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

SEP 29 1987

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#7G3525. Rovral on stored corn grain. Review and Evaluation of Residue Data. MRID No. 40189101. RCB No. 2663.

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Rhone-Poulenc Inc. is requesting a temporary tolerance for combined residues of the fungicide iprodione [3-(3,5-dichlorophenyl) -N-(methyl-ethyl)-2,4-dioxo-1-imidazolidinecarboximide], its isomer [3-(1-methylethyl)-N-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidine-carboximide], and its metabolite [3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboximide] expressed as iprodione equivalents, in or on field corn grain at 20 ppm.

Tolerances have been established for the 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-imidazolidine-carboxamide on various raw agricultural commodities of plant origin at levels ranging from 0.05 ppm to 150 ppm [40 CFR 180.399 (a)].

Tolerances have been established for the 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-imidazolidine-carboxamide] and [N-(3,5-dichloro-4-hydroxyphenyl)-ureido-

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carboxamide], all expressed as iprodione equivalents in or on raw agricultural commodities of animal origin at levels ranging from 0.05 ppm to 3.0 ppm [40 CFR 180.399 (b)].

A Registration Standard for iprodione has not been completed.

Conclusions:

1. The metabolism of iprodione in plants and animals is adequately understood. In plants the residues of concern, expressed as iprodione equivalents, are iprodione, [3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide] (RP-26019); 3-(1-methylethyl)-N-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide (RP-30228); and 3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide (RP-32490). The residues of concern in animals are iprodione; 3-(1-methylethyl)-N-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide (RP-30228); 3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide (RP-32490); and N-(3,5-dichloro-4-hydroxy-phenylureidocarboxamide (RP-36115), all expressed as iprodione.

2. Adequate methods are available for enforcement purposes. Enforcement methods are available in Pesticide Analytical Manual, Vol. II (PAM-II). The petitioner has conducted the FDA multiresidue protocols for iprodione and its metabolites.

3. The 20 ppm proposed tolerance will not be adequate to cover all residues of iprodione which may occur on corn grain which has been treated at the maximum recommended application rate. A tolerance level of 44 ppm to cover residues of iprodione on corn grain treated as proposed would be acceptable.

4. Residues of iprodione do not concentrate in the various fractions of processed corn. No data are available for grain dust.

5a. The tolerances established to cover secondary residues of iprodione in milk and the fat, kidney, liver, meat and meat-by-products of cattle, goats, hogs, horses, and sheep and the meat and meat by-products (except kidney and liver) of poultry will not be exceeded as a result of livestock ingesting treated corn bearing maximum anticipated residues of iprodione at levels up to 44 ppm (as well as the feed items with established tolerances).

5b. The existing tolerances will not be adequate to cover all secondary residues of iprodione which may occur in eggs and the fat, kidney, and liver of poultry as a result of poultry ingesting corn grain treated as proposed.

Recommendations

For the reasons given in Conclusions 3 and 5b, we recommend against the proposed temporary tolerance of 20 ppm to cover combined residues of iprodione on corn grain.

For a favorable recommendation the petitioner should be advised to submit a revised Section F requesting temporary tolerances to cover total combined residues of iprodione which may occur as a result of the proposed use as follows:

Corn Grain	44.0 ppm
Fat, Poultry	4.0 ppm
Liver, Poultry	7.0 ppm
Eggs	2.0 ppm

For a permanent tolerance the petitioner should be advised to follow 40 CFR 158 and the Residue Chemistry and Product Chemistry Guidelines. The registrant should be informed that the minimum RCB will require for a permanent tolerance to cover residues of iprodione on corn grain will be the following:

1. Residue data on corn grain reflecting the maximum recommended application rate.

2. Data on iprodione residue levels in the grain dust that is generated when treated corn is moved through grain transport and storage facilities.

3. The petitioner needs to submit a revised Section B/label which adequately addresses the problem of possible over-tolerance residues arising from multiple treatment of grain by different personnel.

Detailed Considerations

Formulation and Proposed Use

The iprodione formulation proposed for use is Rovral® Fungicide EPA Reg. No. 359-685, a 50% wettable powder. All inerts have been cleared under 40 CFR 180.1001. RCB has previously concluded that residue problems from either inert ingredients or manufacturing impurities are not anticipated.

A single application of Rovral® is to be applied at dosage rates of 4-8 oz. of product (2-4 oz. a.i.) per 100 bushels of corn using 300-400 ounces of water (44 ppm on a calculated basis).

For ambient air (low temperature) drying, harvest corn at 25% moisture or less. Treat corn immediately with Rovral®. Turn on fan immediately and achieve 1 CFM air flow. Continue to dry until corn moisture is 16%.

For combination drying (heated and ambient air), harvest corn at 25% moisture or less. Use heat to dry corn to 18% moisture. Apply Rovral® to corn after drying. Turn on fan immediately and achieve 0.5-1.0 CFM air flow. Continue drying until corn moisture is 16%.

Nature of the Residue

Plant Metabolism - There were no additional plant metabolism studies submitted with this request. Plant metabolism studies have been reported on strawberries and wheat (A. Rathman, PP#8G2087, March 2, 1979), peaches (R. Perfetti, May 13, 1984, PP#2F2596), lettuce (N. Dodd, April 11, 1983, PP#3G2801), peanuts (N. Dodd, May 31, 1984, PP#4G3037) and rice (R. W. Cook, PP#6F3443/FAP#6H5507, March 17, 1987).

We reiterate the conclusion reached in the above petitions that the residues of concern in plants are iprodione [3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide]; [3-(1-methylethyl)-N-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide][RP-30228]; and [3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide][RP-32490].

Animal Metabolism - The metabolism of iprodione in cows, goats, and rats has been evaluated in our review of PP#2F2728 (M.F. Kovacs, October 25, 1982, almonds). Poultry studies have been reviewed (R. Cook, February 21, 1984, PP#3F2964/FAP#4H5415). We have previously concluded that the residues of concern in animals are iprodione (RP-26019) [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][RP-30228], and its metabolites [3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide] [RP-32490], and N-(3,5-dichloro-4-hydroxyphenyl ureidocarboxamide) (RP-36115), all expressed as iprodione equivalents. We reiterate that conclusion.

Analytical Method

The analytical method for iprodione in or on corn grain is entitled "Rhone-Poulenc Analytical Method No. 162 determination of iprodione and its metabolites in/on grain and hay by GLC and TLC. ASD No.: 83/021." The method determines RP-26019, RP-30228, and RP-32490. Iprodione residues in ground-up samples are extracted twice with aqueous acetone. After initial extraction, the organic solvent is removed by rotary-evaporation. The next step is liquid-liquid partition with 10% ethyl acetate in methylene chloride which concentrates the residues in the organic fraction. Additional cleanup steps include gel permeation chromatography (mobile phase ethyl acetate/toluene); acetonitrile-hexane cleanup; Florisil column chromatography with 20% ethyl acetate in hexane for fraction 1 [RP-26019 (iprodione) and RP-30228(iprodione isomer)] and 30% ethyl acetate in hexane for fraction 2 [RP-32490 (iprodione metabolite)]. Quantitative determination of residues is by ^{63}Ni electron capture gas chromatography.

Untreated samples of corn grain were spiked with 0.05 ppm, 0.10 ppm, and 0.20 ppm with parent (RP-26019), its isomer (RP-30228), and metabolite (RP-32490) prior to the extraction step. Recovery values ranged from 87.0% to 114.0% for RP-26019; 69.0% to 116.8% for RP-30228; and 81.4% to 116.4% for RP-32490.

Various other substrates spiked at levels ranging from 0.05 ppm to 100 ppm showed recoveries ranging from 67.4% to 122.1% for RP-26019; 65.2% to 119.9% for RP-30228; and 63.0% to 118.5% for RP-32490. The limit of detection for parent, its isomer, and metabolite is considered to be 0.05 ppm.

Untreated samples of corn grain were spiked on Day 0, Day 28, Day 56, and Day 84 with 0.5 ppm, 5.0 ppm, 10.0 ppm, and 20 ppm of iprodione. Recoveries ranged from 65.5% to 131.6% for RP-26019; 58.4% to 120.1% for RP-30228; 96.3% to 135.3% for RP-32490.

Validation data were also submitted for the processed fractions of corn including grits, flour, meal, crude oil, refined oil, and starch.

The thin-layer chromatography confirmation procedure utilizes ethyl acetate in benzene or methylene chloride on silica gel plates with Bratton-Marshall reagent for visualization of the reddish pink spots.

An interference study conducted to determine if eleven other pesticides which might be used in an intergrated pest control program showed that after going through the analytical procedure, none of the eleven pesticides tested caused any interference.

We conclude that adequate analytical methods are available for enforcing the proposed temporary tolerance on corn grain. Enforcement methods are available in PAM II.

Residue Data

Corn grain was treated with iprodione at 5, 10, and 20 ppm (0.5X the maximum recommended application rate) in a special mixing chamber before being placed in storage. Special sampling ports were located on the vertical axis of the silo which allowed corn sampling from the bottom, middle, and top of the silo. Samples were taken on the day of treatment (Day 0) as well as 28, 56, and 84 days later. The following table shows the maximum residue reported on corn grain treated with 20 ppm iprodione (0.5X the maximum recommended application rate).

Location in Bin	Day of Treatment	RP-26019	RP-30228	RP-32490
Middle	Day 0	20.06	0.00	0.51
Middle	Day 28	19.23	0.00	0.14
Bottom	Day 56	14.36	0.34	0.76
Bottom	Day 84	14.07	0.25	0.11

There were no residue data submitted reflecting the maximum recommended application rate of 44 ppm. From the submitted data, we can conclude that a 20 ppm tolerance will not be adequate to cover all residues of iprodione which may occur in or on corn grain as a result of this proposed use. In the absence of residue data

reflecting the maximum recommended application rate, we are unable conclude what an actual residues of iprodione on corn grain will be. However, RCB would accept the 1X application rate of 44 ppm to be an appropriate level for a temporary tolerance. For a permanent tolerance residue data reflecting the maximum proposed application rate must be submitted.

Processed Fractions

Corn grain was treated with 20 ppm and 40 ppm iprodione and then dry milled. Processed fractions from the dry milled corn showed the following residues:

Plant Part	Dosage Rate	R-26019	RP-30228	RP-32490
Whole Corn	20 ppm	18.00	---	---
	40 ppm	43.50	---	---
Grits	20 ppm	1.89	0.00	0.00
	40 ppm	4.02	0.09	0.00
Flour	20 ppm	13.66	0.00	0.00
	40 ppm	34.74	0.16	0.08
Meal	20 ppm	9.94	0.17	0.00
	40 ppm	23.75	0.37	0.00
Crude Oil	20 ppm	10.44	0.29	0.05
	40 ppm	11.22	0.40	0.07
Refined Oil	20 ppm	0.06	0.48	0.00
	40 ppm	0.06	0.58	0.00

After the wet milling of corn grain treated with 20 ppm of iprodione, residues detected in the starch were 10.42 ppm RP-26019, 0.10 ppm RP-30228, and N.D. RP-32490.

The wet and dry milling studies submitted with this petition show that residues of iprodione do not concentrate in the various processed fractions.

There was no submission of data reflecting residues of iprodione in grain dust resulting from treated corn. In a future request for a permanent tolerance, such data will be needed.

Meat, Milk, Poultry and Eggs

Corn grain may constitute up to 80% of the beef cattle diet, 50% of the dairy cattle diet, 70% of the poultry diet, and 80% of the swine diet.

Dairy cattle feeding studies have been conducted for 28 days at levels of 5, 15, 50, and 200 ppm. (For a detailed review

of these studies, see M. F. Kovacs, Jr. PhD. Memo dated October 25, 1982, Correspondence File PP#2F2728). Maximum combined residues of iprodione reported for milk were 0.389 ppm from the 200 ppm feeding level plateauing at 17 days. The table below shows the total maximum residues of iprodione in tissues at the 15, 50, and 200 ppm feeding level.

	Feeding Level		
	15 ppm	50 ppm	200 ppm
Muscle	<0.05	0.07	0.13
Kidney	0.16	0.80	2.87
Fat	<0.05	0.21	0.52
Liver	0.13	0.66	1.95

Total maximum residues of iprodione in poultry muscle tissue at 28 days were <0.05, 0.32, and 1.68 ppm at the 2, 20, and 100 ppm feeding levels. Comparable residues in fat were 0.18, 2.57, and 8.62 ppm, respectively. Residues in liver were 0.61, 4.10, 13.4 ppm and in kidney were 0.33 ppm, 2.30 ppm, and 6.87 ppm, respectively.

In eggs, the 2 ppm feeding level resulted in maximum detectable residues of 0.137 ppm at 7 days through 28 days. At levels of 20 and 100 ppm, the maximum detected residues were 0.75 and 2.17 ppm, respectively.

Assuming a 44 ppm tolerance to cover total residues of iprodione on corn grain the dietary burden of livestock ingesting treated corn would be 36 ppm for beef cattle, 22 ppm for dairy cattle, 31 ppm for poultry, and 36 ppm for swine. There are additional feed items with established tolerances. The highest tolerances have been established on peanut forage and peanut hay at 150 ppm.

The following tolerances established to cover residues of iprodione will not be exceeded with the additional burden of corn grain bearing iprodione residues of 44 ppm:

Fat of cattle, goats, hogs, horses and sheep	0.5 ppm
Kidney of cattle, goats, hogs, horses and sheep	3.0 ppm
Liver of cattle, goats, hogs, horses and sheep	3.0 ppm
Meat of cattle, goats, hogs, horses and sheep	0.5 ppm
Meat by-products (except kidney and liver) of cattle, goats, hogs, horses, and sheep	0.5 ppm
Meat of poultry	0.5 ppm
Meat by-products (except kidney and liver) of poultry	0.5 ppm
Milk	0.5 ppm

However, the following tolerances established to cover secondary residues of iprodione will not be adequate to cover all residues which may result from poultry ingesting corn grain bearing iprodione residues of 44 ppm.

Eggs	0.8 ppm
Poultry Fat	2.0 ppm
Poultry Liver	3.0 ppm

A revised Section F requesting the following temporary tolerances to cover all residues of iprodione occurring as a result of the maximum proposed use should be submitted:

Corn Grain	44.0 ppm
Fat, Poultry	4.0 ppm
Liver, Poultry	7.0 ppm
Eggs	2.0 ppm

cc: Reading File, Circulation, Subject File, Reviewer, PP#7G3525, TOX, PMSD/ISB
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