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

FEB 15 1985

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#4F3150. (RCB #210). Iprodione on Dry, Snap, and Lima Beans. Evaluation of Analytical Methods and Residue Data. Accession No. 072912, 072913.

FROM: Cynthia Deyrup, Ph.D., Chemist
Residue Chemistry Branch
Hazard Evaluation Division (TS-769)

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

TO: Henry Jacoby, Product Manager No.21
Registration Division (TS-767)

and

Toxicology Branch
Hazard Evaluation Division (TS-769)

Rhone-Poulenc proposes the establishment of permanent 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 des-isopropyl metabolite, 3-(3,5-dichlorophenyl)-2,4-dioxo-1-imidazolidinecarboxamide in/on the following raw agricultural commodities:

Beans, succulent	2 ppm
Beans, dry	2 ppm
Bean forage	30 ppm
Bean hay	90 ppm

1/20

Permanent tolerances for iprodione, its isomer, and its metabolite have been established on a number of crops ranging from 0.05 ppm on almond meat to 20 ppm on stone fruits (40 CFR 180.399).

A tolerance for the combined residues of iprodione, its isomer, and the des-isopropyl metabolite was established on grapes in the Federal Register (12/5/84) at 60 ppm. Also established at this time were tolerances for iprodione and its non-hydroxylated metabolites in the fat, meat, and meat by-products (except liver and kidney) of cattle, goats, hogs, horses, and sheep at 0.4 ppm; kidney and liver of cattle, goats, hogs, horses, and sheep at 3 ppm; meat and meat by-products (except liver) of poultry at 0.4 ppm; poultry liver at 3 ppm; poultry fat at 2 ppm; and eggs at 0.8 ppm. A tolerance for iprodione and its hydroxylated and non-hydroxylated metabolites in milk at 0.3 ppm was also established at this time.

Food additive tolerances for iprodione, its isomer, and the des-isopropyl metabolite on raisins and raisin waste (300 ppm) and grape pomace (225 ppm) have been approved and are in the process of being established.

Tolerances for the combined residues of iprodione, its isomer, and the des-isopropyl metabolite are pending on peanuts (0.5 ppm), peanut forage and hay (150 ppm), peanut hulls (7 ppm), crude peanut oil (1 ppm), and soapstock (10 ppm) in PP#4F3129/4H5440. Also pending in that petition are tolerances for iprodione and its non-hydroxylated metabolites (expressed as iprodione equivalents) in the meat, fat, and meat by-products (except liver and kidney) of cattle, hogs, goats, horses and sheep at 0.6 ppm; kidney of cattle, hogs, goats, horses, and sheep at 3.0 ppm; liver of cattle, hogs, goats, horses and sheep at 2.0 ppm; meat, fat, and meat by-products of poultry at 0.05 ppm; and eggs at 0.01 ppm. PP#4F3129/4H5440 also proposes a tolerance for iprodione and its hydroxylated and non-hydroxylated metabolites on milk at 0.4 ppm.

Conclusions

1a. Residue data on succulent beans and bean forage reflect PHI's ranging from 3-21 days; therefore, the residue data on succulent beans and forage are relative to the proposed use. The residue data for bean hay reflect a 45 day PHI only. Although this PHI is reflective of dry bean hay, a PHI of 2 weeks is more reflective for snap bean hay. Because the proposed use implies PHI's ranging from 2-6 weeks, the petitioner will need to submit residue data on bean hay reflecting a PHI of about 14 days (see also the Proposed Use and Residue Data sections of this review).

1b. Since the forage residue data reflect PHI's of 3-21 days, the petitioner should restrict foraging to 3 days after treatment with iprodione in a revised Section B/label. The present label would permit foraging directly after application, and no data were submitted to reflect a 0 day PHI.

2a. RCB concludes that the nature of the residue in plants is adequately understood. The residues of concern are iprodione per se, its isomeric metabolite RP-30228, and the des-ispropyl metabolite RP-32490.

2b. The nature of the residue in milk is adequately understood. The residues of concern are iprodione and its hydroxylated and non-hydroxylated metabolites.

2c. Presently, the residues of concern in meat, fat and meat by-products of cattle, goats, hogs, horses, and sheep are iprodione per se and its non-hydroxylated metabolites. However, the major metabolite in goat kidney is apparently hydroxylated.

However, as a result of this re-review, RCB now has reservations concerning the structural assignment of 3,5-dichloro-4-hydroxyphenylurea to Compound X. According to ASD Report No. 83/007, Lab. Ref. No. 83/088/BHL/AG (submitted with PP#3F2964), Compound X is identified by mass spectrometry as 3,5-dichloro-4-hydroxyphenylurea. However, in "Addendum to ADC Project #622, 'Preliminary Characteristics of Unknown X from Kidney'" (also submitted with PP#3F2964), the investigators concluded that Compound X is a non-hydroxylated metabolite of iprodione. The petitioner should resolve these apparently conflicting conclusions regarding the structure of Compound X.

2d. RCB has previously concluded that the nature of the residue in animals is adequately understood. However, the tolerance expression for animal commodities is being reconsidered (PP#4F3129 - see Other Considerations).

2e. RCB has previously concluded that the nature of the residue in poultry tissues and eggs is adequately understood. However, the present tolerance expression for animal commodities is being reconsidered (PP#4F3129 - see Other Considerations).

3a. The petitioner should furnish recovery data for metabolites RP-30228 and RP-32490 from dry beans and bean hay.

3b. Sample chromatograms were submitted of iprodione and RP-30228 standards, snap bean check samples and snap beans fortified with iprodione and RP-30228. The petitioner should also submit the corresponding chromatograms for lima beans, dry beans, bean forage, and bean hay. In addition, the petitioner will need to furnish representative chromatograms reflecting check samples and samples fortified with RP-32490 for succulent beans, dry beans, bean forage, and bean hay for RCB's evaluation. RCB can't judge the adequacy of the methodology used to generate the submitted residue data until representative chromatograms have been submitted.

The petitioner should submit more than one check sample chromatogram per commodity.

4a. The petitioner needs to provide residue data for iprodione residues on lima beans grown in CA. RCB needs residue data from CA, not only because CA is a leading producer of lima beans, but also because residue levels on lima beans from CA may differ from residue levels observed in other areas because of California agricultural practices, such as irrigation.

4b. The petitioner will need to submit additional residue data from MI and CA on dry beans in order to achieve adequate geographic representation.

4c. The petitioner has provided one chromatogram of a check sample of snap beans, one of treated snap beans, and one of treated bean forage. The treated snap bean chromatogram

reflected an analysis for iprodione, and the treated bean forage reflected an analysis for RP-30228. The petitioner should submit pertinent representative chromatograms of treated succulent beans, dry beans, forage, and hay reflecting analyses for iprodione, RP-30228, and RP-32490.

4d. Both bean hay field trials reflect a PHI of 45 days. Although this PHI is relative to the proposed use for dry bean hay, about 2 weeks would be a more relative PHI for snap bean hay. The petitioner will need to submit residue data for bean hay reflecting about a 14 day PHI. (See Residue Data section of this review).

4e. Although the maximum level of combined residues of iprodione/metabolites observed in bean forage was 13.3 ppm after a 9 day PHI, and the maximum level of combined residues of iprodione/metabolites observed in bean hay was 19.1 ppm after a 45 day PHI, the petitioner has proposed iprodione tolerance levels of 30 ppm on bean forage and 90 ppm on bean hay. The petitioner needs to explain why he feels that tolerances of 30 ppm and 90 ppm are necessary for residues of iprodione/metabolites on bean forage and bean hay respectively.

4f. At this time RCB can not judge the appropriateness of the proposed tolerances for the reasons summarized below:

i. Residue data on lima beans from CA are needed.

ii. Residue data on dry beans from CA and MI are needed.

iii. Pertinent representative chromatograms of check samples, fortified samples, and treated samples reflecting analyses for iprodione, RP-30228 and RP-32490 need to be submitted for dry and succulent beans, bean forage and bean hay.

iv. Residue data for bean hay reflecting about a 14 day PHI are needed.

v. Once the deficiencies involving the residue data have been resolved, the petitioner may find it appropriate to repropose lower tolerance levels for iprodione/metabolites on bean forage and hay in a revised Section F.

4g. At this time RCB will defer its conclusions on whether secondary residues of iprodione/metabolites in meat, milk, poultry and eggs resulting from the proposed use on beans would exceed established or proposed tolerances (see also PP#4F3129) until those issues stated above in 4f have been resolved.

5a. Codex has established a tolerance for residues of iprodione per se on dry beans at 0.2 ppm. Canada has established a tolerance for iprodione (presumably parent) residues at 0.1 ppm. If the proposed tolerances on dry and succulent beans are established, there will be a compatibility problem.

Recommendations

RCB recommends against the establishment of the proposed tolerances for iprodione, its isomer, and its des-isopropyl metabolite on succulent beans, dry beans, bean forage and bean hay at 2.0, 3.0, 30, and 90 ppm for the reasons given above in our conclusions 1a, 1b, 2c, 3a, 3b, 4a, 4b, 4c, 4d, 4e, 4f, and 4g.

The petitioner must also be notified that since an apparently hydroxylated metabolite in goat kidney has been detected, the question of the tolerance expression for animal commodities is being reconsidered in PP#4F3129. Presently, the tolerance expression for meat, poultry and eggs includes iprodione and its non-hydroxylated metabolites, whereas the tolerance expression for milk includes iprodione and its non-hydroxylated and hydroxylated metabolites.

Detailed Considerations

Manufacturing and Formulation

The synthesis of iprodione was discussed in RCB review of PP#8G2087 (memo of A. Rathman, 3/2/79). Technical iprodione is 95% pure. The impurities are not expected to cause a residue problem.

Iprodione is formulated as Rovral, a wettable powder, which contains 50% active ingredient. The inerts are cleared under 40 CFR 180.1001.

Proposed Use

For use on succulent and dry beans, iprodione is to be applied at early bloom (25-50% of the plants with at least one bloom) at the rate of 0.75-1.0 lb a.i./A in 20-40 gal water/A. A second application may be made at peak bloom (maximum number of open blooms). Both aerial and ground equipment application are permissible. Garlic and leafy vegetables may be rotated after harvest; root crops, cereal grains, soybeans, and tomatoes may be rotated the year following treatment. No specific PHI is imposed.

The last application of iprodione coincides with the peak bloom period of the beans.

Harvesting of the beans could take place 2 weeks after the last application in the case of snap beans, whereas in the case of dry beans, harvesting would not take place until around 6 weeks after the last application of iprodione. Residue data on succulent bean and bean forage reflect PHI's ranging from 3-21 days; therefore, the residue data on succulent beans and forage are relative with regard to the proposed use. However, the residue data for bean hay reflects a 45 day PHI only. Although this PHI is reflective for dry bean hay, a PHI of 2 weeks is more reflective for snap bean hay. Because the proposed use implies PHI's ranging from 2-6 weeks, the petitioner will need to submit residue data on bean hay reflecting a PHI of about 14 days.

Since the forage residue data reflect PHI's of 3-21 days, the petitioner should restrict foraging to 3 days after treatment with iprodione in a revised Section B/label. The present label would permit foraging directly after application.

Nature of the Residue

Plants

No new plant metabolism studies were submitted with this petition. However, metabolism studies on peanuts (PP#4G3037), lettuce (PP#3G2801), strawberries and wheat (PP#8G2087), and peaches (PP#2F2596) have been previously submitted. All the metabolism studies exhibited the same general pattern. RCB concludes that the nature of the residue in plants is adequately understood. The residues of concern are iprodione per se, its isomeric metabolite RP-30228, and the des-isopropyl metabolite RP-32490.

Animals

No new metabolism studies were submitted with this petition, but metabolism studies with ^{14}C ring labeled iprodione have been carried out in cows and goats (PP#2F2728) and chickens (PP#3F2964). Further work leading to the identification of additional goat metabolites was also described in PP#3F2964.

Cow

Two cows were dosed orally with ^{14}C phenyl ring iprodione at a daily rate of approximately 2 mg/kg of body weight, which corresponds to approximately 60 ppm based on daily feed intake. One cow received a single dose; the other cow received multiple doses over a 5 day period. Seven days after dosage, excretion of radioactivity became insignificant, and the cows were then slaughtered. The tissue distribution of radioactive iprodione equivalents is given below.

TOTAL ^{14}C-RESIDUES IN TISSUE

A. Single Dose Study

Tissue	Average ppm
Liver	0.131
Kidney	0.027
Muscle	0.003
Fat	0.033
Heart	0.005
Blood	0.013

B. Multidose Study

Tissue	Average ppm
Liver	0.447
Kidney	0.047
Muscle	0.003
Fat	0.050
Heart	0.009
Blood	0.031

The liver contained the highest levels of radioactive iprodione equivalents, of which only 10% were extractable with acetone. Acidic acetone extracted an additional 9% of the total radioactive residue from the filter cake remaining after acetone extraction. Acid, base and enzymatic (pronase) hydrolysis liberated up to 60, 73 and 29% of the total radioactive residue respectively. Following acid hydrolysis, only 9% of the total radioactive residue was recovered by ethyl acetate extraction.

Since it was not possible to characterize or identify any of the residues in cow liver because of the bound nature of the residue a fractionation study was carried out. The following distribution of ^{14}C-residues resulted:

Fraction	% of Total ^{14}C-Residue
Organosoluble	17.3
Glycogen	2.2
Lipid	13.8
Nucleic Acid	2.2
Protein	8.6
Insoluble	51.2

The petitioner tentatively concluded that the distribution of radioactivity indicated that the ^{14}C residues in liver may result from iprodione breakdown and reincorporation of iprodione fragments.

Milk

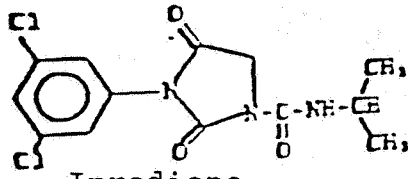
In the multidose study the concentration of iprodione equivalents in milk increased (to 0.432 ppm) until dosing was stopped on the fifth day so that a plateau was never attained. The level of iprodione residues had decreased to 0.01 ppm by 96 hours post-treatment.

Acetone extraction of milk followed by enzymatic hydrolysis (Glusulase) resulted in 75% of the total radioactive residue partitioning into ethyl acetate for the single dose experiment and 86% for the multidose experiment. TLC resulted in the identification of 65% of the total extractable residue in the single dose cow and 62% in the multidose cow. The major metabolites in milk are RP-36114, which is hydroxylated, and RP-32490, which is not hydroxylated.

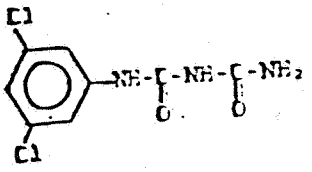
See Figure 1 for structures.

The nature of the residue in milk is adequately understood. The residues of concern are iprodione and its hydroxylated and non-hydroxylated metabolites.

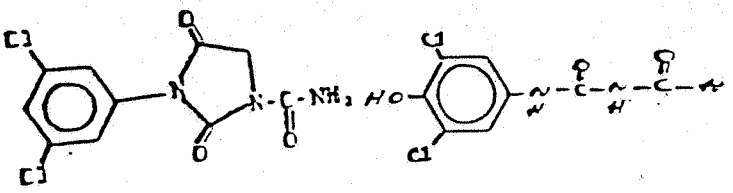
Figure 1.



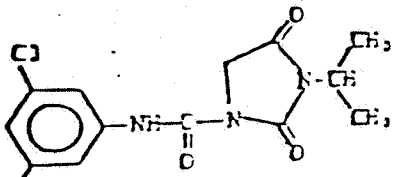
Iprodione
RP-26019



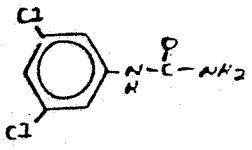
RP-36115



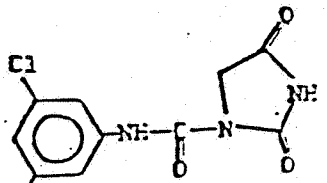
RP-23490 RP-36114



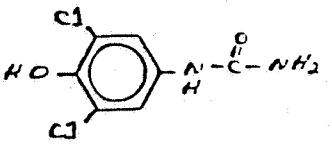
RP-30228



RP-44247



RP-36112



Compound X*

*RCB has reservations concerning this structure. See Nature of the Residue.

Goat

A goat metabolism study was submitted with PP#2F2728, and results of the additional investigation of previously unidentified metabolites were submitted with PP#3F2964.

One goat was dosed for 5 days with ^{14}C-phenyl iprodione at a daily rate of approximately 2 mg/kg which corresponds to about 200 ppm based on daily feed intake. The goat was slaughtered 4 hours after the final dose.

The initial study (PP#2F2728, memo of M. Kovacs, Jr., 10/25/82) yielded the following distribution of metabolites in tissue.

Tissue	Major Residues	% of Extractable Residue Identified
Liver	Iprodione RP-32490 Compound X Compound Y	40
Kidney	RP-32490 RP-36115 Compound X	32
Muscle	RP-32490	44
Fat	RP-32490	82

Further investigation of Compound X and Compound Y (see PP#3F2964) resulted in the identification of Compound Y as 3,5-dichlorophenylurea (RP-44247) and Compound X as 3,5-dichloro-4-hydroxyphenylurea so that 55% of the total extractable residue in goat kidney is now identified. RCB concluded that while 55% identification is less than desirable, the rapid depuration of iprodione residues upon withdrawal of the dosing permitted the conclusion that the metabolism of iprodione is adequately understood (memo of R. Cook, PP#3F2964/4H5415, 2/21/84).

Presently the residues of concern in meat, fat and meat by-products of cattle, goats, hogs, horses, and sheep are iprodione per se and its non-hydroxylated metabolites. However, the major metabolite in goat kidney is apparently hydroxylated.

However, as a result of this re-review, RCB now has reservations concerning the structural assignment of 3-5-dichloro-4-hydroxyphenylurea to Compound X. According to ASD Report No. 83/007, Lab. Ref. No. 83/088/BHL/AG (submitted with PP#3F2964), Compound X is identified by mass spectrometry as 3,5-dichloro-hydroxyphenylurea. However, in "Addendum to ADC Project #622, 'Preliminary Characteristics of Unknown X from Kidney'" (also submitted with PP#3F2964), the investigators concluded that Compound X is a non-hydroxylated metabolite of iprodione.

The latter investigators concluded that Compound X was non-hydroxylated because application of the enforcement analytical methodologies for hydroxylated and non-hydroxylated metabolites led exclusively to the formation of the heptafluorobutyryl (HFB) - derivative of 3,5-dichloroaniline. Had a 4-hydroxyl substituent been present, the HFB derivative of 3,5-dichloro-4-methoxyaniline would have been formed. The petitioner should resolve these apparently conflicting conclusions regarding the structure of Compound X.

Data submitted with PP#3F2964 show that Compound X is fully accounted for by the analytical methodology for hydroxylated metabolites. However, the use of the methodology for non-hydroxylated metabolites results in a 41% conversion to the HFB-3,5-dichloroaniline derivative. The latter method omits both the acid hydrolysis (which cleaves conjugates) as well as the methylation step used in the analysis for hydroxylated metabolites.

RCB has previously concluded that the nature of the residue in animals is adequately understood. However, the present tolerance expression for animal commodities is being reconsidered (PP#4F3129 - see Other Considerations).

Poultry

A poultry metabolism study was submitted with PP#3F2964 (memo of R.W. Cook, 2/21/84). Leghorn hens were dosed with ^{14}C-phenyl iprodione for 15 days.

In chicken liver, the major metabolites were RP-32490, RP-4427, and unknown Z. Unknown Z possesses the 3,5-dichloroaniline nucleus and is fully accounted for by enforcement methodology for non-hydroxylated metabolites which converts RP-32490, RP-44247, and unknown Z to the HFB - derviative of 3,5-dichloraniline. Unknown Z appears to be similar to Compound X (found in goat kidney; see above) in that both appear to contain the 3,5-dichloroaniline nucleus. The major difference is that the enforcement methodology for non-hydroxylated metabolites fully accounts for unknown Z, but does not fully account for unknown X. TOX concluded that further identification of Unknown Z was unnecessary (PP#3F2964, memo of A. Arce, 5/30/84). In muscle tissue and fat, the terminal residues consisted primarily of RP-32490 and iprodione.

Eggs

The primary metabolites found in eggs (PP#3F2964, memo of R.W. Cook, 2/21/84) are RP-32490, RP-36112, RP-36115, and RP-44247, all of which are non-hydroxylated. Almost all of the total radioactive residue (97.8%) was extracted from eggs with dichloromethane and ethyl acetate. TLC identified 95% of the total extractable residue from eggs.

RCB has previously concluded that the nature of the residue in poultry tissues and eggs is adequately understood. However, the tolerance expression for animal commodities is being reconsidered (PP#4F3129 - see Other Considerations).

Analytical Methodology

All succulent samples were analyzed for iprodione and the metabolites RP-30228 and RP-32490 according to Rhone Poulenc Method No. 151. This method is similar to the procedure which has undergone a successful method trial on kiwi fruit (PP#2F2596, memo of R.B. Perfetti, 5/13/82). Briefly, the method consists of acetone extraction, liquid-liquid partitioning, gel permeation chromatography, florisil column clean-up, and analysis with GLC using a ^{63}Ni electron capture detector.

Method No. 162 was used to analyze dry samples. This method differs from method No. 151 in that the samples are extracted with aqueous acetone, a more active florisil column is used to achieve clean-up, and an acetonitrile - hexane partitioning was added prior to florisil chromatography.

Recoveries were as follows:

Crop	Fortification Level (ppm)	% Recoveries Iprodione	RP-30228	RP-32490
Green Beans	0.05 - 2.0	73 - 114		
	0.05 - 1.0		70 - 93	71 - 108
Dry Beans	0.1 - 0.2	99 - 115	_____	_____
Forage	0.5 - 5.0	92 - 111		
	0.2		73	88
Bean Hay	0.2 - 20.0	74 - 119	_____	_____

The limit of determination for succulent and dry samples is given as 0.05 ppm.

The petitioner should furnish recovery data for metabolites RP-30228 and RP-32490 from dry beans and bean hay.

Sample chromatograms were submitted of iprodione and RP-30228 standards, snap bean check samples, and snap beans fortified with iprodione and RP-30228. The petitioner should also submit the corresponding chromatograms for lima beans, dry beans, bean forage, and bean hay. In addition, the petitioner will need to furnish representative chromatograms reflecting check samples and samples fortified with RP-32490 for succulent beans, dry beans, bean forage, and bean hay for RCB's evaluation. RCB can not judge the adequacy of the methodology used to generate the submitted residue data until representative chromatograms have been submitted. The petitioner should submit more than one check sample chromatogram per commodity.

Residue Data

Field trials of snap beans were carried out in 5 states (FL, MI, NY, OR, and WI) which produce 70% (Agricultural Statistics, 1983) of the nation's snap beans. There was also one lima bean field trial, located in DE. Bean forage residue data were also generated from the succulent bean field trials described above. Residue data for dry beans and dry bean hay were generated from field trials in ID and NE which produce 23% of the nation's dry beans (Agricultural Statistics, 1983).

The petitioner needs to provide residue data for iprodione residues on lima beans grown in CA. According to the Census of Agriculture, Volume 1, Geographic Area Series, the acreage planted in lima beans in CA is double the acreage planted in lima beans in DE, the #2 state. RCB needs residue data from CA, not only because CA is a leading producer of lima beans, but also because residue levels on lima beans from CA may differ from residue levels observed in other areas because of California agricultural practices, such as irrigation. No residue data on snap beans were submitted from CA field trials; thus, no residue data on any succulent beans from CA have been submitted.

The petitioner will need to submit additional residue data from MI and CA on dry beans in order to achieve adequate geographic representation. The states of NE, ID, MI and CA together produce about 69% of the nation's dry beans.

All samples were initially stored frozen, shipped in dry ice, and then stored at 0°F until analyzed. One sample was stored one year, and all other samples were stored 2-3 months before analysis. No storage stability data for residues of iprodione/metabolites on dry and succulent beans, bean forage, and bean hay were submitted with this petition, but data submitted with PP#8G2087 indicated that residues of iprodione and RP-30228 on stone fruit are stable under frozen conditions for ca. one year. Since most of the analyses were carried out 2-3 months after sampling, RCB concludes that appropriate storage stability data have been submitted.

All field trials reflected 2 applications of 1 lb a.i./A. PHI's of 3-45 days were observed. The following ranges of residue levels were observed:

RAC	PHI (days)	Iprodione	RP-30228	RP-32490
Snap Beans	3 - 18	0.06 - 0.8	ND - 0.08	ND
Lima Beans	21	0.1	ND	ND
Snap Bean Forage	3 - 19	1.4 - 12.8	0.1 - 0.8	ND - 0.6
Lima Bean Forage	21	0.9	0.4	0.4
Dry Beans	45	ND	0.1	ND
Dry Bean Hay	45	6.9 - 15.5	1.5 - 3.3	0.3 - 0.8

The petitioner has provided chromatograms of check samples of snap bean, treated snap beans, and treated bean forage. The treated snap bean chromatogram reflected an analysis for iprodione, and the treated bean forage reflected an analysis for RP-30228. The petitioner should submit pertinent representative chromatograms of treated succulent beans, dry beans, forage, and hay reflecting analyses for iprodione, RP-30228, and RP-32490.

Both bean hay field trials reflect a PHI of 45 days. Although this PHI is relative to the proposed use for dry bean hay, about 2 weeks would be a more relative PHI for snap bean hay. The petitioner will need to submit residue data for bean hay reflecting about a 14 day PHI (see also the Proposed Use section of this review). This conclusion was finalized because of a weak correlation between the residue data for forage and hay. Observe the following residue data:

Forage	19-day PHI	12 ppm total residue
Forage	21-day PHI	1.6 ppm total residue
Hay (submitted only 2 values)	45-day PHI	9 - 19 ppm total residue

First, there is a very steep drop in the maximum residue values on forage going from 19-day PHI to 21-day PHI. Second, if it is assumed that the maximum residue found on forage at a 21 day PHI is the same as that residue that could be found on forage at 45-day (actually, it should be lower than 1.6 ppm at 45-day PHI), then there could be about a 12X concentration factor going from forage to hay. Further, this could mean that hay reflective of a 19-day PHI could contain close to 150 ppm total residue. Thus, RCB reiterates that residue data for bean hay reflecting about a 14-day PHI are needed.

Although the maximum level of combined residues of iprodione /metabolites observed in bean forage was 13 ppm after a 9 day PHI, and the maximum level of combined residues of iprodione/ metabolites observed in bean hay was 19.1 ppm after a 45 day PHI, the petitioner has proposed iprodione tolerance levels of 30 ppm on bean forage and 90 ppm on bean hay. The petitioner needs to explain why he feels that tolerances of 30 ppm and 90 ppm are necessary for residues of iprodione/metabolites on bean forage and bean hay respectively. The proposed tolerance level should not be larger than is needed for the proposed use (see EPA Guidelines, Subdivision O: Residue Chemistry). Once the deficiencies involving the residue data have been resolved, the petitioner may find it appropriate to repropose lower tolerance levels for iprodione/metabolites on bean forage and hay in a revised Section F.

At this time, RCB can not judge the appropriateness of the proposed tolerances for the reasons summarized below:

1) Residue data on lima beans from CA are needed.

2) Residue data on dry beans from CA and MI are needed.

3) Pertinent representative chromatograms of check samples, fortified samples, and treated samples reflecting analyses for iprodione, RP-30228 and RP-32490 need to be submitted for dry and succulent beans, bean forage, and bean hay.

4) Residue data for bean hay reflecting about a 14 day PHI are needed.

5) Once the deficiencies involving the residue data have been resolved, the petitioner may find it appropriate to repropose lower tolerance levels for iprodione/metabolites on bean forage and hay in a revised Section F.

Meat, Milk, Poultry and Eggs

No new animal feeding studies were submitted with this petition, but a cattle feeding study had been submitted in conjunction with PP#2F2728 (memo of M. Kovacs, Jr., 10/25/82), and a poultry feeding study was submitted with PP#3F2964 (memo of R.W. Cook, 2/21/84).

Meat and Milk

In the cattle feeding study, technical iprodione was fed at levels of 5, 15, 50, and 200 ppm to lactating cows for 29 days. Iprodione and its non-hydroxylated metabolites were determined in meat, and iprodione and its hydroxylated and non-hydroxylated metabolites were determined in milk. The results of the cattle feeding study are tabulated below at the 200 ppm feeding level:

Commodity	Iprodione Equivalents (ppm)
Muscle	0.13
Fat	0.52
Liver	1.95
Kidney	2.87
Milk (28th day)	0.33

Permanent tolerances for the combined residues of iprodione, RP-30228, and RP-32490 have been established or are in the process of being established on the following livestock feed items:

Almond hulls	0.25 ppm
Grape pomace	225 ppm
Raisin waste	300 ppm

Proposed permanent tolerances for iprodione/metabolites are pending on the following feed items:

Peanuts	0.5 ppm
Peanut forage & hay	150 ppm
peanut hulls	7.0 ppm
Peanut soapstock	10.0 ppm
Succulent beans	2.0 ppm
Bean forage	30.0 ppm
Bean hay	90.0 ppm

A possible diet consisting of 30% grape pomace, 20% bean seed, 5% peanut soapstock, 25% peanut hay, and 20% bean hay would impose a dietary burden of iprodione residues of ca. 124 ppm upon beef cattle. A possible diet for dairy cows (20% grape pomace, 20% bean seed, 60% peanut hay) would impose a dietary burden of iprodione residues of ca. 135 ppm upon dairy cattle.

Current and proposed tolerances on meat and milk RAC's are listed below:

Commodity	Currently established Tolerances	Tolerances Proposed in PP#4F3129
Meat, fat, meat by-products of cattle, goats hogs, horses, sheep	0.4	0.6 (except liver and kidney)
Kidney of cattle, goats, hogs, horses, sheep	3.0	3.0
Liver of cattle, goats hogs, horses, sheep	3.0	2.0
Milk	0.3	0.4

Poultry

In the chicken feeding study submitted in conjunction with PP#3F2964, technical iprodione was fed to laying hens at levels of 2, 20, and 100 ppm for 28 days. The feeding of iprodione rather than aged residues was acceptable because both plants and animals metabolize iprodione to the des-isopropyl metabolite RP-32490 (memo of R.W. Cook, 2/21/84). The results of the feeding at 20 ppm are tabulated below:

Commodity	Iprodione Equivalent (ppm, 20 ppm feeding level)
muscle	0.3
fat	2.6
liver	4.1
kidney	2.3
eggs	0.8

The following iprodione/metabolites tolerances on poultry feed items are either proposed or are in the process of being established:

Feed Item	Proposed Tolerances (ppm)
succulent bean seed	2.0
grape pomace	225.0 (establishment pending)
peanuts	0.5
peanut soapstock	10.0

A diet consisting of 15% succulent bean seed, 5% grape pomace, 10% peanut meal, and 5% peanut soapstock would impose a dietary burden of iprodione residues of 12.1 ppm upon a laying hen. The worst case diet for turkeys and broilers imposes about the same dietary burden of iprodione residues upon these animals.

Tolerances for iprodione and its non-hydroxylated metabolites have been established for poultry fat (2.0 ppm), poultry liver (3.0 ppm), and poultry meat and meat by-products (0.4 ppm), and eggs (0.8 ppm).

At this time, RCB will defer its conclusion on whether secondary residues of iprodione/metabolites in meat, milk, poultry and eggs arising from the proposed use on beans would exceed established or proposed tolerances (see also PP#4F3129) until 1) representative chromatograms have been submitted so that RCB can validate the analytical methodology and residue data on the possible feed items; 2) residue data on lima beans from CA field trials have been submitted; 3) residue data on dry beans from CA and MI have been submitted; 4) residue data for bean hay reflecting about a 14 day PHI have been submitted.

Other Considerations

1. Because of the occurrence of an apparently hydroxylated metabolite in goat kidney, the question of the tolerance expression for animal commodities is being reconsidered in PP#4F3129/4H#5440. Presently, the tolerance expression for meat, poultry and eggs includes iprodione and its non-hydroxylated metabolites, whereas the tolerance expression for milk includes iprodione and its hydroxylated and non-hydroxylated metabolites.

2. Codex has established a tolerance for residues of iprodione per se on dry beans at 0.2 ppm. Canada has established a tolerance for iprodione (presumably parent) residues at 0.1 ppm. If the proposed tolerances on dry and succulent beans are established, there will be a compatibility problem.

cc:R.F., Circu, Reviewer:TOX, EAB, EEB, PP#4F2150/Iprodione
RDI:JHOnley:1/29/85:RDSchmitt:1/31/85
TS-769:RCB:CM#2:RM810:X5664:CDeyrup:wh:2/8/85

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Iprodione

CCPR NO. III

PETITION NO. 4F 3150

Reviewer: C Deyrup

Codex Status

[ ] No Codex Proposal
Step 6 or above

Residue (if Step 9):

iprodione only

Crop(s) Limit (mg/kg)

beans (dry) 2.0

CANADIAN LIMIT

Residue:

presumably parent [1]

Crop Limit (ppm)

white beans 0.1 [2]

Proposed U.S. Tolerances

J. Jones 12/11/90

Residue: iprodione

3-(1-METHYLETHYL)-N-(3,5-DICHLOROPHENYL)-2,4-DIOXO-1-IMIDAZOLIDINECARBOXAMIDE

3-(3,5-DICHLOROPHENYL)-2,4-DIOXO-1-IMIDAZOLIDINECARBOXAMIDE

Crop(s)	Tol. (ppm)
Beans, succulent	2.0
Beans, dry	2.0
Bean Forage	30
Bean Hay	90

MEXICAN TOLERANCIA

Residue:

Crop Tolerancia (ppm

n.a.

NOTES:

[1] Definition of other than "regulable residue" type tolerances

[2] Regulable residue type tolerance.