1-13-84

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

JAN 13 1984

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP# 3E2939 Chlorothalonil on Cranberries. Evaluation of analytical method and residue data (Acc. No. 071773)

FROM: Martin F. Kovacs Jr., Ph.D., Chemist
Residue Chemisty Branch
Hazard Evaluation Division (TS-769)

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

TO: Hoyt Jamerson, Minor Uses Officer
Process Coordination Branch
Registration Division (TS-767C)

and

Toxicology Branch
Hazard Evaluation Division (TS-769)

Interregional Research Project #4 National Director, Dr. R. H. Kupelian, on behalf of the IR-4 Technical Committee and the Agricultural Experiment Stations of Massachusetts, New Jersey, Washington and Wisconsin requests the establishment of a tolerance for combined residues of the fungicide chlorothalonil (tetrachloroisophthalonitrile) and its metabolite 4-hydroxy-2,5,6-trichloroisophthalonitrile in or on the raw agricultural commodity cranberries at 2.0 ppm.

Established tolerances (40 CFR 180.275) range from 0.05 ppm for the edible pulp of bananas to 15 ppm for celery and papayas.

Tolerance proposals are pending for peaches (PP# 3E2815), oranges, grapefruit and citrus oil (PP# OF2405) and for coffee

and cocoa beans (PP# 2E2744). A tolerance proposal for chlorothalonil in or on almonds, rice, wheat, meat, milk, poultry and eggs (PP# 3F2875) is currently in reject status.

SDS Biotech Corp. has submitted a letter (Ralph P. Burton, SDS Biotech Corp, to Mr. Hoyt Jamerson, Minor Uses Officer, EPA) authorizing the use of all confidential information in EPA's files for BRAVO 500 (EPA Reg. No. 677-313) and other chlorothalonil formulations to support the establishment of a tolerance for the use of BRAVO 500 (chlorothalonil) on cranberries. The letter also notes that Diamond Shamrock Corp. has transferred ownership of its chlorothalonil products, labels and data to SDS Biotech Corp.

Conclusions

1a. In the absence of submitted residue data for the impurities HCB and PCBN on cranberries following the proposed use of BRAVO 500 formulations, we calculated maximum theoretical residues of HCB and PCBN on cranberries of $\leq$ 0.002 ppm and $\leq$ 0.05 ppm respectively. Unless TOX Branch objects, we (RCB) consider these calculated maximum impurity levels of no concern. However, if TOX Branch is concerned, then the petitioner must provide RCB with either (1) assay data on the BRAVO 500 formulations used in the residue trials submitted, all reflecting impurity levels of HCB and PCBN at less than [redacted] respectively or as an alternative (2) reanalyses of selected cranberry samples for residues of both HCB and PCBN all treated at the maximum proposed use rate. If reanalyses of these samples reveals finite residues of HCB and PCBN at levels of concern to TOX Branch then these residues may need to be included in a revised tolerance expression for cranberries.

1b. All inerts in BRAVO 500 are cleared under 40 CFR §180.1001.

2a. Toxicological considerations permitting, and in further consideration of the limited human dietary exposure to residues of chlorothalonil as a result of the proposed use on cranberries (which in turn comprise $\leq$ 0.03% of the diet) we (RCB) are recommending that the Registration Standard requirement for additional chlorothalonil plant metabolism studies (see Chlorothalonil Registration Standard dated 11/4/83) be waived for the purpose of the proposed use. Accordingly, we conclude that the nature of the residue in plants is adequately understood.

2b. Since no feed items are involved in this petition our inability to arrive at a final conclusion regarding the adequacy of animal metabolism data (see Chlorothalonil Registration Standard dated 11/4/83) has no bearing on the establishment of a tolerance for chlorothalonil on the rac cranberries.

3. Because of the need for an explanation by the petitioner as to the reason for high control or check values of chlorothalonil residues in the NJ and WA residue trials, resolution of questions relating to the inclusion of HCB and PCBN in the tolerance expression, and submission of chromatograms depicting residues of chlorothalonil in the WA trial (Check Samples #823-826), we cannot conclude that adequate analytical methodology is available to enforce the proposed tolerance on cranberries at this time.

4a. We reserve our final conclusion regarding the adequacy of the proposed tolerance for use of chlorothalonil on cranberries grown in MA, NJ and WI until the petitioner provides information regarding the mode of application (i.e., ground vs aerial) used in the submitted residue studies. If the submitted residue data were obtained by ground application only then Section B must be revised to reflect this use pattern.

4b. We reserve our final conclusion regarding the adequacy of the proposed tolerance for use of chlorothalonil on cranberries grown in WA until conclusion 4a has been resolved and in addition until the petitioner either (1) submits to RCB representative chromatograms of all previous sample analyses including calculations and representative chromatograms of check samples (see our conclusion 3a above) and reanalyzes all samples collected in that residue trial or (2) conducts additional residue studies in WA at the maximum proposed use rates and minimum PHI's permitted on the label. If new residue data are submitted, the mode of application (i.e., ground vs. aerial) must be specified and all sample analyses (including check samples) submitted should include representative chromatograms.

5. No livestock or poultry feed items are involved in the proposed use, therefore there will be no problem of secondary residues in meat, milk, poultry and eggs.

6. The International Tolerance Sheet is attached. There are no Canadian or Mexican tolerances for chlorothalonil residues on cranberries; however, a Codex tolerance of 5.0 ppm for residues of chlorothalonil and its 4-OH

metabolite is at Step 9. This Codex IRL tolerance although incompatible with the 2.0 ppm tolerance proposed in this petition is more than adequate to cover the submitted residue data. However, after the questions relating to the residue data submitted in this petition have been resolved, further consideration will be given

to the compatibility between the proposed U.S. tolerance with the Codex tolerance.

Recommendations

We recommend that the proposed tolerances not be established for reasons given in conclusions 1a, 3, 4a, and 4b. Requirements for resolution of these deficiencies are discussed in the appropriate conclusions above.

Detailed Considerations

Manufacture

The manufacturing process for technical chlorothalonil was discussed in our review of PP #4E1502 (memo of 11/27/74, R. Schmitt).

Hexachlorobenzene (HCB) was reported to be a contaminant (at an average level of [redacted] of 308 batches of technical chlorothalonil that were analyzed (PP #8E2025, memo of 12/28/78 T. McLaughlin). A second impurity in the technical material is pentachlorobenzonitrile (PCBN) which may be present at levels of [redacted] see PP #1E2473, memo of 3/4/82, K. Arne).

IMPURITY INFO IS NOT INCLUDED

The petitioner contends in Section D of this petition that analyses for residues of PCBN and HCB are not necessary to support this tolerance petition since maximum residues for the parent compound did not exceed 2 ppm at the maximum proposed application rate and therefore it is unlikely that detectable levels of PCBN and HCB would be present. We do not concur with the petitioner's rationale for not submitting PCBN and HCB residue data for the following reasons.

None of the BRAVO 500 formulations utilized in the submitted cranberry residue studies were assayed for HCB and PCBN impurity levels. In our M. F. Kovacs, Jr. 11/7/83 review of PP# 3F2875, maximum HCB and PCBN impurity levels reported in the BRAVO 500 formulations applied to almonds, rice and wheat were [redacted]

In the current petition up to 3 applications of BRAVO 500 are permitted on cranberries at 5.2 lbs ai/Application, with a minimum 10-day application interval for a total of 15.6 lbs ai/A with a 50-day PHI. (see Section B Proposed Use).

Assuming that the BRAVO 500 formulations applied to cranberries in this petition contained impurities of HCB and PCBN at the previously reported maximum levels of [redacted] respectively and furthermore by employing the following additional assumptions listed below, we can calculate maximum theoretical residues of these impurities on cranberries following the proposed use as follows:

(1) Avg. cranberry production/acre (based on MA data for low average yield)

80 barrels/acre x 100 lbs/barrel = 8,000 lbs/acre

(2) That the residue dissipation rate for HCB and PCBN on cranberries is the same as that reported for HCB on grass (M.J. Beall, J. Environ. Quality 5 (4) 357 (1976) as reported in the K.H. Arne 4/10/81 review of PP# 1F2473 Chlorothalonil on Mint.

(3) That all of the applied HCB and PCBN would contact the cranberry fruit.

IMPURITY INFO IS NOT INCLUDED

BRAVO 500; 3 Applications, 10-day interval, 50-day PHI following last application and residue dissipation of HCB and PCBN per (2) above:

Residue (ppm) immediately following:

	1st Appl.	2nd Appl.	3rd Appl.	+50 days
HCB	0.13	0.17	0.19	$\leq$ 0.002
PCBN	4.07	5.49	5.99	$\leq$ 0.05

Therefore, 50 days following the last application of BRAVO 500 to cranberries total maximum calculated residues of HCB and PCBN would be $\leq$ 0.002 ppm and $\leq$ 0.05 ppm.

Unless TOX Branch objects, we (RCB) consider the aforecited calculated maximum impurity levels of HCB and PCBN on cranberries following the proposed use to be of no concern. If, however, TOX Branch expresses concern over these maximum potential impurity levels on cranberries then the petitioner must provide RCB with either (1) assay data on the BRAVO 500 formulations used in the residue trials submitted all reflecting impurity levels of HCB and PCBN at less than [redacted] respectively or as an alternative (2) a reanalysis of selected cranberry samples for residues of both HCB and PCBN all treated at the maximum proposed use rate.

If the petitioner opts to reanalyze the selected cranberry samples under item (2) above and the requested reanalysis indicates finite residues of HCB and/or PCBN at levels of concern to TOX Branch, then these residues may need to be included in a revised tolerance expression for chlorothalonil on cranberries (see Chlorothalonil Registration Standard dated 11/4/83 Residue Chemistry Chapter Nature of the Residue in Plants p.2 under Conclusions).

Formulation

The formulation to be used is BRAVO 500 which contains 4.17 lb. active chlorothalonil per gallon or 500 g/liter. This formulation was described in our review of an amendment to PP #6F1799 (see memo of 8/13/80, P. V. Errico). All inerts in BRAVO 500 are cleared under 40 CFR §180.1001. Another registered formulation used for some of the residue studies, BRAVO W-75 contains 75% active ingredient.

Proposed Use

For control of fruit rots, Lophoderium leaf/twig blight in cranberry bogs, BRAVO 500 is to be applied at 6 to 10 pts/A (3.13 to 5.2 lb ai/A) at the late bloom stage. Repeat applications are to be made at 10 to 14-day intervals. Under severe disease conditions use the 5.2 lb ai/A rate on a 10-day schedule. A maximum of 3 applications are permitted per season and a 50-day PHI is imposed. BRAVO 500 may be applied through sprinkler irrigation equipment (solid set systems only); however, application to bogs when flooded and release of irrigation water from bogs within 3 days following application is not permitted. In the absence of specific directions for ground application only (as is the case in this petition) both ground and aircraft methods of application are recommended. According to RCB's Cultural Practices File (Cranberries) approximately two-thirds of the cranberry acreage in the U.S. is treated via ground application with the remainder by air (helicopter or fixed-wing aircraft). In MA and NJ, application is by both air and ground whereas in WI, WA and OR application is by ground only. The proposed use is not limited by a label restriction to any particular state.

Nature of the Residue

Plants

No new plant or animal metabolism studies were submitted with this petition. The metabolism of chlorothalonil in plants and animals has been reviewed in detail in conjunction with earlier petitions (PP#s 7F0599, 1F1024, 2F1230, 4E1502, 6F1799 and 8G1871).

Although it was concluded in the earlier petitions cited above that the residue in plants (corn and tomatoes PP#7F0599 and potatoes PP#9F0743) is mainly surface in nature, and not translocatable with no uptake from roots to aerial plant parts with the parent compound and the 4-hydroxy metabolite the residues of concern, we now conclude that the metabolism studies cited in the earlier petitions are not translatable to the currently proposed use on cranberries. The earlier plant metabolism studies reflected primarily soil applications of chlorothalonil with the resultant translocated residues characterized in immature plant tissue. On the other hand, the currently proposed use involves multiple foliar applications of chlorothalonil to cranberries approaching maturation, a physiological condition which would lend itself to a different rate and pattern of metabolite formation than that previously observed in earlier metabolism studies.

Our conclusions arrived at above concerning the non-translatability of previously submitted chlorothalonil metabolism studies to the currently proposed use on cranberries are based upon the identified inadequacies of these studies (see Chlorothalonil Registration Standard. 11/4/83, Residue Chemistry Chapter, Nature of the Residue in Plants p. 2 under Conclusions).

However, toxicological considerations permitting, and in further consideration of the limited human dietary exposure to residues of chlorothalonil as a result of the proposed use on cranberries (which in turn comprise $\leq$ 0.03% of the diet) we (RCB) are recommending that the Registration Standard requirement cited above for additional chlorothalonil plant metabolism studies be waived for the purpose of the proposed use.

For the purpose of establishing a tolerance on the rac cranberries as proposed in this petition, we therefore conclude that the nature of the residue in plants is adequately understood.

Animals

Although, as cited above, the metabolism of chlorothalonil in animals has been reviewed in earlier petitions and the conclusion arrived at that the parent compound and the 4-OH metabolite are the residues of concern, RCB has concluded (see Chlorothalonil Registration Standard 11/4/83. Residue Chemistry Chapter Nature of the Residue in Animals p. 12) that, since the metabolism of chlorothalonil in plants is not adequately understood, a final decision as to the animal metabolism data requirements cannot be made and accordingly the animal metabolism of chlorothalonil as well as the metabolic residues of concern in feed items are not presently

understood. However, since no feed items are involved in this petition, our inability to arrive at a final conclusion regarding the adequacy of animal metabolism data has no bearing on the establishment of a tolerance for chlorothalonil on the rac cranberries.

Analytical Methodology

The source of the proposed method of enforcement for the determination of chlorothalonil and its 4-hydroxy metabolite in cranberries was cited by the petitioner in "Analytical Methods for Pesticides and Plant Growth Regulators, G. Zweig, Editor, Vol. VIII, Academic Press 1976, Chapter 15 (Chlorothalonil) Authors D. L. Ballee, W. C. Duane, D. E. Stallard and A. L. Wolfe pp. 263-274. The cited method basically describes the enforcement method contained in PAM II for the determination of chlorothalonil and its 4-OH metabolite which involves extraction of the parent and metabolite with acidified acetone, separation and cleanup of the two compounds on a Florisil column, methylation of the metabolite and determination of the derivative and parent by MC- or EC-GLC. This method was validated in PAM II for potatoes and with modifications for extraction of oily crops such as peanuts, further validated by EPA on peanuts (PP# 1F1024, memos of May 18, 1971 and August 10, 1972).

The modification of the PAM II method as also described above in Chapter 15 of Analytical Methods for Pesticides and Plant Growth Regulators, Vol. VIII, 1976, involved the separation of residues of chlorothalonil from its 4-OH metabolite in cranberries by selective partitioning between 0.4 M $NaHCO_3$ solution and isopropyl ether rather than separation and cleanup of the two compounds on a Florisil column as described in the PAM II method. This modified procedure as submitted by the petitioner was also referred to as "Chlorothalonil on Cranberries 1-83." Recovery of chlorothalonil from cranberries ranged from 91 to 108%, avg., 98% at fortification levels of 0.2 to 0.4 ppm; recovery values for the hydroxy metabolite ranged from 90 to 110% avg. 97% at a fortification level of 0.2 ppm. However, in 1982 New Jersey and Washington cranberry residue trials, control values for chlorothalonil were reported as 0.08 to 0.31, avg. 0.20 ppm and 0.70 to 1.90, avg. 1.36 ppm respectively. Control values for the 4-OH metabolite were reported as 0.01 to 0.014, avg. 0.011 ppm and $\leq$ 0.10 ppm for the respective trials cited above. The petitioner should provide an explanation for the high control values for residues of chlorothalonil in the New Jersey and Washington residue trials and in particular submit chromatograms depicting residues of chlorothalonil in the Washington trial (Check samples #823-826). Notwithstanding the high control values for chlorothalonil observed in the residue trials cited above, we

consider the sensitivity of the method to be about 0.01 ppm for chlorothalonil and 0.1 ppm for its 4-OH metabolite. Accompanying chromatograms support these limits of detection.

We cannot conclude that adequate analytical methods are available to enforce the proposed tolerance on cranberries because of the need for an explanation by the petitioner as to the reason for high control or check values of chlorothalonil residues in the NJ and WA residue trials, resolution of questions as to whether or not HCB and PCBN should be included in the tolerance expression, and submission of chromatograms depicting residues of chlorothalonil in the WA trial.

Residue Data

No storage stability studies for chlorothalonil and its metabolite 4-OH chlorothalonil were submitted for the rac cranberries for which a tolerance is proposed in this petition. However, RCB has concluded (see Chlorothalonil Registration Standard 11/4/83 Residue Chemistry Chapter Storage Stability Data p. 17) that chlorothalonil residues are relatively stable in plant samples when stored at sub-freezing temperatures for 6-14 months. Accordingly, we are not raising any questions with respect to the accuracy of the submitted residue data on cranberries since all cranberry samples were stored in a frozen condition (-10°C) for periods of time ranging from 2 to 7 1/2 months prior to analysis.

Residue experiments were carried out during 1981 and 1982 in MA, NJ, WA and WI. These states represent the major cranberry producing areas of USA. Residue data on cranberries were provided only for chlorothalonil and its 4-OH metabolite and not for the potential impurities HCB and PCBN (see our discussion and calculations under Manufacture above on maximum potential residues of HCB and PCBN on cranberries as a result of the proposed use). In conjunction with the 1981 and 1982 MA residue trials, residue data was also provided for chlorothalonil and its 4-OH metabolite in cranberry bog and ditchwater. (Note that the proposed labeling in Section B prohibits release of irrigation water from bogs for at least 3 days following application).

The formulation used for a majority of the residue experiments was BRAVO 500, however, two applications each were made with BRAVO W-75 formulation in the 1981 MA residue trial at 0.43 and 0.50X the maximum recommended rate.

Overall, following application (method not specified) of BRAVO 500 to cranberry bogs in MA, NJ, WA and WI during 1981 and 1982 at 3 to 20 pts/A or 1.56 to 12.0 lbs ai/A (the recommended rates range from 3.13 to 5.2 lb ai/A) in 2 to 3

applications at 10 to 18 day intervals (a maximum of 3 applications at a minimum of 10-day intervals is recommended) with PHI's ranging from 50 to 100 days (50 days recommended) uncorrected apparent residues of chlorothalonil and its 4-OH metabolite were reported as (<0.01 to 4.96) avg. 1.09 ppm and <0.1 ppm respectively.

Of the 5 residue trials submitted only the NJ trial reflected the proposed use as described in Section B, that is, 5.2 lbs ai/A, 3 applications at 10-day intervals and a PHI of 50 days. In that trial uncorrected residues of chlorothalonil and its 4-OH metabolite were reported as (1.01 to 1.65 ppm) avg. 1.36 ppm, we calculate corrected residues at (0.81 to 1.45 ppm) avg. 1.16 ppm.

No detectable residues of either chlorothalonil (<0.02 ppm) or its 4-OH metabolite (<0.02 ppm) were found in bog and ditch water following application rates up to 2X at either the 1981 or 1982 MA residue trial sites.

We conclude that the submitted residue data will clearly support the proposed use in NJ. However, we can also extend this conclusion to the residue data submitted from both MA and WI notwithstanding the fact that the residue data generated in those states reflected longer PHI's (63-90 days vs the 50 days recommended) and fewer numbers of applications made (2 vs. 3 recommended) than specified in Section B. Our conclusions regarding the adequacy of the proposed tolerance for use of chlorothalonil on cranberries in both MA and WI is based on the relatively low residue levels observed for chlorothalonil in those state trials (i.e., in MA 0.35 ppm following 2 applications at a 2X rate and 82-day PHI and in WI 0.83 ppm following 2 applications at a 2.3X rate and a 72-day PHI).

On the other hand, we question the validity of the residue data submitted from WA because of the magnitude of the chlorothalonil check values which ranged from <0.01 to 1.90 ppm, averaged 0.78 ppm and possibly contributed to the reported high uncorrected maximum residue values of chlorothalonil ranging up to 1.98 ppm at a 100-day PHI. Before we can render a favorable tolerance recommendation regarding the use of chlorothalonil on cranberries grown in WA, the petitioner should reanalyze all samples collected in that trial and submit to RCB representative chromatograms of all sample analyses including calculations and representative chromatograms of check samples. As an alternative to the reanalyses of previously submitted residue data from WA, the petitioner should conduct additional residue studies on cranberries in WA at the maximum proposed label use rates, including the maximum number of applications permitted at the minimum proposed PHI of 50 days. The new residue data generated

should specify the mode of application (i.e., ground vs. aerial) and all sample analyses (including check samples) submitted should include representative chromatograms.

Our favorable conclusion regarding the adequacy of the proposed tolerance is also contingent upon clarification by the petitioner as to the mode of application of chlorothalonil to cranberries (i.e., ground vs aerial) since the proposed labeling in Section B does not preclude aerial application (which is commonly practiced in MA and NJ). If the residue data submitted in this petition were obtained by ground application only then Section B must be revised to reflect this use pattern.

Meat, Milk, Poultry, and Eggs

Since no livestock or poultry feed items are involved there will be no problem of secondary residues in meat, milk, poultry and eggs.

Other Considerations

The International Residue Limit (IRL) Status sheet is attached. According to it, there are no Canadian or Mexican tolerances for chlorothalonil residues on cranberries. The Step 9 Codex IRL of 5.0 ppm for combined residues of chlorothalonil and its 4-OH metabolite on cranberries although incompatible with the 2.0 ppm tolerance proposed in this petition is more than adequate to cover the submitted residue data. However, after the questions relating to the residue data submitted in this petition have been resolved, further consideration will be given to the compatibility between the proposed U.S. tolerance and the Codex tolerance.

cc: R.F., Circu, Reviewer, TOX, EEB, EAB, FDA, PP#3E2939, Robert E. Thompson
RDI:Section Head:JHOnley:Date:12/28/83:RDSchmitt:Date:12/28/83
TS-769:RCB:Reviewer:MFKovacs:,DCR-34334 RM-1123-CM#2:557-7484:bje:revised 45801 1/11/84:tar:corrected by LDT:date:1/12/84

INTERNATIONAL RESIDUE LIMIT STATUS Reviewer - Marty Kovacs

CHEMICAL Chlorothalonil

PETITION NO 3E2939

CCPR No. 81

Codex Status

/ / No Codex Proposal
Step 6 or above

Residue (if Step 9): Chlorothalonil and 4-hydroxy-2,5,6-trichloro-1,3-benzene dicarbonitrile

Cranberries	5.0

Proposed U.S. Tolerances

for Sec. 180.275

Residue: Chlorothalonil and metabolite*

Crop(s)	Tol. (ppm).
Cranberries	2.0

CANADIAN LIMIT

Residue: _____

Crop	(Limit (ppm)
None on this commodity	

MEXICAN TOLERANCIA

Residue: _____

Crop	Tolernacia (ppm)
None on this commodity	

Notes: *4-hydroxy-2,5,6-trichloroisophthalonitrile