FSA/PB
1 - PP #6F0474

MEMORANDUM OF TELEPHONE CONVERSATION

May 12, 1966

AF 12-868

BETWEEN:

Dr. A. J. Lemin (The Upjohn Company
Kalamazoo, Michigan

J. Wolff ( PB, FSA

SUBJECT: PP #6F0474. Botran on various crops.

I called Dr. Lemin to inquire about the proposed use on currants. A tolerance of 15 ppm was proposed for this crop in section F; but no conditions of use were included in the revised labels submitted with his letter to PCB of April 19, 1966. Dr. Lemin replied that after discussions with the plant pathologists at the USDA, the Upjohn Company has decided to withdraw the proposed use on currants.

We also discussed the use directions on cucumbers which state that the treatment may be repeated after 14 days. Dr. Lemin stated that the intent is to repeat every 14 days, if necessary.

J. Wolff

cc:

PCB
FSA/OD
FSA/PB--file PP #6F0474
FSA/Wolff

JWolff:dep
5/13/66

RD/I--GJBeusch

Lemin agrees to withdraw proposed use on currants.
7-29-66.

# End of Document

UNITED STATES DEPARTMENT OF AGRICULTURE
AGRICULTURAL RESEARCH SERVICE
PESTICIDES REGULATION DIVISION
WASHINGTON, D. C. 20250

To: William Stokes, Assistant to the Director
BSSE, Food and Drug Administration
Department of Health, Education, and Welfare

From: R. O. White, Acting Director

Subject: Pesticide Petition Number 6F0474 requesting tolerances for 2,6-dichloro-4-nitroaniline, submitted by Upjohn Company, and filed February 18, 1966.

We have completed our examination of the residue data, analytical methods employed, and other pertinent information contained in this petition for tolerances of fifteen parts per million (ppm) for 2,6-dichloro-4-nitroaniline in or on brambles (including blackberry, boysenberry, and red raspberry) and currants; ten ppm in or on celery and rhubarb; and five ppm in or on carrots, cucumbers, Irish potatoes, plums and prunes, and spinach. In accordance with the requirements of Public Law 518, 83rd Congress, we herein offer an opinion as to whether the proposed tolerances reasonably reflect the amount of residues likely to result when this pesticide chemical is used as proposed.

It is the opinion of the Department that the proposed tolerances reasonably reflect the amounts of residue likely to result in brambles (including blackberry, boysenberry, and red raspberry), currants, celery, rhubarb, carrots, cucumbers, Irish potatoes, and spinach, contingent upon the following changes to which the petitioner has agreed:

1. Brambles, including blackberry, boysenberry, and raspberry (red): Limit to four applications.

2. Carrot: Delete spray use. Limit dip to 10 seconds.

3. Cucumber (greenhouse): Apply to diseased areas of plants. Additional application may be necessary after 14 days.

4. Celery: Seven day preharvest interval.

5. Irish potato: Fourteen day preharvest interval. Do not feed treated potatoes to livestock.

The proposed tolerance for spinach reflects only the residue likely to result from the growing of spinach as a follow-up crop on previously treated soil, not from the use on spinach.

The data are insufficient to serve as a basis for an opinion on the amount of residue likely to result in plums and prunes.

# End of Document

FSA

Gilpatrick
Busch

AF 12-868

February 18, 1966

Pesticide Petition No. 6F0474

Dr. A. J. Lemin
Agricultural Products Division
The Upjohn Company
Kalamazoo, Michigan 49001

Dear Dr. Lemin:

We have your letter of February 7, 1966, transmitting in duplicate a petition to establish tolerances for residues of the fungicide 2,6-dichloro-4-nitroaniline. We acknowledge receipt of the accompanying check for $3000.

This petition has been designated Pesticide Petition No. 6F0474.

We also received your letter of February 10, 1966, transmitting in triplicate a revised Section F for this petition and page 110 which had been omitted from the original petition.

As revised, this petition requests the following tolerances:

15 parts per million in or on brambles (preharvest only, including blackberry, boysenberry, raspberry (red) and currants).

10 parts per million in or on celery (preharvest only), rhubarb (preharvest only).

5 parts per million in or on carrots (postharvest only), cucumbers (preharvest only), Irish potatoes (preharvest only), plums and prunes (preharvest only), spinach (preharvest only).

This petition is being filed today. Further action awaits completion of scientific review and evaluation.

Sincerely yours,

Drew M. Baker, Jr.
Assistant to the Director
Bureau of Scientific Standards
and Evaluation

cc: Pesticides Regulation
Division, ARS, USDA

DMBaker:rh 2/18/66
RD DMB:aeg 2/17/66

cc: PCB FSA DTE BSSE FB ACR RD intl WStokes 2/17/66

# End of Document

FSA 60th day 5/27/66
90th day - 6/27/66

UNITED STATES DEPARTMENT OF AGRICULTURE
AGRICULTURAL RESEARCH SERVICE
PESTICIDES REGULATION DIVISION
WASHINGTON, D. C. 20250

Objection Branch

To: William Stokes, Assistant to the Director,
B.S.S.E., Food and Drug Administration,
Department of Health, Education, and Welfare

From: Justus C. Ward, Director

Subject: Certification of usefulness of the pesticidal chemical,
2,6 dichloro-4-nitroaniline

On February 7, 1966, The Upjohn Company, Kalamazoo, Michigan, submitted a petition to establish tolerances for residues of 2,6 dichloro-4-nitroaniline (Botran). This petition numbered 6F0474 was filed on February 18, 1966.

Pursuant to Section 408 (l) of Public Law 518 (68 Stat. 511), the petition and related data have been analyzed. It is hereby certified that the pesticide chemical is useful for the purposes for which tolerances are sought on blackberries, Boysenberries, raspberries (red), currants, celery, rhubarb, carrots, cucumbers, Irish potatoes, plums, prunes and spinach.

Received
FSA/Pest. Br.
MAR 30 1966

# End of Document

OPTIONAL FORM NO. 10
5010-104

UNITED STATES GOVERNMENT

# *Memorandum*

TO : L. L. RAMSEY, Acting Ass't Director
for Regulatory Programs

DATE: May 24, 1966

FROM : F. J. McFarland
Petitions Control Branch, SCI-R

Upjohn Company
Kalamazoo, Mich. (AF 12-868)

SUBJECT: Pesticide Petitions No. 6F0490 and No. 6F0474

File PP# 6F0474

Attached for your concurrence is a draft of a letter filing Pesticide Petition No. 6F0490 requesting a tolerance of 0.05 ppm for the fungicide Botran on cottonseed. The Upjohn Company has requested that we consider 6F0490 before Petition 6F0474 which was filed February 18, 1966, for Botran on various fruits and vegetables at 15, 10, and 5 ppm. Their request is based upon an earlier need for the use of Botran on cotton.

Upjohn sent PRD, USDA, a request for no residue registration March 31, 1966, for the use of Botran on cotton. On May 3, 1966, PRD sent us the residue data with a memo saying that they had concluded the use would be acceptable under the former no residue procedure and requested our opinion whether the residue data were adequate. FSA advised PCB May 9, 1966, that the use on cotton involved direct contact with the crop, that in their opinion residues would occur from the usages involved, and that registration should be proposed on a tolerance rather than on a no residue basis. PCB advised PRD of this May 10, 1966.

We recommend that Petition 6F0490 be considered before Petition 6F0474, and that action on the petition be expedited to the extent possible.

Concur R. L. Ramsey 5/26/66

Note

Received
FSA/Pest. Br.
MAY 27 1966

AGRICULTURAL
PRODUCTS
DIVISION

THE UPJOHN COMPANY

KALAMAZOO, MICHIGAN

TELEPHONE
Area Code 616
343-1511

AGRICULTURAL CHEMICAL RESEARCH
Office of
ALAN STEMP
Manager

August 5, 1966

Mr. William Stokes
Bureau of Scientific Standards
and Evaluations
Food and Drug Administration
200 C Street, SW
Washington, D.C.

Dear Mr. Stokes:

Subject: Petition No. 6F0474 (Botran)

We would like to make the following changes in our Petition No. 6F0474 (BOTRAN):

1. Reduce requested tolerance of 5 ppm on potatoes to read 1 ppm.
2. Reduce requested tolerance of 5 ppm on plum and prunes to read 1 ppm.
3. Withdraw our requested tolerance on spinach.
4. Celery:
   A. Additional 1966 residue results are attached from California and Michigan to supplement our request for 10 ppm at 7 days.
   B. Pertaining to the previously submitted Michigan evaluations: after closer investigations of these particular samples, we find that, as indicated on the residue report, these particular samples were contaminated with soil and were not washed prior to running the analysis. We are in the process of collecting additional residue samples here in Michigan this week and will forward the results to you as soon as they are available.
   C. In line with your advice, we would like to request a change in the tolerance of 10 ppm to 15 ppm with a seven day limitation to harvest.



PCB

AUG 15 1966

Should you have questions, we would appreciate it if you would contact my office, Area Code 616, 345-5571, extension 7234, or E. M. Beckman, extension 7615.

Sincerely yours,

A. J. Lemin
Manager,
Plant Health Products, R & D

jfc
Enc.

...ue Determination for DCNA on Celery (California, 1966)

ANALYST REFERENCE: 6075-WRN-16 REPORT DATE: February 25, 1966

STUDY 1

| Sample No. | Treatment Rate (Lbs. Active/100 Gal.) | Treatment-Harvest Interval (Months) | Residue Found (PPM) |
|---|---|---|---|
| [illegible] | 1.5 | 2.3, 1.9 | 0.2 |
| [illegible] | 1.5 | 2.3, 1.9 | 0.[illegible] |
| [illegible] | 1.5 | 2.3, 1.9, 1.1 | 2.9 |
| [illegible] | 1.5 | 2.3, 1.9, 1.1 | 3.9 |
| [illegible] | 1.5 | 2.3, 1.9, 1.1, 0 | 13.6 |
| [illegible] | 1.5 | 2.3, 1.9, 1.1, 0 | 20.0 |
| [illegible] | 3.0 | 2.3, 1.9 | 1.4 |
| [illegible] | 3.0 | 2.3, 1.9 | 0.5 |
| [illegible] | 3.0 | 2.3, 1.9, 1.1 | 4.6 |
| [illegible] | 3.0 | 2.3, 1.9, 1.1 | 5.0 |
| [illegible] | 3.0 | 2.3, 1.9, 1.1, 0 | 30.3 |
| [illegible] | 3.0 | 2.3, 1.9, 1.1, 0 | 30.0 |

GENERAL OF STUDY 1:

COOPERATOR: Albert O. Paulus and Albert N. Holland, Santa Ana, California.
FIELD LOCATION: Santa Ana, California
CROP: Celery
PLANTING DATE: HARVEST DATE: February 13, 1966
TREATMENT DATES: December 6, December 20, 1965; January 12 and February 13, 1966.
FORMULATION: Botran 75% WP
METHOD OF TREATMENT: Hand spray

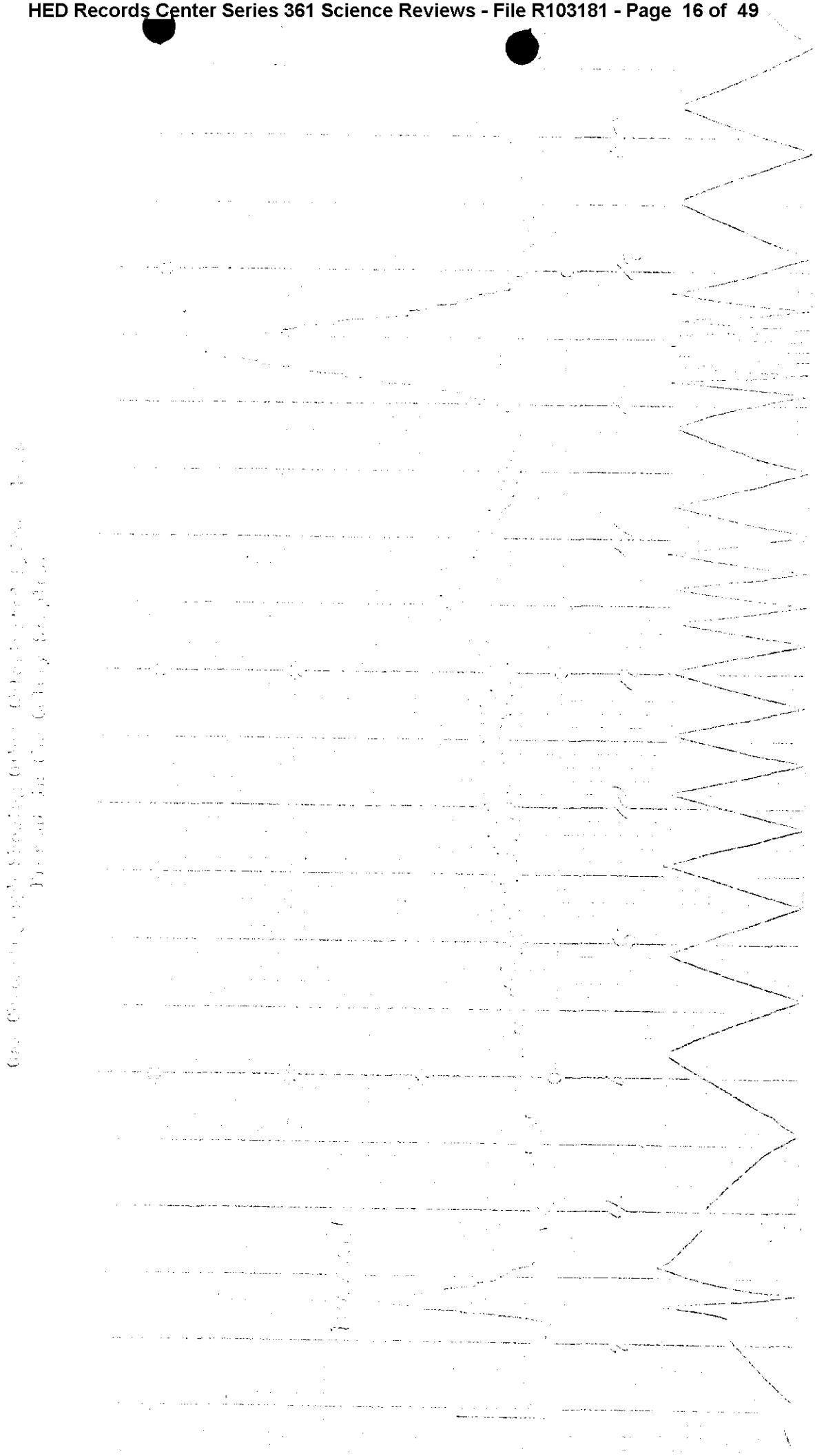
[illegible] OF SAMPLES:

STORAGE CONDITIONS: None SHIPPING CONDITIONS: Frozen
MODE OF SHIPMENT: Air Express ARRIVAL CONDITIONS: Frozen - good.
LABORATORY PROCEDURE: Standard microcoulometric vapor phase chromatographic procedure.
COMMENTS: Peaks of other chlorinated pesticides were seen as peaks in the gas chromatograph scan. Extra cleanup was required (column chromatography).

[illegible]: Kent Beckman FILING CODE: DCNA - Celery 1966, California, Paulus Holland

bab

| [illegible] | Sample No. | Remarks | Wt. Sample (g) | Dilution (ml) | ppm | Wt. Aliquot (g) | Dilution (ml) | ppm | [illegible] | [illegible] |
|---|---|---|---|---|---|---|---|---|---|---|
| 25-66 | | Standard, 1.2 ppm | 2.5 | 1610 | 12.8 | 1.61 | - | - | - | - |
| | 58 | Untreated | - | - | 12.8 | - | [illegible] | - | | |
| | 59 | Untreated, fortified 5.0 ppm | 2.5 | 720 | 12.8 | 0.72 | 412.5 | 297.0 | - | [illegible] |
| | 60 | Untreated | 2.6 | 40 | 12.8 | 0.04 | 412.5 | 16.50 | [illegible] | - |
| | 61 | Untreated | 2.5 | 100 | 12.8 | 0.10 | 412.5 | 40.25 | [illegible] | - |
| | 62 | Untreated | 2.6 | 70 | 12.8 | 0.07 | 412.5 | 28.88 | [illegible] | - |
| | 63 | Treated | 2.6 | 170 | 12.8 | 0.17 | 82.5 | 14.03 | [illegible] | 0.95 |
| | 64 | Treated | 2.5 | 180 | 12.8 | 0.16 | 82.5 | 14.85 | [illegible] | 0.84 |
| | 65 | Treated | 2.5 | 1090 | 6.4 | 2.18 | 82.5 | 179.85 | [illegible] | [illegible] |
| | 65 | Treated | 2.5 | 990 | 6.4 | 1.98 | 82.5 | 163.35 | 2.72 | [illegible] |
| | 66 | Treated | 2.5 | 1400 | 6.4 | 2.80 | 82.5 | 231.0 | 3.85 | [illegible] |
| | 67 | Treated | 2.5 | 560 | 6.4 | 1.12 | 825.0 | 924.0 | 15.40 | [illegible] |
| | 68 | Treated | 2.5 | 720 | 6.4 | 1.44 | 825.0 | 1188.0 | 19.80 | [illegible] |
| | 69 | Treated | 2.5 | 1040 | 12.8 | 1.04 | 82.5 | 85.8 | 1.43 | [illegible] |
| | 70 | Treated | 2.5 | 370 | 12.8 | 0.37 | 82.5 | 30.53 | 0.51 | [illegible] |
| | 71 | Treated | 2.5 | 165 | 6.4 | 0.33 | 825.0 | 272.25 | 4.54 | [illegible] |
| | 72 | Treated | 2.5 | 180 | 6.4 | 0.36 | 825.0 | 297.0 | 4.95 | [illegible] |
| | 73 | Treated | 2.5 | 1090 | 6.4 | 2.18 | 825.0 | 1798.5 | 30.00 | [illegible] |
| | 74 | Treated | 2.5 | 1080 | 6.4 | 2.16 | 825.0 | 1782.0 | 29.70 | [illegible] |
| | | 8073-EXP-16 | | | | | | | | |



Analysis of Celery for DCNA Residue (Michigan, 1965)

Ref: 76L5WNW106 November 10, 1965

Summary

| Sample No. (1965) | Treatment Rate (Lbs. Active/Acre) | Treatment-harvest Interval (Days) | DCNA Found (P.P.M.) |
|---|---|---|---|
| 591 | 2 | 50,43,36,28,21,13,7,1 | 5.6 |
| 652 | 2 (Last spray 4.1) | 54,47,40,32,25,17,11,5,0 | 22.2 |
| 653 | 2 (Last spray 4.1) | 57,50,43,35,28,20,14,8,3 | 14.2 |
| 826 | 2 (Last spray 4.1) | 60,53,46,38,41,23,17,11,6 | 6.6 |

Source of Samples

The samples were taken from the farm of Jon Slager, 6129 Market Avenue, Comstock, Michigan, by Upjohn personnel. The plot was 450 square feet. The celery was sprayed on 7/12/65, 7/19/65, 7/26/65, 8/5/65, 8/10/65, 8/18/65, 8/24/65 and 8/30/65 using 2.7 pounds of BOTRAN 75W per acre. A sample (No. 591) was taken on 8/31/65. There was rain between the last spray and the sampling. No bottom or roots were taken, only that part above ground. The celery was sprayed again on 9/4/65 with a knapsack sprayer using a suspension of BOTRAN 75W at two pounds per 100 gallons. The rate was 275 gallons per acre. Samples were taken the same day, on 9/7/65 and on 9/10/65. All were taken to nearby Kalamazoo immediately.

Method of Analysis

Sample 591 consisted of only that part of the plant above ground. The other samples consisted of the whole saleable plant. The lower part of the stalk was washed, since this is always done commercially. The samples were chopped in a Hobart food chopper and held frozen so that all were analyzed at the same time.

The microcoulometric vapor phase chromatography method was used, without column chromatography. The data are given on the attached table. Figure 1 shows a pseudo first order plot of the last three analyses, indicating a half-life of 3.85 days.

Code: DCNA - Celery - 1965
Michigan, Slager

cll

DCNA on Celery (Michigan, 1965)

| DATE OF ASSAY | SAMPLE NUMBER | HISTORY | RETENTION TIME (min) | RETENTION COUNT | CORR. | DCNA EQUIV. (mcg) | DILUTION FACTOR | DCNA FOUND (mcg) | DCNA FOUND (P.P.M.) ANALYST | DCNA FOUND (P.P.M.) CHECK (RECOVERY) |
|---|---|---|---|---|---|---|---|---|---|---|
| 9/15/65 | 654 | Untreated | - | - | 12.8 | - | 412.5 | - | nil | |
| 9/15/65 | 654 | Untreated, fortified 5.0 ppm. | 2.7 | 720 | 12.8 | 0.72 | 412.5 | 297.0 | 4.95 | (99%) |
| 9/15/65 | 591 | 2 lbs./acre | 2.7 | 795 | 12.8 | 0.80 | 412.5 | 330.0 | 5.50 | 5.6 |
| 9/15/65 | 652 | 2 lbs./acre (last spray 4.1) | 2.7 | 800 | 6.4 | 1.60 | 825.0 | 1320.0 | 22.0 | 22.2 |
| 9/15/65 | 653 | 2 lbs./acre (last spray 4.1) | 2.7 | 505 | 6.4 | 1.01 | 825.0 | 841.5 | 14.0 | 14.2 |
| 9/15/65 | 826 | 2 lbs./acre (last spray 4.1) | 2.7 | 960 | 12.8 | 0.96 | 412.5 | 396.0 | 6.6 | 6.7 |
| 9/15/65 | | Standard, DCNA, 1.5 mcg. | 2.7 | 1495 | 12.8 | 1.495 | $\frac{1.495}{1.500} \times$ | 100 = 100% | | |
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| 11 1/9/65 | | | | | | | | | | |

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FSH PP 6F0474

Petitions Control Branch and
Division of Toxicological Evaluation

August 9, 1966

AF 12-863

Pesticides Branch, Division of Food
Standards and Additives

PP #6F0474, Botran on various crops. Evaluation of analytical methods and residue data.

The Upjohn Company proposes the following tolerances for residues of the fungicide 2,6-dichloro-4-nitroaniline (trade name Botran):

15 ppm - blackberries, boysenberries, raspberries (red) and currants

10 ppm - celery and rhubarb

5 ppm - carrots, cucumbers, Irish potatoes, plums and prunes, and spinach

Tolerances ranging from 5-20 ppm already have been established on 12 crops under section 120.200.

The petitioner agreed informally on July 29, 1966, to withdraw the tolerances proposed for currants and spinach, but has not done so officially.

Conclusion

1. Adequate methods are available for enforcing the proposed tolerances.

2. When the pesticide is used as directed, the proposed tolerances would not be exceeded by the residues on blackberries, boysenberries and raspberries (red), rhubarb, and cucumbers.

3. Residues on carrots would exceed the proposed 5 ppm tolerance. A 10 ppm tolerance would be adequate.

4. The 10 ppm tolerance proposed for celery is inadequate. It would be adequate with a 14-day rather than a 7-day preharvest interval.

5. The 5 ppm tolerances proposed for potatoes and plums (prunes) are higher than necessary. Lower tolerances of 0.25 ppm for potatoes, and of 1 ppm for plums (prunes) would be adequate.

6. With a tolerance of 0.25 ppm on potatoes, in conjunction with the label restrictions, we would not reasonably expect residues to transfer to meat and milk.

7. The residue in dried prunes would not exceed the level of 1 ppm and a food additive tolerance would not be needed here.

8. The tolerance proposed for spinach is intended to cover incidental residues which result on spinach as a follow-up crop, and not from the purposeful use of Botran on spinach. A residue problem is likely only when spinach follows onions, and the soil is treated in connection with the growing of the onion crop. This type of a tolerance probably should have been proposed under Section 406 of the Act, but in view of the petitioner's verbal agreement to withdraw the proposed tolerance, this question may be moot.

9. In the absence of a described use for currants, we are unable to evaluate the adequacy of the proposed tolerance for currants.

Recommendation

1. Pharmacological considerations permitting, we recommend that the tolerances proposed on the crops enumerated in Conclusion 2 above be established.

2. We could recommend favorably on carrots if the proposed tolerance were increased to 10 ppm.

3. We could recommend favorably for the tolerance for celery if the preharvest interval were increased from 7 to 14 days.

4. We could recommend favorably if the proposed tolerances were reduced to 1 ppm for plums (prunes) and 0.25 ppm for potatoes.

5. We are making no recommendations on the tolerances proposed for currants and spinach as we understand the proposals are being withdrawn.

## Detailed Considerations

Proposed Use

The use recommendations for different crops are given below under Residue Data. All uses are preharvest except for that on carrots.

Nature of the Residue

As we stated in our memo of 6/3/65 (see PP #5F0434), dissipation of residues on plants is effected chiefly by volatilization.

The parent compound is considered the only toxic component of the residue on plants.

Animals metabolize Botran to 3,5-dichloro-4-aminophenol and excrete it in conjugated form, chiefly in the urine.

Analytical Methods

Colorimetric - The colorimetric method was used in one study on carrots which had been submitted previously. This procedure was evaluated and subjected to a method tryout in connection with PP #5F0434. It was considered adequate for enforcing the previously established tolerances and we consider it to be adequate for enforcing the proposed tolerances on the crops of this petition.

MCGC - The MCGC method used for the residue determinations was discussed in detail in the aforementioned memo in PP #5F0434. Cheng and Kilgore (see J. Food Sci., 31, 259; 1966) recently applied a simplified version of this method to various fruits using electron-capture detection.

Overall, we consider the sensitivity of this method to be 0.05-0.1 ppm which is satisfactory in relation to the contemplated tolerances. A few values of 1-3 ppm were obtained on red raspberries and carrots and may represent inadequate cleanup of these samples.

Recoveries on samples fortified with 0.25-5 ppm of Boram are also satisfactory ranging overall from 75% (on blackberries) to 124% (on celery).

We consider this method to be adequate for obtaining residue data or for use as an alternate enforcement procedure.

Residue Data

Blackberries, Boysenberries, and Raspberries (Red) - Pacific Northwest only--use 1 lb act/100 gals or 3 lbs act/A as dust just prior to bloom and then at 10-day intervals, maximum of four applications, 7-day PHI. Considering that up to 250 gallons of spray liquid may be used per acre, the rate for the dust formulation is not out of line.

In the absence of a described use for currants, we are unable to evaluate the adequacy of the proposed tolerance for currants.

Seven studies made in Washington and Oregon include dissipation data, and data reflecting both multiple applications and excessive doses of sprays and dusts. Residue values from four applications at the proposed 7-day PHI (derived from plots of the data with adjustments for dosage where necessary) range from 0.5-12 ppm. Only two values are in the 11-12 ppm range.

We conclude that residues from the described use would not exceed the proposed 15 ppm tolerance.

Celery - Use 1.5 lbs act/100 gals and 100 gals/A at 7-day intervals beginning 10 weeks before harvest, 7-day PHI.

Four studies made in Florida, Michigan, and California are available. All of the data reflect multiple applications and one study with dissipation data shows a half-life of about 4 days for residues on celery grown in Michigan during midsummer.

Three of the four studies show that the tolerance would not be exceeded. However, the remaining Michigan study indicates that the tolerance may be crowded or possibly exceeded at 7 days which is the proposed preharvest interval. An increase in this preharvest interval to 14 days would provide the needed margin of safety.

Rhubarb (hothouse) - Use 1 lb act/100 gals at weekly intervals beginning when first buds emerge from crown, 3-day PHI.

Three studies made in Washington are available. Since applications to this minor crop are to be made within the hothouse, the climatic factor is not so important as it would be otherwise. Therefore we raise no objection to what would appear to be inadequate geographic representation. Although in one study the PHI was 18 days, all studies reflect excessive dosages varying from 1.5-3.5 lbs/100 gals. The residue range is 1.2-10.0 ppm at these excessive rates. At the proposed rate, the residue would not exceed roughly 6 ppm. We conclude that residues from the recommended use would not exceed the proposed 10 ppm tolerance.

Carrots - Postharvest--use solution containing 0.75 lb act/100 gals (equivalent to 900 ppm) for 10-second dip. The solution is to be replenished with up to half the amount of fungicide after treating 500 bushels. The dipping solution is to be discarded after treating 1000 bushels of carrots. This is in line with the practice for dipping sweet potatoes.

Two of the four studies show residue values for unwashed, unpeeled carrots at zero-day and up to 14 days after dipping. In the first of these studies, the residues range from 3.6-4.9 ppm. The second study involves dipping in a 1200 ppm solution rather than the 900 ppm proposed. Here residues corrected to the proposed concentration range from 2.7-9.3 ppm. (These values were not corrected for blanks ranging from nil to 1.4 ppm.) Seven of the 19 values exceed 5 ppm. The remaining studies were made in cooperation with the Campbell Soup Company, and show residues in dipped carrots stored for 3.5-5.5 months under commercial conditions. Values for the unpeeled roots are 3.7 ppm, for the peeled 2.1 ppm, and canned 0.2 ppm or less.

Although it would defeat the purpose of the treatment, we must expect that treated carrots could be withdrawn from storage almost immediately after treatment.

We therefore conclude that residues on carrot roots could exceed the proposed 5 ppm tolerance. A tolerance of 10 ppm would be more appropriate.

Cucumbers (Greenhouse) - Use 1 lb/100 gals on diseased parts, with additional application if necessary after 14 days, no PHI.

Four studies made in California and Oregon include data reflecting excessive dosages and multiple applications. The highest residues are of the order of 2 ppm where a 25% excess of fungicide was used. (One value reflects a 50-day PHI for a soil treatment with Botran, which is not pertinent here.) Most residue values are <0.2 ppm, but a few approach 2 ppm.

Since the studies reflect applications to the whole crop rather than just the diseased parts, residues would be even lower than these, and we conclude that residues on cucumbers would not exceed the proposed 5 ppm tolerance.

Irish Potatoes - Michigan only--use 1.5 lbs/100 gals and 100 gals/A beginning at lay-by and continuing at 10-14 day intervals, 14-day PHI. Do not feed treated potatoes to livestock.

The use pattern is such that only very minor contaminative residues would be expected. The source of the residues would be soil contamination from foliar applications. [In the case of DDT (a much more persistent pesticide) on sweet potatoes (a related crop), we estimated an increment of 0.1 ppm on tubers from foliar applications at 2.5 lbs act/A - see PP #395.]

Both of the two available studies reflect excessive treatments. In a New York study the potato plants received 10 sprays at intervals of 5-11 days and were harvested 3 days earlier than the proposed 14-day PHI. All samples show less than 0.05 ppm. In a Michigan study there was a pre-emergent soil application at 4.5 lbs act/A (soil applications are not proposed) plus 4 weekly applications. At harvest 21 days later, all reported residues are less than 0.2 ppm. Even this value is excessive as the potatoes were unwashed.

On the basis of the proposed use pattern and the data available, we consider the proposed 5 ppm tolerance to be too high. In our opinion, a nominal tolerance of 0.25 ppm would be adequate.

Since the application is a foliar one, residues are not normally to be expected on the tubers. Occasionally small residues, not in excess of 0.25 ppm, will be found from contamination by soil. The question of transfer of residues to meat and milk from the feeding of cull and surplus potatoes is therefore only a minor one and the label warning against the feeding of treated potatoes to livestock should serve to prevent the occurrence of such transfer.

Plums and Prunes - Use 1 lb act/100 gals at popcorn and full bloom.

Two of the three available studies reflect postharvest or post-blossom applications and are not pertinent to the proposed use. PBD, USDA in its memo of 3/29/66 states that the data are insufficient to serve as a basis for an opinion of the residues likely to result on this crop. While we agree that the data do not permit a precise determination of the residue levels, the use pattern is such that only very minor residues would be expected. In the one pertinent study, quadruple the recommended dosage was used; but no detectable residues are reported at harvest. In another study, plums on the trees were sprayed and harvested the next day. The resulting residue reported is only 2.5 ppm.

We therefore conclude that the proposed 5 ppm tolerance is too high. In our opinion, a nominal tolerance of 1 ppm (about three times the highest blank reported) would be adequate.

Data in PP #5F0434 show that residues in fruit are reduced by 60-99% on commercial drying. Therefore establishing a tolerance on plums and prunes would not necessitate establishing a food additive tolerance for dried prunes.

Spinach - No purposeful applications are proposed, but a tolerance is requested to cover possible residues from treatments made on previous crops. The maximum previous use would be that on onions where soil treatments are permitted using up to 30 lbs act/A.

In one study, a very high dosage of 70--125 lbs act/A was used. Residues of 2-3 ppm are reported for 9.9 months; but at 10.6 months after application, only trace residues below the 0.05 ppm practical limit of sensitivity are reported. In a second study, a residue of 0.23 ppm is reported, but here the crop was harvested only 6 months after the application of 30 lbs act/A. In a third study, spinach harvested 10.9 months after soil treatment with 30 lbs act/A shows no residues (<0.05 ppm).

We are dubious about the need for a tolerance in this situation. Even at the maximum application rate (for onions) it seems unlikely that residues would be present in spinach 7 or 8 months after the initial treatment for the proceeding crop. In addition a residue problem is likely to arise only where spinach follows onions; and the petitioner already has a warning on his label for onions to plow and cross-disc treated areas before seeding with spinach, which is sensitive to Botran. The warning itself would discourage the rotation of onions and spinach.

Since the petitioner has agreed verbally to withdraw the tolerance proposed for spinach, we are making no recommendations on this.

PP #6F0474

7

Other Considerations

The persistence of Bolran residues in soil was discussed in our memo of 6/3/65 in PP #5F0434. The half-life in soil is about 3 months and we would not expect residues to accumulate on the soil from yearly treatments.

J. Wolff

cc:
LEB
LCI-CD
CGI-R
DFC(Jones)
ERC(L.Johnson)
FSA/CD
FSA/PB
PP #5F0434
PP #6F0474

JWolff:jrf
8/9/66
RD/I - C.Deusch, JAlpert

# End of Document

FSA

AGRICULTURAL
PRODUCTS
DIVISION

THE UPJOHN COMPANY

KALAMAZOO, MICHIGAN

TELEPHONE
Area Code 616
345-3571

AGRICULTURAL CHEMICAL RESEARCH
Office of
ALAN J. LEMIN
Manager

August 12, 1966

Mr. William Stokes
Bureau of Scientific Standards
and Evaluation
Food and Drug Administration
200 C Street, SW
Washington, D.C. 20204

Dear Mr. Stokes:

Report
Beach
Cummings
Wolff

File: PP 6F0474

SUBJECT: Petition No. 6F0474 (BOTRAN)

REFERENCE: Letter of August 5, 1966 to Mr. W. Stokes from Dr. A. Lemin

Confirming my telephone conversation with Mr. Drew Baker today, I wish to make the following changes in our 6F0474 petition:

1. Change the requested tolerance for potato from 1.0 ppm. to 0.25 ppm.
2. Change the requested tolerance for carrots from 5 ppm. to 10 ppm.
3. Confirm the withdrawal of a request for a tolerance for currants.
4. Confirm our request for a tolerance of 15 ppm. for celery with a pre-harvest interval limitation of seven (7) days.

Should you have additional questions or suggested changes, I would appreciate you calling my office, Area Code 616, 345-3571, extension 7234 or K. M. Beckman, extension 7615.

Yours sincerely,

A. J. Lemin

A. J. Lemin, Manager
Plant Health Products R & D

Received
FSA/Pest. Br.
AUG 16 1966

jlc

# End of Document

PB for SA
PP# 6F0474

Pesticides Control Branch and
Division of Toxicological Evaluation

September 23, 1966

Pesticides Branch, Division of Food
Standards and Additives

AT 12-610

PP 6F0474, Ferbam on various crops. Addendum

The Upjohn Company by its letter of August 5 and 12, 1966 has revised the proposed tolerances for carrots, celery, potatoes, plums and prunes. Also submitted at that time were data for residues on celery with an indication that more would be forthcoming. However these have not yet been submitted, and we are now being asked by the petitioner to proceed with the data that are presently available. (Telephone conversation, Baker-Kerr, 9/19/66).

The proposed new tolerances reflect our original recommendations (see DDA memo of 8/9/66) for carrots, potatoes, plums and prunes, or plums (prunes) as designated in the regulations.

The proposed new tolerance of 15 ppm in conjunction with a 7-day preharvest interval for celery differs from our finding that a 10 ppm tolerance with a 14-day interval would be needed. Our finding stemmed from the higher residues believed to be present on fall celery (although the data of the Michigan study - see our memo of 8/9/66 - were complicated by the presence of soil on the samples which would have increased the residue level). The new data recently submitted for celery grown and treated in California during December, January and February, reinforces our view that exceeding or exceeding of a tolerance at 10 ppm and even at 15 ppm could occur with a 7-day preharvest interval, particularly if previous applications are made at 7-day intervals as proposed. In fact the level of residues indicated are higher than we had anticipated. The rate of dissipation under winter conditions is equivalent to a half-life of 11-15 days (vs. 6 days during the summer months).

However the data do support a tolerance of 15 ppm, in conjunction with a 7-day preharvest interval provided previous applications are made at 14 (instead of 7) day intervals in the fall or winter applications. Since this raises the problem of efficacy, we are asking for the petitioner's comment on this question. We would, if efficacy considerations permit, recommend for the proposed tolerance if the intervals between applications for fall or winter celery were extended from 7 to 14 days.

Currants and spinach have now been withdrawn from consideration of a tolerance.

[illegible] 2

Recommendations

Pharmacological considerations permitting, we can recommend that tolerances for residues of 2,6-dichloro-4-nitroaniline be established at:

15 ppm for blackberries, boysenberries and raspberries (red)
10 ppm for carrots and rhubarb
5 ppm for cucumbers
1 ppm for plums (prunes)
0.2 ppm for potatoes

We do not recommend that the proposed 15 ppm tolerance for celery be established. We would recommend favorably for such a tolerance, if repeat applications were to be made at 7-day intervals during the summer, and 14-day intervals during the fall and winter, in conjunction with a 7-day preharvest interval.

Should such an extension of the intervals between applications adversely affect the usefulness of the fungicide, we also could recommend affirmatively for a tolerance of 15 ppm with a 14-day preharvest interval.

C.J. Rauch

cc:
[illegible]
RD [illegible]

[illegible]
[illegible]

[illegible]

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File - PP# 6F0474

FSA - Output

Mr. Drew M. Baker
Petitions Control Branch

October 4, 1966

George E. Whitmore
Division of Toxicological Evaluation
Petitions Review Branch

Botran - 15 ppm boysenberries, raspberries, blackberries, and celery; 10 ppm carrots and rubarb; 5 ppm spinach; 1 ppm plums and prunes; 0.25 ppm potatoes (white)

PESTICIDE PETITION NO. 6F-0474

The Upjohn Company
Kalamazoo, Michigan
(AF 12-868)

Data supporting the safety of Botran residues for Pesticide Petition No. T-421 (21 June 1964 memo), Pesticide Petition No. 434 (23 February 1965 memo) and Pesticide Petition No. 490 (9 June 1966) demonstrated 100 ppm no-effect diets in 2 year dog and rat feeding experiments, 100 ppm no effect diet for a 3 generation rat reproduction study, similar rat and human metabolism, and no effects in human males consuming 10 mg/day for 3 months.

Additional data provided with this petition that is pertinent to safety is a "Semara" test in rabbits. Female New Zealand strain of albino rabbits were fed Botran diets of 0, 100 and 1000 ppm from the eighth day of pregnancy until the sixteenth day of pregnancy. Ten, 12 and 14 females were exposed to diet levels of 0, 100 and 1000 ppm respectively. Observations for effects included; behavior, appearance, survival (parents), breeding cycle, live births, litter size, sex ratio, unborn viability, 24 hour survival, 21 day survival, 21 day pup weights, parental pathology (gross examination-implantation sites), fetal resorption, offspring pathology (gross), and skeletal examination of pups by alizarin red staining. Observations did not reveal compound related influences.

The provided toxicity data supports the safety of 1.5 mg/day for humans (1 ppm diet-1500 gram daily intake). Tolerances established by Pesticide Petition No. 3F-0434 could result in a daily Botran intake of approximately 1.43 mg/day if all consumed residue crops contained maximum allowed residue (discussed in Pesticide Petition No. 3F-0434 memorandum). Establishment of requested tolerances of this petition could add approximately 0.32 to this previously calculated intake. This is assuming maximum allowable residues would be present on the tolerance crops. A total possible intake would amount to 1.43 mg plus 0.32 mg/day. The calculated 1.5 mg/day safe intake would be exceeded by 0.25 mg/day.

Factors for consideration of the safety of the requested Botran ~~[illegible]~~, besides the toxicity data, include the following:

1. Unlikelihood of maximum residues to occur.
2. Unlikelihood of all tolerance crops being treated with Botran.
3. Unlikelihood of man simultaneously ingesting all tolerance crops.

Valid calculations involving the above conditions aren't possible. However, it is reasonable to assume actual intake would be many times reduced from the possible calculated amount. Assuming as much as ½ of the calculated highest possible intake as the highest possible actual intake demonstrates that approximately 0.9 mg/day is well below the calculated safe amount.

Probably any one of the above three residue influencing conditions could reduce actual possible intake by ½ or more. These conditions in combination therefore assure that even a presumed possible actual intake of 0.9 mg/day would be most unlikely to occur.

CONCLUSION:

Toxicity data demonstrating 100 ppm no effect long term rat and dog diets, similar rat and human Botran metabolism, 3-month no effect feeding of man of 10 mg/day, no effect 100 ppm diet in a 3 generation rat reproduction study, 1000 ppm no effect pregnant rabbit exposure test, and residue data related to the difference between calculated and possible actual residues support the safety of the requested residue tolerances.

INIT:HAlmquist

cc: DTE
LIB (Dr. Jacobson)
FP No. T-421
FP No. 434
FP No. 6F-0490
FP No. 5F-0434
FP No. 6F-0474

CEWhitmore:dpe 10-6-66

# End of Document

~~Export~~ ~~Branch~~ FSA ~~Staff~~

AF 12-868

October 5, 1966

File: PP 6F0474

Pesticide Petition No. 6F0474

Dr. A. J. Lemin
Agricultural Products Division
The Upjohn Company
Kalamazoo, Michigan 49001

Dear Dr. Lemin:

This refers to Pesticide Petition No. 6F0474 requesting the amendment of section 120.200 to include the following tolerances for residues of the fungicide 2,6-dichloro-4-nitroaniline:

15 ppm in or on brambles (pre-harvest only) including blackberries, boysenberries, raspberries (red) and celery.

10 ppm in or on carrots (post-harvest only) and rhubarb (pre-harvest only).

5 ppm in or on cucumbers (pre-harvest only)
1 ppm in or on plums/prunes (pre-harvest only).
0.25 ppm in or on potatoes (pre-harvest only).

As discussed with you and your associates in our meeting on September 30, 1966, the question of the 15 ppm tolerance in or on celery is still open. As stated in our meeting, the 15 ppm tolerance may be adequate provided that repeat applications will be made at 7 day intervals during the summer and 14 day intervals during the fall and winter in conjunction with a 7 ddy pre-harvest interval.

As you had indicated agreement with the above we look forward to receiving a confirmation of the changes and revised copies of the label.

Sincerely yours,

James B. Lamb
Petitions Control Branch
Bureau of Science

cc: Pesticides Regulation Division
ARS, USDA

Received
FSA/Pest. Br.
OCT 6 1966

cc: PCB FSA DTE ACC SCI-R
JBLamb:mcs 10/5/66 :mak 10/5/66

TJA/PB
PP#6F0474

Petitions Control Branch and
Division of Toxicological Evaluation

October 17, 1966

Pesticides Branch, Division of Food
Standards and Additives

AF 12-868

PP #6F0474: Botran on various crops. Addendum 2, with special reference to celery.

The Upjohn Company by its letter of October 10, 1966, has revised the proposed usage in accord with one of the two suggestions made in our memo of September 28, 1966. Applications would now be made at 7-day intervals in summer or at 14-day intervals in fall and winter, in conjunction with a 7-day preharvest interval.

Pharmacological considerations permitting, we now recommend that the proposed tolerance of 15 ppm be established for celery.

G.J. Beusch

cc:
DFE
BPC
SCI
SCI-R
SCI-OD
FSA/OD
FSA/PB
PP #6F0474

GJBeusch:md
10/17/66

RD/I--JAlpert

# End of Document

Upjohn
Berueck
Lehmann
Wolff

# MEMORANDUM OF CONFERENCE

**November 1, 1966**

**PRESENT:** Dr. R. R. Herr — Upjohn Company, Kalamazoo, Mich.
Dr. R. L. Johnson — " "
(AF 12-868)

File: PP#6F0474

and

Mr. F. J. McFarland — Petitions Control Branch
Mr. J. B. Lamb — " " "

**SUBJECT:** Status of Pesticide Petition No. 6F0474 (Botran)

The meeting which was requested by Dr. Herr concerned the present status of Upjohn's petition No. 6F0474 which requested tolerances for Botran on various agricultural crops.

Dr. Herr stated that they were very concerned about getting the requested tolerances in time for the November-December celery planting season. Mr. McFarland informed them that the petition is in the final stage and that we would let them know by telephone when an order will be published just as soon as we are in a position to do so.

F. J. McFarland

J. B. Lamb

cc: PCB FSA DTE
JBLamb:mcs 11/1/66 :rh 11/1/66

Received
FSA/Pest. Br.
NOV [illegible] 1966

# End of Document

Dept Branch Secretary Woodruff FDA File: PP# 6F0474

COMMISSIONER OF FOOD AND DRUGS

November 3, 1966

Jesse B. Lamb
Petitions Control Branch, SCI-R

SUBJECT: MEMORANDUM
The Upjohn Company
Kalamazoo, Mich. (AF 13-[illegible])

Establishment of tolerances for residues of the fungicide, 2,6-dichloro-4-nitroaniline; Pesticide Petition No. 6F0474

Botran is the trade name used by the Upjohn Company for the fungicide, 2,6-dichloro-4-nitroaniline. Tolerances have been established at levels from 5 to 20 ppm on twelve fruits and vegetables.

This petition requests tolerances for residues of Botran as follows:

15 ppm in or on blackberries, boysenberries, raspberries (red), and celery.

10 ppm in or on carrots (from postharvest application) and rhubarb.

5 ppm in or on cucumbers.

1 ppm in or on plums (fresh prunes).

0.25 ppm in or on potatoes.

The Pesticides Regulation Division, USDA, has certified to the usefulness of Botran on the above agricultural commodities. They find that the proposed tolerances reasonably reflect the amount of residues likely to result from the proposed usage.

The Division of Food Standards and Additives finds that adequate analytical methods are available for the enforcement of the proposed tolerances. They find that the residues from the proposed use of Botran will not exceed the proposed tolerances. They advise there is no need to limit the tolerance for raspberries to the red variety.

The Division of Toxicological Evaluation has informed us that these tolerances are safe and will protect the public health.

The Fish and Wildlife Service, USDI, has no objection to the proposed tolerances.

We recommend that the attached order be signed and published.

APPROVED:

F. J. McFarland, Chief
Petitions Control Branch
Bureau of Science

L. L. Ramsey, Acting Asst. Director
for Regulatory Programs
Bureau of Science

cc: FCB SCI-R FBW GC(Hearing Clerk) William Stokes 10/20/66
JBLamb:mca 11/3/66 rfa 9/20/66 - GWhitmore 10/18/66 -/OCFitzhugh 10/20/66
R/D Init: GJBeusch 10/14/66

# End of Document

~~July~~ FSA

Mr. William Stokes
Petitions Control Branch

December 20, 1966

Dr. O. G. Fitzhugh
Division of Toxicological Evaluation

File: OPP FF6F0474

Botran

PESTICIDE PETITION NO. 6F-0474

Upjohn Company
Kalamazoo, Michigan
(AF 12-363)

Regarding Dr. Whitmore's memo of 10-6-66 concerning possible daily intake of 1.75 mg botran if allowable residues were present on all crops on which use is authorized and proposed for authorization in this petition, the following comments are offered. In content of these calculations there is no significant difference toxicologically between a calculated 1.8 and calculated 1.75 mg. The decimal places are not significant. It is not possible to be that precise, scientifically.

It is not conceivable that a regular intake of this magnitude could be approached -- and even if it could, the margin of safety between the maximum daily intake of Botran realistically expected from the proposed tolerance levels and the no-effect level in the feeding experiments is ample, approximately 100.

cc: DTE
FP No. 6F-0474

RSR/OGFitzhugh:dps 12-20-66

# End of Document

AF 120868

Pesticide Petition No. 6F0474

January 10, 1967

Dr. Rosa E. Herr
Pesticide Regulatory Affairs
Plant Health Products
The Upjohn Company
Kalamazoo, Michigan 49001

Dear Dr. Herr:

Now that the tolerances proposed in Pesticide Petition No. 6F0474 have been established, we wish to advise you that the maximum acceptable daily intake for residues of the fungicide 2,6-dichloro-4-nitroaniline ("Botran") has been reached based on the no-effect levels indicated by the data in the various Botran petitions. Accordingly, we will be unable to consider the establishment of additional tolerances for residues which will result in a toxicologically significant increase in the total dietary intake of Botran.

Sincerely yours,

Drew M. Baker, Jr.
Petitions Control Branch
Bureau of Science

cc: Pesticides Regulation Division
ARS, USDA

cc: PCB / FSA DTE SCI-R ACC PP7F0558

DMBaker:mmm 1/10/67; rh 1/5/67

R/D Initialed:HBlumenthal 1/5/67
OGFitzhugh 1/6/67
WStokes 1/6/67
FJMcFarland 1/10/67
LLRamsey 1/10/67

Received
FSA/Pest. Br.
JAN 19 1967

# End of Document

File 3B F474

Mr. William Stokes
Petitions Control Branch

February 21, 1967

W. G. A. Waitmore
Division of Toxicological Evaluation
Petitions Review Branch

Botran (2,6-dichloro-4-nitroaniline) 0.05 ppm in or on almond meats
0.5 ppm in or on almond hulls

PESTICIDE PETITION NO. PP-3E5S

Upjohn Company
Kalamazoo, Michigan
(AF 12-668)

Toxicity data provided for Botran Pesticide Petition No. P-421 (June 22, 1964 memo), Pesticide Petition No. 490 (June 9, 1966 memo) and Pesticide Petition No. 474 (October 6, 1966 memo) demonstrated 100 ppm no effect diets in 2 year dog and rat studies, 100 ppm no effect diet in a 3 generation rat reproduction study, similar rat and human metabolism, no effects in human males consuming 10 mg/day/3 months, and a no effect in a, "Lesser", rabbit test for teratogenicity.

These data support the safety of the requested negligible residue tolerances of 0.05 ppm in or on almond meats.

TOX defers to PM relative to the safety of livestock consuming 0.5 ppm of Botran in or on almond hulls.

Enclosures
cy memo 6-9-65
cy memo 6-22-66
cy memo 10-6-66

INIT:Blumenthal

cc: FSA
TOX
LIB (Dr. Jacobson)
PP Res. PP-0355 - P-421
490 & 474

GAW/Waitmore:dps 2-21-67

Received
FSA/Pest. Br.
MAR 3 1967

13544

# R103181

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|---|---|
| **Chemical:** | **Dicloran** |
| **PC Code:** | **031301** |
| **HED File Code** | **11500 Petition Files Chemistry** |
| **Memo Date:** | **10/26/2004** |
| **File ID:** | **00000000** |
| **Accession Number:** | **412-05-0090** |

**HED Records Reference Center**
**01/27/2005**