6-16-83

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

JUN 16 1983

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#2F2728 Iprodione on Almonds
Amendment of February 23, 1983

FROM: Martin F. Kovacs Jr., Ph.D., Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

THRU: Charles L. Trichilo, Chief
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

TO: Henry M. Jacoby
Product Manager (21)
Registration Division (TS-767)

and

Toxicology Branch
Hazard Evaluation Division (TS-769)

This amendment was submitted by Rhone-Poulenc Inc. in response to Henry M. Jacoby's November 4, 1982 letter which was based on our review (October 25, 1982 of PP#2F2728). The November 4, 1982 letter to Rhone-Poulenc Inc. listed the following deficiencies:

1. The analytical methodology must be validated by method trials completed by this Agency to establish enforcement analytical methods for residues in meat, fat, meat by-products and milk.

2. The residue data submitted for almond nutmeats and hulls do not reflect the proposed use that permits aerial applications of Rovral® to almond trees. You must either submit additional residue data reflecting aerial application of Rovral® at the recommended label rates or resubmit Section B to delete aerial application of Rovral® to almonds.

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3. In the dairy cattle feeding study, milk and liver samples were stored prior to analysis. A conclusion on appropriate meat and milk tolerances cannot be made until you have submitted storage stability data at 0°F for residues of iprodione in milk and liver for a period of 4 and 8 months, respectively, and until the results of the requested method tryout are available.

4. Provided the deficiency mentioned above is resolved, a more appropriate tolerance proposal for milk would be 0.02 ppm and for meat, fat and meat byproducts of cattle, goats, hogs, horses, and sheep would be 0.1 ppm. If the deficiency in item 3 above can be resolved, you should resubmit Section F to propose these tolerance levels.

1. Deficiency No. 1 cannot be resolved until the results of the requested method trial (see M.F. Kovacs' October 22, 1982 memo re. Iprodione on Almonds) have been received and evaluated by RCB. The requested MTO is currently underway at the Anal. Chem. Lab Section, Chemical Operations Br., Benefits and Use Div. and the results should be forthcoming shortly (March 23, 1983, Telecom between R. Thomas ACS, COB, BUD; and M.F. Kovacs, Jr.).

2. In response to deficiency no. 2, the petitioner has proposed that the residue data from the aerial tests for iprodione applied to stone fruits be used to justify the aerial application of iprodione on almonds since stone fruits and almonds are of the same genus Prunus. In this regard, the petitioner cites that Rovral 50 WP is currently registered for use on peaches, cherries and nectarines with an established tolerance of 20 ppm. This registered use allows a total of 5 applications to be made either aerially or by ground equipment at a rate of 1 lb ai/acre/application up to and including the day of harvest (0 day PHI).

The petitioner specifically cites residue data submitted in support of the above established tolerance. The residue studies cited were conducted using aerial applications, 3 peach (2 California, 1 South Carolina) and 1 cherry residue test. In all of these studies, reported residues of iprodione were below 2 ppm for a 0-7 day PHI. Furthermore, the petitioner references the proposed almond label (submitted in conjunction with PP#2F2728) which allows for only 2 applications of Rovral at a rate of 0.5 lb. ai/A/application. The proposed spray

schedule for iprodione on almonds results in a PHI of approximately 200 days.

The petitioner concludes that, considering the timing of Rovral almond sprays (2 applications at blossom with a PHI of approximately 200 days) in contrast to the 5 applications at 1 lb. ai/acre/ application permitted on stone fruits up to and including the day of harvest (0 day PHI), there is no reason to expect aerial applications of Rovral on almonds to result in increased residues.

Our Comments/Conclusions on the Petitioner's response to Deficiency No. 2

We have reexamined the cherry and peach residue data previously submitted in Section D of PP# 8G2087 and PP#3F2810 containing in part tests describing residues of iprodione following ground (PP#8G2087) and aerial (PP#3F2810) applications of Rovral 50 WP.

Following 5 ground applications of Rovral 50 WP at 1.0 lb ai/A/appl. (1X) to cherries with a 0 day PHI, reported residues of iprodione were 1.90, 12.00 ppm; for comparable aerial applications reported residues were 1.4 ppm.

Following 4 ground applications of Rovral 50 WP at 1.0 lb ai/A/appl., 6 to 9 applications at 0.75 or 0.50 lb ai/A/appl., or 3 to 4 applications at 1.0 or 0.75 lb ai/A/appl. to peaches with a 0 day PHI, reported residues of iprodione were 4.60 ppm; 1.57 ppm, 0.82 ppm; and 5.85 ppm respectively; for comparable aerial applications reported residues were 0.61 ppm, 1.1 to 1.4 ppm, and 0.05 and 0.08 ppm respectively.

In the R.B. Perfetti March 21, 1983 memo re. PP#3F2810 (Iprodione on Stonefruit) it was concluded that no significant difference was observed in the reported residue data on cherries, prunes, peaches, nectarines, plums and apricots when iprodione was applied aerially vs. using ground equipment. In fact, in the cherry and peach residue data we have reexamined above it appears as if ground application tended to result in somewhat higher residues than those reported for aerial applications at comparable application rates.

Based on our reevaluation of the above surrogate iprodione residue data on stonefruit we are of the opinion that aerial application of iprodione will not result in increased residues on almonds and the requested additional residue data reflecting aerial application of Rovral or a revised Section B deleting aerial application of Rovral to almonds will not be needed.

Therefore, we can now conclude that the proposed tolerances for the combined residues of the fungicide iprodione, its isomer RP 30228 and its non-hydroxylated metabolite RP 32490 in or on almond nutmeat at 0.05 ppm and almond hulls at 0.25 ppm are adequate to cover residues expected on these commodities resulting from the proposed use.

We consider Deficiency No. 2 to be resolved.

3. In response to deficiency No. 3 the petitioner has submitted an iprodione storage stability study entitled "The Investigation of the Stability of Iprodione Residues in Milk and Animal Tissues Stored under Frozen Conditions."

Samples of cow milk and goat liver from the ^{14}C metabolism studies (see the M.F. Kovacs October 25, 1982 review of PP#2F2728) were used for this study. Iprodione and its non-hydroxylated metabolites were determined in the milk by analytical procedure (ADC#623-A) and in goat liver by analytical procedure (ADC #623-B). Hydroxylated metabolites of iprodione in milk were determined by Rhone-Poulenc Method No. 159. All of the above analytical procedures which employ electron capture gas chromatography as the final determinative step have been discussed in detail in the above review.

All residue values (expressed as iprodione equivalents) reported following sample storage were corrected for average recovery values of 73%, 68% and 96% respectively for iprodione and its non-hydroxylated metabolites, its hydroxylated metabolite in milk and iprodione and its non-hydroxylated metabolites, in goat liver. Representative chromatograms were submitted for each sample type. The petitioner did not indicate if the initial residue values reported for each sample prior to storage were corrected for the average recovery values reported above.

Following 22 months storage at <0°C, residues of iprodione and its non-hydroxylated metabolites in milk were reported as 0.13 ppm as compared to 0.11 ppm prior to storage. Residues of the hydroxylated metabolites in milk after 13 months storage at <0°C were reported as 0.10 ppm compared to 0.11 ppm prior to storage. Following 13 months storage at <0°C, residues of iprodione, and its non-hydroxylated metabolites in goat liver were reported as 3.54 ppm as compared to 4.25 ppm prior to storage.

Our Comments/Conclusions on the Petitioners' Response to Deficiency No. 3

As noted above, we have no indication that the residue values reported by the petitioner for milk and liver samples taken prior to storage were corrected for the average recovery values reported on these same samples analyzed following storage. However, applying the same recovery values obtained on the post-storage samples to the pre-storage samples (assuming the latter residue values were uncorrected for average recovery values) we can recalculate pre-storage residues of iprodione and its non-hydroxylated metabolites in milk, its hydroxylated metabolite in milk and iprodione and its non-hydroxylated metabolites in goat liver to be 0.15 ppm, 0.16 ppm and 4.43 ppm respectively. These calculated residue values translate into a 9% loss of iprodione and its non-hydroxylated metabolites in milk following 22 months storage, a 37% loss of the hydroxylated metabolite in milk following 13 months storage and a 20% loss of iprodione and its non-hydroxylated metabolites in goat liver following 13 months storage; all at <0°C.

Calculated on the basis of only 4 months' storage in milk, the loss of iprodione and its non-hydroxylated metabolites and its hydroxylated metabolite would be 1.6% and 11.4% respectively. Calculated on the basis of only 8 months storage in liver, the loss of iprodione and its non-hydroxylated metabolites would be 12.3%.

In light of the storage stability data provided by the petitioner which in turn served as the basis for our above calculations regarding the requested storage stability of iprodione and its metabolites following 4 and 8 months storage respectively in milk and liver, we consider that the calculated

residue losses during storage at <0°C are relatively insignificant. Therefore, pending the successful completion of the initiated method trial, we can now finally conclude that the dairy cattle feeding study previously submitted in this petition can serve as a valid basis for the establishment of appropriate meat and milk tolerances which are now proposed below by the petitioner in a revised Section F.

We consider Deficiency No. 3 to be resolved.

4. In response to Deficiency No. 4, the petitioner has submitted a revised Section F as follows:

Raw Agricultural Commodity

It is hereby proposed the establishment of permanent tolerances for the combined residues of the fungicide iprodione 3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide and its metabolites 3-(1-methylethyl)-N-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide and 3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide, in or on the raw agricultural commodities almond nutmeat at 0.05 parts per million and almond hulls at 0.25 parts per million, as a result of pre-harvest (blossom) applications.

Commodity	Tolerances (ppm)
Almond Nutmeat	0.05
Almond Hulls	0.25

Meat and Meat Byproducts

It is also hereby proposed the establishment of permanent tolerances for the combined residues of 3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide and its non-hydroxylated metabolites, typically 3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide, by converting the non-hydroxylated phenyl ring moiety to the N-heptafluorobutyrate derivative of 3,5-dichloroaniline common moiety, as iprodione equivalents:

Commodity	Tolerances (ppm)
Meat & meat byproducts (meat, kidney, fat, liver) of cattle, goats, hogs, horses and sheep	0.1

Milk

It is also hereby proposed the establishment of permanent tolerances for the combined residues of 3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide, 3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide, and N-(3,5-dichloro-4-hyroxyphenyl)-ureido carboxamide by converting respectively, the hydroxylated and the non-hydroxylated moiety to the 4-methoxy-3,5-dichloroaniline and the 3,5-dichloroaniline heptafluorobutyrates, as iprodione equivalents:

Commodity	Tolerances (ppm)
Milk	0.02

Our Comments/Conclusions on the Revised Section F

We conclude that the petitioner has adequately responded to our request to propose more appropriate tolerance proposals for milk at 0.02 ppm and for the meat, fat and meat byproducts of cattle, goats, hogs, horses, and sheep at 0.1 ppm. However, we feel that the proposed tolerance expressions for Meat and Meat Byproducts and Milk are too cumbersome and unwieldy. We suggest that the petitioner revise and resubmit the above tolerance proposals as follows:

Meat Fat and Meat Byproducts

Permanent tolerances are proposed for the combined residues of 3-(3,5-dichlorophenyl)-N-(1-methylethyl) -2,4-dioxo-1-imidazolidinecarboxamide and its non-hydroxylated metabolites (expressed as iprodione equivalents) in or on the following raw agricultural commodities:

Commodity	Tolerances (ppm)
Meat, fat and meat byproducts of cattle, goats, hogs, horses and sheep.	0.1

Milk

Permanent tolerances are proposed for the combined residues of 3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide and its non-hydroxylated and hydroxylated metabolites (expressed as iprodione equivalents) in or on the following raw agricultural commodity:

Commodity	Tolerances (ppm)
Milk	0.02

We conclude that Deficiency No. 4 has been resolved provided that the petitioner resubmits a revised Section F containing the revised tolerance expressions we have proposed above.

Recommendations:

TOX considerations permitting and pending both the successful completion of the initiated method trial and the receipt of a Revised Section F containing the petitioner's reproposed tolerance expressions under Meat, fat and meat byproducts and milk which we have recommended and detailed under Deficiency No. 4 above, we recommend for the establishment of tolerances for the combined residues of the fungicide iprodione and its non-hydroxylated metabolites in or on the raw agricultural commodities almond nutmeat at 0.05 ppm and almond hulls at 0.25 ppm; for combined residues of iprodione and its non-hydroxylated metabolites in meat, fat and meat by-products of cattle, goats, hogs, horses and sheep at 0.1 ppm and for combined residues of iprodione and its non-hydroxylated and hydroxylated metabolites in milk at 0.02 ppm.

There are no Canadian, Mexican or Codex International residue limits established for combined residues of iprodione on almonds (nutmeats and hulls).

If and when the proposed meat and milk tolerances are established, the specific metabolites to be regulated and analyzed for should be listed in the analytical method to be published in PAM.

Reviewer: Marty Kovacs

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL IPRODIONE

PETITION NO. 2F2728

CCPR NO. III

Codex Status

/____/ No Codex Proposal
Step 6 or above

Residue (if Step 9):

parent (on other commodities)

Crop(s) Limit (mg/kg)

None (on these commodities)

Proposed U.S. Tolerances

Residue:

3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide, its isomer and hydroxylated and non-hydroxylated metabolites

Crop(s)	Tol. (ppm)	
Almond Nutmeat	0.05	Parent & isomer & hydroxylated and non-hydroxylated metabolites
Almond Hulls	0.25	
Meat + Meat byproducts (meat, kidney, fat, liver) of cattle, goats, hogs, horses and sheep	0.1	(Parent + non (hydroxylated (metabolites. (
Milk	0.02	(Parent + hydr (xylated and (non-hydroxy- (lated metabo- (lites.

CANADIAN LIMIT

Residue: _____

_____

Crop	Limit (ppm)
None (on these commodities)	

MEXICAN TOLERANCIA

Residue: _____

_____

Crop	Tolerancia (ppm
None	

NOTES:

cc: R.F.
Circu
Reviewer
FDA
TOX
EEB
EFB
PP# No. 2F2728
Robert E. Thompson (Res. Triangle Park, NC)
RDI:Section Head:RSQ:Date-4/14/83:RDS:Date-4/14/83:DCR-17347
TS-769:RCB-15:Reviewer-Kovacs:efs:Rm810:CM#2:x77324:4/18/83
REVISED:DCR#18004:jad:4/20/83