R.F.
4-6-87

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

APR 6 1987

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#7E3474 - Iprodione In or On Carrots - Evaluation of Analytical Method and Residue Data - EPA Accession No. 265922
RCB No. 1631

FROM: V. Frank Boyd, Ph.D., Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

TO: Hoyt Jamerson, PM 43
Registration Support and Emergency Response Branch
Registration Division (TS-767C)

and

Toxicology Branch
Hazard Evaluation Division (TS-769C)

THRU: John H. Onley, Ph.D., Section Head
Tolerance Petition Section II
Residue Chemistry Branch
Hazard Evaluation Division (TS-769C)

The petitioner, Interregional Research Project No. 4 (IR-4), State Agricultural Experiment Station, Rutgers University, New Brunswick, New Jersey, on behalf of the IR-4 Technical Committee, and the Agricultural Experiment Station of Florida, proposes tolerances for the combined residues of the fungicide iprodione [3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide (tradename Rovral® Fungicide)] and 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 the raw agricultural commodity (RAC) carrots at 5 ppm.

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Note: Established tolerances are "(expressed as iprodione equivalents)". We presume the petitioner intended to express the residues as above, but a revised Section F including this expression is needed.

No Registration Standard has been completed for iprodione.

Conclusions:

1. The residues of concern in plants are 3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide [iprodione, 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-imidazolidine-carboxamide [RP-32490]. The residue of concern in animals are 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-hydroxyphenylureidocarboxamide), all expressed as iprodione equivalents.

2. Adequate methods are available for enforcement purposes.

3a. Combined residues of iprodione and its metabolite and isomer are not likely to exceed the proposed tolerance level of 5.0 ppm in the RAC carrots from the use as proposed.

3b. Established meat, milk, poultry, and egg tolerances are not likely to be exceeded from the use as proposed.

4. A revised Section F proposing the tolerance in terms of residue "(expressed as iprodione equivalents)" is needed.

5. There are no Codex, Mexican or Canadian tolerances for iprodione on carrots, therefore, no compatibility problems are expected.

Recommendations:

We recommend for the establishment of a 5.0 ppm tolerance for iprodione residues in carrots, providing a revised Section F as indicated in Conclusion 5 is submitted, Toxicology Branch and Exposure Assessment Branch considerations permitting.

Detailed Considerations

Formulation:

The formulation proposed for use is Rovral® Fungicide, EPA Registration No. 359-685, a wettable powder formulation containing 50% iprodione. Formulation inerts are cleared under 40 CFR 180.1001.

We have previously concluded residue problems are not anticipated from either inert ingredients or manufacturing impurities.

Directions for Use:

Apply Rovral® as a foliar spray for control of Alternaria Blight on carrots at 1.0 to 2.0 lb/A (0.5-1.0 lb/ai/A). Make the first application in the spring when conditions become favorable for disease development and continue at 7 to 10-day intervals, using shorter intervals and higher rates for severe disease conditions. Do not make more than 8 applications per season. Apply up to day of harvest.

Nature of the Residue:

Plants:

Plant metabolism studies have been reported on strawberries and wheat (A. Rathman, March 2, 1979, PP#8G2087), peaches (R. Perfetti, May 13, 1984, PP#2F2596), lettuce (N. Dodd, April 11, 1983, PP#3G2801), and peanuts (N. Dodd, May 31, 1984, PP#4G3037). In ^{14}C-iprodione plant metabolism studies in strawberries, wheat, peaches, and peanuts, the primary residue from foliar application was the parent compound iprodione and smaller amounts of its isomer RP 30228. Soil applications resulted in these two compounds plus small amounts of the metabolite RP-32490.

No new plant metabolism studies are submitted. We would expect metabolism in carrot plants to proceed along the pathways previously identified. We reiterate our conclusion that the residues of concern in plants are iprodione [3,-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide] 3-(1-methylethy)-N-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide [RP-30228]; and 3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide [RP-32490].

Animals:

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-32490), and its metabolites 3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide (RP-36112), and N-(3,5-dichloro-4-hydroxyphenylureidocarboxamide) (RP-36115), all expressed as iprodione equivalents. We reiterate that conclusion.

Analytical Methods:

The PAM II method for the determination of iprodione residues is Rhone-Poulenc Analytical Method No. 151. The method employs sample extraction, liquid-liquid partition using ethylacetate/methylene chloride, followed by column chromatography on Florisil and analysis of residues by GLC using ^{63}Ni Electron Capture. Determination of the amount of parent compound required a capillary column coupled to a Nitrogen/Phosphrous detector due to the presence of massive substrate interference. The isomer and metabolite were calculated conventionally by use of EC detector coupled to regular OV-17 column, as per the PAM II method. All calculations were achieved by computerized comparison to an external standard.

Method sensitivity for the isomer and metabolite is at 0.05 ppm. Method sensitivity for iprodione was hampered by apparent contamination of 3 checks and values of 0.05 to 0.07 in 4 other of the 10 checks analyzed (Table 1). A sensitivity of 0.05 ppm is assumed by discarding the contaminated check values. Recovery values of 107% mean for spiked recoveries of iprodione at 0.1 to 5.0 ppm are reported. At 0.1 to 1.0 ppm

spiking levels for the isomer (RP-30228) and the metabolite (RP-32490) the mean recoveries were 80 percent and 95 percent, respectively.

The analytical methodology is considered to be adequate for determination of iprodione residues in carrots.

Residue Data:

The chopped and frozen samples of carrots were spiked for recovery determination within a week following harvest. Analyses were performed within 3 months after harvest. Recovery determinations with each set of sample analyses proved satisfactory storage stability.

The carrot field plots were treated with 8 or 13 applications of Rovral 50WP at 1.0 or 2.0 lb/ai/A of iprodione, using ground equipment only. Initial applications were make at onset of early leaf and continued on a weekly basis with the last spray on day of harvest. A total of 10 tests were conducted in Arizona (1), California (3), Florida (1), Michigan (1), New Jersey (1), Oregon (1), and Texas (2). The residue data are presented in Table 1 below.

Table 1. Iprodione Residues In/On Carrot Roots Harvested at 0-Day Preharvest Interval (PHI).

Location and Site No.	Total Application (lb/ai/A)	Residues of Iprodione (ppm)*			
		Total Residues	Iprodione	Isomer	Metabolite
TX-1	-	0.00	0.00	0.00	0.00
CA-1	-	0.00	0.00	0.00	0.00
MI	-	0.00	0.00	0.00	0.00
FL	-	0.05	0.05	0.00	0.00
CA-2	-	0.06	0.06	0.00	0.00
NJ	-	0.06	0.06	0.00	0.00
AZ	-	0.07	0.07	0.00	0.00
TX-2	-	0.11	0.11	0.00	0.00
CA-3	-	0.14	0.14	0.00	0.00
OR	-	1.61	0.00	0.00	0.00
TX-2	8.0	0.49	0.49	0.00	0.00
FL	8.0	0.61	0.61	0.00	0.00
CA-3	8.0	0.73	0.63	0.10	0.00
MI	8.0	0.64	0.64	0.00	0.00
OR	8.0	1.67	1.67	0.00	0.00
NJ	8.0	2.13	2.13	0.00	0.00
CA-2	8.0	2.57	2.52	0.05	0.00
AZ	8.0	2.90	2.80	0.10	0.00
CA-1	8.0	3.18	3.13	0.05	0.00
TX-1	13.0	1.63	1.32	0.31	0.00
CA-3	16.0	0.91	0.77	0.14	0.00
TX-2	16.0	0.87	0.87	0.00	0.00
MI	16.0	1.39	1.34	0.05	0.00
FL	16.0	2.57	2.41	0.08	0.08
OR	16.0	3.12	3.06	0.06	0.00
NJ	16.0	3.23	3.13	0.05	0.05
CA-2	16.0	4.48	4.40	0.08	0.00
AZ	16.0	6.94	6.84	0.10	0.00
CA-1	16.0	7.39	7.22	0.17	0.00
TX-1	26.0	2.79	2.24	0.55	0.00

* Corrected for recovery

In Table 1 the check sample data indicate a slight contamination or background problem in four tests with results of 0.06 to 0.14 ppm of apparent iprodione. These data are not a problem since finite residues in carrots treated at 1X (8.0 lb/ai/A) range from 0.49 to 3.13 ppm iprodione. The Oregon check sample analysis of 1.61 ppm corresponds to the 1.67 ppm iprodione found in 1X treated carrots, indicating a definite field sampling or application error.

Total residues in carrots treated at 8.0 lb/ai/A range from 0.49 to 3.18 ppm. The 2X (16.0 lb/ai/A) data for total residues range from 0.87 to 7.39 ppm, indicating a direct ratio between application rate of Rovral 50WP and the total residues of iprodione resulting in carrot roots.

The total data presented in Table 1 were generated by field tests across the United States representing a geographic distribution covering 80 percent of the carrot-producing area of the United States. These data show that the maximum residue expected from application of Rovral 50WP according to label use would be 3.18 ppm, iprodione residues. The proposed tolerance of 5.0 ppm iprodione residues is considered adequate.

Meat, Milk, Poultry and Eggs:

Tolerances for residues of iprodione and its hydroxylated and nonhydroxylated metabolites under 180.399(b) are established at the following levels: milk at 0.5 ppm; meat, fat, and meat byproducts of cattle, goats, hogs, horses, and sheep at 0.5 ppm; poultry meat and meat byproducts at 0.4 ppm, poultry fat at 2 ppm, and poultry liver at 3 ppm, and eggs at 0.8 ppm.

Carrots are not considered to be a major animal feed item but 30 percent of all carrot production in the U.S. is fed to cattle. In our previous considerations (M.F. Kovacs, October 25, 1983, PP#2F2728), in cattle fed 200 ppm of iprodione for 28 days, maximum residues were 0.389 ppm (of total hydroxylated and nonhydroxylated metabolites) in milk at 17 days. Maximum residues of nonhydroxylated metabolites were 0.13 ppm in muscle, 0.52 ppm in fat, 2.87 ppm in beef kidney, and 1.95 ppm in liver. The diet of both dairy and beef cattle can consist of up to 30 percent of cull carrots, yielding a dietary burden of (30% x 5 ppm) about 1.5 ppm iprodione.

The animal dietary burden from consuming a 100 percent diet of cull carrots bearing residues of 5.0 ppm is significantly less than the animal dietary burden from other animal feedstuffs bearing iprodione residues at significantly higher residue levels, for example raisin waste at 300 ppm, dried grape pomace at 225 ppm, peanut hulls at 7 ppm, and peanut hay or forage at 150 ppm. Further, the animal dietary burdens resulting from 100 percent intake of treated carrots bearing residues at the proposed tolerance level of 5.0 ppm are still numerically less than the established meat and milk tolerances. Thus, we can conclude that the established meat and milk tolerances are not likely to be exceeded as a result of the use of iprodione as proposed. Carrots are not a feed item for poultry.

OTHER CONSIDERATIONS

International Tolerances:

There are no Codex, Canadian, or Mexican tolerances for residues of iprodione in or on carrots. Codex MRL for iprodione on other commodities are based on levels of iprodione *per se*, that is, the "indicator compound concept." Since the majority of the iprodione residues on carrots are parent compound, the indicator compound concept could be applicable in the present instance. Therefore, we might anticipate a compatability problem. A Codex sheet is attached.

cc: R.F., Circu., V.F. Boyd, EAB, EEB, PMSD/ISB, PP#7E3474
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4/3/87

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Iprodione (Rovral®)

PETITION NO. 7E3474
V.F.Boyd 4/3/87

CCPR NO. 111

Codex Status

/ / No Codex Proposal
Step 6 or above

Residue (if Step 9):

Iprodione

Crop(s) Limit (mg/kg)

None (on carrots

Proposed U.S. Tolerances

Residue: Parent, its isomer and the dealkylated metabolite

Crop(s) Tol. (ppm)

CARROTS 5.0

CANADIAN LIMIT

Residue:

Crop Limit (ppm)

None (on carrots)

MEXICAN TOLERANCIA

Residue:

Crop Tolerancia (ppm

NOTES:

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