer 3-(1-methylethyl)-N-(3,5dichlorophenyl)-2,4 dioxo-1-imidazolidinecarboxamid and its metabolite 3-(3,5-dichlorophenyl)2,4-dioxo-1-imidazolidin
Residue: carboxamide

Crop(s)	Tol. (ppm)
Stonefruit	20

CANADIAN LIMIT

Residue:

Crop	Limit (ppm)
none (on stonefruit)	

MEXICAN TOLERANCIA

Residue:

Crop	Tolerancia (ppm)
none	

★ Consideration of U.S. residue definition compatibility needed in addition to numerical values.

Notes: