4-18-86

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

APR 18 1986

MEMORANDUM

OFFICE OF PESTICIDES AND TOXIC SUBSTANCES

SUBJECT: PP6F3366/FAP6H5496: Iprodione in or on Potatoes. Evaluation of Analytical Method and Residue Data. EPA ACCESSION NUMBER 261265, 261266. [RCB # 636, 637]

TO: H. Jacoby, PM 21
Registration Division (TS-767)

and

Toxicology Branch
Hazard Evaluation Division (TS-769)

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

FROM: R. W. Cook, Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

Agrochemical Division, Rhone-Poulenc Inc. proposes 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 the raw agricultural commodities potatoes at 0.5 ppm, and food additive tolerances for processed potatoes dried potatoes (flakes) and potato chips at 2.5 ppm.

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.

Tolerances for combined residues of 3-(3,5-dichlorophenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidinecarboxamide [iprodione] 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 (expressed as iprodione equivalents) have been established under 40 CFR 180.399(a) in or on a variety of raw agricultural commodities at levels from 0.05 (almond nutmeats)to 60 ppm (grapes). Tolerances in meat, milk, poultry and eggs are established under 40 CFR 180.399(b) in milk

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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 0.4 ppm, poultry fat 2 ppm, and poultry liver at 3 ppm, and eggs at 0.8 ppm, 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-hydroxyphenylureidocarboxamide), all expressed as iprodione equivalents. Tolerances for residues of iprodione (as above) are established under 21 CFR 193 at 300 ppm in raisins and also established under 21 CFR 561 for residues in dry grape pomace at 225 ppm, raisin waste at 300 ppm, and in peanut soapstock at 10 ppm. Tolerances are currently pending for beans; a Section 18 use of iprodione on rice in Texas has recently been recommended by RCB.

A Registration Standard does not exist for iprodione at this time.

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-imidazolidine-carboxamide [RP-30228], and 3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide [RP-32490]. The residue of concern in animals are iprodione [3-(3,5-dichlorophenyl)-N-(1-methylethyl)2,4-dioxo-1-imidazolidine carboxamide], 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-hydroxyphenylureidocarboxamide), all expressed as iprodione equivalents.

2a. 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 0.5 ppm in the raw agricultural commodity potatoes from the use as proposed.

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

3c. We are unable to determine the appropriate levels of food additive tolerance for processed potato products, if needed. Residue data from potato processing studies utilizing potatoes bearing residues near the tolerance level are needed to determine the adequacy of the proposed food additive tolerance levels. Exaggerated application rates may be necessary to obtain potatoes with adequate residues for processing studies.

4a. A revised Section F including the term "(expressed as iprodione equivalents)" is needed.

4b. The food additive tolerances should be proposed in terms of "Potatoes, processed (including chips).", not chips and flakes.

Recommendations:

We recommend against the establishment of the proposed tolerances, for the reasons cited in Conclusions 3c, and 4. For a favorable recommendation, the petitioner should be advised that the following information is needed.

1. Residue data from potato processing studies utilizing potatoes bearing residues near the tolerance level are needed to determine the adequacy of the proposed food additive tolerance levels. Exaggerated application rates may be necessary to obtain potatoes with adequate residues for processing studies.

2. A revised Section F including the term "(expressed as iprodione equivalents)" is needed. Further, the food additive tolerances should be proposed in terms of "Potatoes, processed (including chips).", rather than as "Chips" and "Flakes".

DETAILED CONSIDERATIONS:

Formulation:

The formulation proposed for use is formulated from Iprodione, EPA Reg. No. 359-684. It is 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 manufacturing impurities or inerts.

Directions for Use: Potatoes:

For early blight (Alternaria solani), apply 2 pounds product (1 lbai/A). Begin applications when conditions first become favorable for disease development. Up to 3 subsequent applications can be applied at 7-10 day intervals or as required. For white mold (Sclerotinia sclerotiorum), apply 2 pounds product (1 lbai/A). Apply immediately prior to row closing and if conditions are favorable for disease development, again 28 days later. A single, flat fan, or cone nozzle should be centered and adjusted to provide complete coverage of each row. Do not apply within 14 days of harvest. Up to 4 applications can be made per season.

Nature of the Residue:

Plants:

Plant metabolism studies have been reported on strawberries and wheat (A. Rathman, 3/2/79, PP8G2087), peaches (R. Perfetti, 5/13/84, PP2F2596), lettuce (N. Dodd, 4/11/83, PP3G2801), and peanuts (N. Dodd, 5/31/84, PP4G3037). 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 that metabolism in potato plants to proceed along the pathways previously identified. We reiterate our conclusion that the residues of concern in plants are iprodione [3-(3,5-dichloro phenyl)-N-(1-methylethyl)-2,4-dioxo-1-imidazolidine carboxamide]; 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].

Animals:

The metabolism of iprodione in cows, goats, and rats has been evaluated in our review of PP2F2728 (M. F. Kovacs, 10/25/82, almonds). Poultry studies have been reviewed (R. Cook, 2/21/84, PP3F2964/FAP4H5415). 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-imidazolidine carboxamide], 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-imidazolidine carboxamide (RP-36112), and N-(3,5-dichloro-4-hydroxyphenyl ureidocarboxamide) (RP-36115), all expressed as iprodione equivalents. We reiterate that conclusion.

Analytical Methods:

The analytical method for iprodione, marked "CONFIDENTIAL", is entitled "RHONE-POULENC ANALYTICAL METHOD NO. 151 (Revised, 1981), DETERMINATION OF RP 26019 AND ITS METABOLITES IN/ON STONE FRUIT AND NUT CROPS BY GLC AND TLC", (PDD Report No.: 81/008, REF.No.: 81/234/BHL/AG). The method is claimed to be suitable for the analysis of iprodione in stonefruit and nut crops. In principle, iprodione residues in frozen, crushed and blended, plant tissues are extracted twice into acetone. Extraction involves liquid-liquid partition using ethyl acetate/ methylene chloride, cleanup on Florisil and analysis for iprodione residues by GLC with ^{63}Ni electron capture detection. Processed potato products are rehydrated prior to extraction. The method determines RP26019, RP-36112, and RP-36115. Recovery values for RP 26019 in tubers and cull potatoes ranged from 69 to 130% at fortification levels of 0.1 to 2 ppm, while recoveries of RP 30228 and RP 32490 ranged 70 to 131% and 72 to 107%, respectively, at fortification levels of 0.1 to 0.5 ppm. Recoveries, respectively, of these three compounds in processed potato products chips and flakes were 122-129, 71-153, and 100-104%.

A successful trial of the ~~PAM II~~ method was conducted on kiwifruit in conjunction with PP3F2810 (R. Perfetti, 3/21/83).

work

We conclude that adequate methods are available for enforcement purposes.

Residue Data:

Previously, under 85-WA-07, we considered 6 field trials with iprodione on potatoes, 4 in WA and 2 in OR. Five trials were conducted at 1 lbai/A by sprinkler irrigation, and only one trial used conventional application equipment. All harvest samples were obtained at >48 days after last application. Combined residues of iprodione in these potatoes were reported at <0.05 ppm, the limit of detection. Since the interval after last application (48 days) is much greater than the 14 day PHI proposed in the current submission, we conclude that the residue data contained in 85-WA-07 is not pertinent to our current considerations.

Field trials were conducted in 10 states (CA, CO, FL, ID, ME, ND, NJ, NY, OR, WA). Geographic representation is considered adequate. Potatoes were treated with 4 (or in some trial 6) applications of either 1 or 2 lbai/A (1X or 2X), with 6 to 30 days after last application. In six trials, applications were made with tractor sprayers, while in the remainder of the trials, backpack sprayers were used. At harvest, samples of tubers and culls were collected and frozen for storage prior to analysis usually within 2 months. Prior stability data indicate no problems during short storage intervals. Additional samples of tubers from two trial were processed into chips and dried flakes.

Combined residues of iprodione and its metabolite and isomer were below the proposed 0.5 ppm tolerance level in all tuber samples from either the 1X or 2X application rates, at 14 days PHI. In fact, most samples of tubers were <0.05 ppm (limit of detection). In cull potatoes, combined residues were somewhat higher, with levels of 0.39 ppm from 4 x 2 lbai/A at 14 days. Residues appeared to be generally higher in the culls than in the tubers. The petitioner speculates that cull potatoes may have more residue than tubers because the culls have "more blemishs, cuts and odd shapes and therefore more opportunity for chemical adsorption and/or soil contamination." While the data do not clearly indicate dosage rate differences, we consider them to adequately reflect the expected residues, since iprodione is applied to the above ground portion of the potato plant while the residue samples are from the underground portions of the plant.

The distribution of the residue is different in potatoes than in previously reported studies. In potato tubers and cull potatoes the presence of the metabolite or the isomer did not necessarily coincide with the presence of the parent compound. That is, residues of the metabolite or the isomer were present without detectable residues of the parent compound.

We conclude that combined residues of iprodione and its metabolite and isomer are not likely to exceed the proposed

tolerance level of 0.5 ppm in the raw agricultural commodity potatoes from the use as proposed herein.

No residue data are available for potato vines, but since potato vines are not considered an animal feed item, residue data for this plant portion are not needed.

Processed Potato Fractions:

Potatoes treated in two of the above discussed residue trials were processed into potato chips and dried potato flakes. In one trial, potato tubers bearing iprodione residues at <0.05 ppm (i.e. at the limit of detection) were processed into chips and flakes. Flakes contained combined residues of 0.05 ppm (the limit of detection) while chips were < 0.05 ppm. In the second trial, tubers bearing 0.06 ppm (slightly greater than detection limit) showed combined residues at 0.39 ppm in chips from the 2X treatment (8 lbai/A). The petitioner then concluded that 5X is the appropriate concentration factor and proposes food additive tolerances of 2.5 ppm in processed potato fractions.

We believe concentration factors should be calculated from RACs bearing field residues at or near the tolerance level, not calculated from RAC with barely detectable residues. Residue data from potato processing studies utilizing potatoes bearing residues near the tolerance level are needed to determine the adequacy of the proposed food additive tolerances. Exaggerated application rates may be necessary to obtain potatoes with adequate residues for processing studies.

We are unable to draw conclusions on the adequacy of the proposed food additive tolerances for processed potato products. The food additive tolerances should be proposed in terms of "Potatoes, processed (including chips)." rather than as "Chips" and "Flakes".

Residues in 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 0.4 ppm, poultry fat 2 ppm, and poultry liver at 3 ppm, and eggs at 0.8 ppm.

Potatoes are a major animal feed item. In our previous considerations (M. F. Kovacs, 10/25/83, PP2F2728), 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% of cull potatoes, yielding a dietary burden

of 30 % X 0.5 ppm = 0.15 ppm iprodione. Poultry diets may consist of up to 20% potatoes (dietary burden = 20% X 0.5 = 0.1 ppm), while the diet of swine can consist of 50% potatoes (dietary burden = 50% X 0.5 = 0.25 ppm.

The animal dietary burden from comsuming 100% diet of cull potatoes bearing residues of 0.5 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% intake of treated potatoes bearing residues at the proposed tolerance level of 0.5 ppm are still numerically less than the established meat, milk, poultry, and egg tolerances. Thus, we can conclude that the established meat, milk, poultry and egg tolerances are not likely to be exceeded as a result of the use of iprodione as proposed.

OTHER CONSIDERATIONS:

International Tolerances:

There are no Codex, Canadian, or Mexican tolerances for residues of iprodione in or on potatoes or potato byproducts. 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 potatoes are not parent compound, the indicator compound concept is not applicable in the present instance. Therefore, we do not anticipate any compatibility problems. A Codex sheet is attached.

Attachment 1: International Residue Limit Status Sheet.
cc: R.F., Circu, R. W. Cook, PP#6F3366/FAP6H5496, PMSD(ISB), TOX.
TS-769:RCB:Reviewer:RWCook:Date:4/16/86:CM#2:RM:810:557-7377
RDI:Section Head:RSQuick:Date:4/16/86:RDSchmitt:Date:4/16/86

8.

I. L.
4/14/86

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Iprodione [Rovral®]

PETITION NO. ~~6F3179~~ 6F3366 / ~~6H5440~~ 6H5496
R. W. Cook
~~11/9/84~~ 4/4/86

CCPR NO. 111

Codex Status

|__| No Codex Proposal Step 6 or above

Residue (if Step 9):
Iprodione

Crop(s)	Limit (mg/kg)
none (on potatoes)	

Proposed U.S. Tolerances

Residue:
Iprodione, 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)
Pototoes	0.5
Processsed potatoes	2.5

CANADIAN LIMIT

Residue: Iprodione including metabolites 3-isopropyl-N-(3,5-dichlorophenyl)-2,4-dioxo-imidazolidine-1-carboxamide and 3-(3,5-dichlorophenyl)-2,4-dioxo-imidazolidine-1-carboxamide.

Crop	Limit (ppm)
none (on potatoes)	

MEXICAN TOLERANCIA

Residue:

Crop	Tolerancia (ppm)
None	

Comments: