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

JUN 26 1985

MEMORANDUM

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: PP#5F3241 [RCB #962]. Iprodione in/on Almonds.
Evaluation of Analytical Methodology and Residue
Data (Accession Numbers 073473 and 073474).

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CT

TO: Henry Jacoby, Product Manager Number 21
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and

Toxicology Branch
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In conjunction with a proposal for amending the currently registered use of its fungicide Rovral® containing the active ingredient (ai) iprodione on almonds, Rhone-Poulenc, Inc. requests the establishment of a revised tolerance for combined residues of 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/on the raw agricultural commodity almond hulls at 2 ppm.

Tolerances have previously been established for residues of iprodione (plus its isomer and metabolite) in/on almonds (nut meat) and almond hulls at 0.05 and 0.25 ppm, respectively, in conjunction with PP#2F2728, as well as in/on several other plant, r.a.c.'s at levels ranging from 10 to 60 ppm (see 40 CFR 180.399 (a)).

Tolerances have been established under 40 CFR 180.399(b) for combined residues of 3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide [iprodione] and its nonhydroxylated metabolites (expressed as iprodione equivalents) in or on:

- meat, fat, and meat byproducts (except liver and kidney) of cattle, goats, hogs, horses, and sheep at 0.4 ppm;
- liver and kidney of cattle, goats, hogs, horses, and sheep at 3 ppm;
- in eggs at 0.8 ppm;
- in poultry meat and meat byproducts (except liver) at 0.4 ppm;
- in poultry fat at 2 ppm;
- in poultry liver at 3 ppm.

Tolerances have been established under 40 CFR 180.399(c) for combined residues of iprodione and its hydroxylated and nonhydroxylated metabolites (expressed as iprodione equivalents) in or on the raw agricultural commodity milk at 0.3 ppm.

In conjunction with PP#4F3129, proposed tolerances are pending which would raise the level of residues allowed in meat, fat and meat byproducts (excluding liver and kidney) of cattle, goats, hogs, horses and sheep to 0.6 ppm. The petitioner was advised by RCB (see R. Cook memo of 5/3/85 re: PP#4F3129) to revise the tolerance expression under 40 CFR 180.399(b) to read:

Combined residues of 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 metabolites 3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide and N-(3,5-dichloro-4-hydroxyphenyl)-ureidocarboxamide, all expressed as iprodione equivalents.

At this time, tolerance proposal for iprodione are pending in conjunction with PP#4E3129 (peanuts), PP#4F3150 (beans), and PP#5E3214 (small berries), while RCB has recommended for a tolerance of 0.5 ppm in/on dry bulb onions.

No Registration Standard has been issued or is anticipated in the near future for iprodione.

Conclusions

1. In addition to the registered use of iprodione on almonds at pink bud stage and again at full bloom, the use proposed in conjunction with the subject petition would allow two additional applications - one at petal fall and another at 5 weeks after petal fall.
2. The nature of the residue in plants and animals is considered adequately understood.

For plant commodities, the residues of concern consist of iprodione [3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide] (RP-26019), its isomer 3-(1-methylethyl)-N-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide (RP-30228), and its metabolite 3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide (RP-32490).

For animal commodities, the residues of concern include 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 metabolites 3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide and N-(3,5-dichloro-4-hydroxyphenyl)-ureidocarboxamide.

3. RCB concludes that adequate analytical methodologies are available for enforcement purposes with regard to almonds (nutmeat, hulls) and animal commodities.
4. While the residue data adequately support the proposed 2.0 ppm tolerance for almond hulls, the established 0.05 ppm tolerance for almond nutmeat is not supported (see Residue Data Section of this review).

Normalizing the residue data reflecting total treatment at 1.25X, the residue level in almond nut meat resulting from iprodione treatment at the proposed 1X rate would be 0.19 ppm. Taking into consideration the preceding, the adequacy of the analytical procedure, and the limited number of field trials (4), the petitioner will need to submit a revised Section F in which a tolerance of 0.3 ppm ppm is proposed for almond nutmeat.

- 5a. The only animal feed of concern in conjunction with the subject petition is almond hulls, which can account for 25% of the diet for beef and dairy cattle and up to 50% of the diet for finishing lambs.

- 5b. RCB concludes that the established tolerances for milk (0.3 ppm); meat, fat and meat byproducts (except liver and kidney, of cattle, goats, hogs, horses and sheep (0.4 ppm); and kidney and liver of cattle, goats, hogs, horses, and sheep (3.0 ppm) will be adequate to cover secondary residues resulting from the proposed use on almonds as well as previously established uses of iprodione.
- 5c. Since no poultry feed items are included in the subject petition, RCB does not expect a problem with secondary residues in poultry (meat, fat, and meat byproducts) and eggs as a result of the proposed use.
6. An International Residue Limit Status sheet is attached to this review. Since there are no established Codex, Canadian, and Mexican limits/tolerances for residues of iprodione in/on almonds, there are no compatibility problems.

Recommendation

At this time, RCB recommends against the proposed tolerance for the reason cited under Conclusion 4.

For further consideration, the petitioner will need to submit a revised Section F in which a tolerance of 0.3 ppm for residues of total iprodione in/on almonds (nutmeat) is proposed.

Detailed Considerations

Manufacture and Formulation

The manufacturing process and a list of impurities in technical iprodione were submitted and reviewed in conjunction with PP#8G2084 (see A. Rathman memo of 3/2/79). Technical iprodione is approximately 95% pure with none of the impurities comprising more [redacted] by weight. RCB does not expect a residue problem resulting from impurities in the technical material.

The formulation proposed for use on almonds, Rovral® fungicide (EPA Reg. No. 359-685), is a wettable powder containing 50% iprodione. All inerts are cleared under 40 CFR 180.1001.

Proposed Use on Almonds

The proposed use is the same as that already registered on almonds in conjunction with PP#2F2728 except that two additional treatments are allowed.

Iprodione is to be used to control brown rot blossom blight (Monilinia laxa) and shothole (Stigmina carpophia) on almonds. A foliar spray is to be applied at the rate of 0.125 lb ai/100 gal in sufficient water to obtain thorough coverage (100 to 400 gal of spray solution by ground equipment and in a minimum of 20 gal of spray solution by aerial means). The use of aerial equipment is not recommended after petal fall.

In addition to the registered uses at pink bud stage and again at full bloom, additional applications would be allowed at petal fall and up to 5 weeks after petal fall if conditions favorable for disease development persist.

The proposed label includes the following restrictions:

Do not make more than 4 applications of Rovral® per season.

Do not graze animals in treated orchards.

Do not feed cover crops grown in treated orchards to livestock.

Nature of the Residue

No new metabolism studies were submitted in the subject petition.

The metabolism of iprodione in plants and animals is discussed in RCB's previous review of a proposal for iprodione tolerances for almonds (nutmeat and hulls) (see M. Kovacs, Jr. memo of 10/25/82 re: PP#2F2728). The nature of the residue is considered adequately understood for the proposed use on almonds.

For plant commodities, the residues of concern consists of iprodione [3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide] (RP-26019), its isomer 3-(1-methylethyl)-N-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide (RP-30228) and its metabolite 3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide (RP-32480).

For animal commodities, the residues of concern include 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 metabolites 3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide and N-(3,5-dichloro-4-hydroxyphenyl)-ureidocarboxamide.

Analytical Methodology

a. Almonds (Nut Meat and Hulls)

The analytical method used to generate the residue data for treated almond hulls and nutmeat submitted in the subject petition, Rhone-Poulenc Analytical Method No. 151, was previously used in conjunction with PP#2F2728 to generate residue data on almonds and found to be acceptable for enforcement of tolerances on almonds (see M. Kovacs, Jr. memo of 10/25/82). This method is basically the same procedure which has successfully undergone a method trial on kiwi fruit (see R. Perfetti memo of 3/21/83 re: PP#3F2810).

In brief, the sample is macerated, residues are then extracted with acidified acetone, cleaned up by gel permeation column chromatography and Florisil column chromatography, and quantitated by gas-liquid chromatography using an electron capture detector.

Control values for iprodione were reportedly <0.05 ppm (number of analyses, n = 4) for almond hulls and <0.05 ppm (n = 3) or 0.02 ppm (n = 4) almonds. Control values for RP-30228 and RP-32490 were reportedly <0.05 ppm.

At fortification ranging from 0.05 to 2.0 ppm in almond hulls, recoveries ranged from 67 to 106% (average of 4 samples = 81%) for iprodione, 62 to 75% (average of 2 samples = 68%) for RP-30228, and 95 to 114% (average of 2 samples = 104%) for RP-32490).

Recoveries from almond nutmeat fortified at 0.05 and 0.5 ppm were 73% for RP-30228, 76% for RP-32490 and ranged from 74 to 103% (average of 3 samples = 92%) for iprodione.

RCB concludes that Rhone-Poulenc Analytical Method No. 151 is adequate for enforcement of the proposed amended tolerance for residues of iprodione (plus RP-32490 and RP-30228) in/on almond hulls.

b. Animal Commodities

The analytical methods for animal commodities have previously been reviewed by RCB in conjunction with PP#2F2728 (see M. Kovacs, Jr. memo of 10/25/82). The methods for iprodione residues in animal tissue are Method ADC #623: Iprodione and its nonhydroxylated metabolites in milk (ADC #623-A) and tissues (ADC 623-B), and Rhone-Poulenc Method 159: hydroxylated metabolites in milk. These methods are based upon the hydrolysis of iprodione metabolites to either of the common moieties dichloroaniline (for nonhydroxylated metabolites) and dichloroaminophenol (as its methyl ester for hydroxylated metabolites). Residues are measured as the heptafluorobutyryl derivative of these common moieties using gas chromatography.

The methods have successfully undergone method trial in conjunction with PP#2F2728 (see M. Kovacs, Jr. memo of 5/24/83).

RCB concludes that adequate analytical methodology is available for enforcement purposes with regard to quantitation of residues in animal tissues and milk.

Residue Data

Four field trials were conducted in the state of California. Almond orchards received iprodione treatments at pink bud, full bloom, petal fall and five weeks after petal fall at the maximum proposed label rate of 0.5 lb ai/A/application, except for one trial in which the last spray was 1.0 lb ai/A. Thus, the total amount of iprodione applied was 2.0 lb ai/A/season (1X) for 3 trials and 2.5 lb ai/A/season (1.25X) for the other trial. PHI's ranged from 132 to 144 days.

Almond samples (nuts and hulls) were stored under frozen conditions approximately 6 months prior to analysis. Storage stability data generated on strawberries, grapes, peaches and cherries submitted in conjunction with PP#8G2087 indicate that overall iprodione residues are stable in fruit samples stored under frozen conditions for about 1 year. Thus, RCB is not concerned about the stability of residues in/on treated almond nuts and hulls analyzed in conjunction with the subject petition.

Although all field trials reflected treatment by ground equipment, in RCB's review of PP#3F2810 (see R. Perfetti memo of 3/21/83) it was concluded that no significant difference was observed in the residue levels found for iprodione treated cherries, prunes, peaches, nectarines, plums and apricots depending on whether the fungicide was applied by ground or aerial equipment.

The reported residue data (corrected for method recovery) are tabularized below:

Sample	Total Applied (lb ai/A)	PHI (days)	Residue Level (ppm)			Total
			iprodione	RP-30228	RP-32490	
almond hulls	2.0	139	1.06	0.48	0.08	1.62
	2.0	144	1.20	0.07	<0.05	1.27
	2.0	144	0.60	0.09	0.09	0.78
	2.5	132	1.29	0.06	0.28	1.63
almond nutmeat	2.0	139	<0.05	<0.05	<0.05	<0.05
	2.0	144	<0.05	<0.05	<0.05	<0.05
	2.0	144	<0.05	<0.05	<0.05	<0.05
	2.5	132	0.18	0.06	<0.05	0.24

While the residue data adequately support the proposed 2.0 ppm tolerance for almond hulls, the established 0.05 ppm tolerance for almond nutmeat is not supported.

Normalizing the residue data reflecting total treatment at 1.25X, the residue level in almond nut meat resulting from iprodione treatment at the proposed 1X rate would be 0.19 ppm. Taking into consideration the preceding, the adequacy of the analytical procedure, and the limited number of field trials (4), the petitioner will need to submit a revised Section F in which a tolerance of 0.3 ppm ppm is proposed for almond nutmeat.

Residues in Meat, Fat, Milk, Poultry and Eggs

The only animal feed of concern in conjunction with the subject petition is almond hulls, which can account for 25% of the diet for beef and dairy cattle and up to 50% of the diet for finishing lambs.

A dairy cattle feeding study was reviewed by RCB in conjunction with PP#2F2728 (see for details M. Kovacs, Jr. memo of 10/25/82). The following results (corrected for method recovery) were reported:

Sample	Feeding Level (ppm)	Maximum Residue Level (ppm)	Total Residue Level (ppm)	Residue Level (ppm)	
		4.6	14.4	50.5	192.2
milk	-----	0.10	0.20	0.39	
muscle	<0.05	<0.05	0.07	0.13	
kidney	<0.05	0.16	0.80	2.87	
liver	<0.05	0.13	0.66	1.95	
fat	<0.05	<0.05	0.21	0.52	

Animal feed items for which iprodione tolerances are established include grape pomace (dry) at 225 ppm, raisin waste at 300 ppm, and cull grapes at 60 ppm. (Note: proposed tolerances for peanut forage and hay at 150 ppm, peanut hulls at 7 ppm, and peanut soapstock at 10 ppm are currently pending in conjunction with PP#3F2964/FAP#4H5415).

The dietary burden of dairy cattle fed almond hulls (2 ppm x 25% = 0.5 ppm) is relatively minor compared to that from the feeding of raisin waste (300 ppm x 10% = 30.0 ppm) or dry pomace (225 ppm x 20% = 45 ppm).

RCB concludes that the established tolerances for milk (0.3 ppm); meat, fat, and meat byproducts (except liver and kidney) of cattle, goats, hogs, horses and sheep (0.4 ppm); and kidney and liver of cattle, goats, hogs, horses, and sheep (3.0 ppm) will be adequate to cover secondary residues resulting from the proposed use on almonds as well as previously established uses.

Since no poultry feed items are included in the subject petition, RCB does not except a problem with secondary residues in poultry (meat, fat and meat byproducts) and eggs as a result of the proposed use.

Other Considerations

An International Residue Limit Status sheet is attached to this review. Since there are no established Codex, Canadian, and Mexican limits/tolerances for residues of iprodione in/on almonds, there are no compatibility problems.

cc:R.F., Circu, Reviewer, TOX, EAB, EEB, PP#5F3241, PMSD/ISB,
Robert Thompson, FDA
RDI:JHOnley:6/3/85:RDSchmitt:6/3/85
TS:769:RCB:CM#2:Rm800:X7484:MPFirestone:wh:6/19/85

INTERNATIONAL RESIDUE LIMIT STATUS

1.2. 5/21/85

CHEMICAL: iprodisone

PETITION NO.: 5F3241

CCPR NO.: 111

REVIEWER: Michael P. Firestone

Codex Status

No Codex Proposal Step 6 or above

Residue (if Step 9): _____

Crop(s) Limit (mg/kg)

none (on almond hulls)

Proposed U.S. Tolerances

Residue: iprodisone, 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

Crop(s) Tol. (ppm)

almond hulls 2

CANADIAN LIMIT

Residue: parent & including metabolites*

Crop(s) Limit (ppm)

none (on almond hulls)

MEXICAN TOLERANCIA

Residue: _____

Crop(s) Tolerancia (ppm)

none

Notes:

* metabolites - 3-isopropyl-N-(3,5-dichlorophenyl)-2,4-dioxoimidazolidin-1-carboxamide and 3-(3,5-dichlorophenyl)-2,4-dioxoimidazolidin-1-carboxamide