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

AUG 13 1987

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

Memorandum:

MEID 164474

SUBJECT: PP#7F3471. Chlorothalonil in/on Pecans. Evaluation of Analytical Method and Residue Data. (Acc#'s 265809, -10, -11, RCB#1696).

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Fungicide-Herbicide Branch
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and

Toxicology Branch
Hazard Evaluation Division (TS-769C)

Fermenta Plant Protection Company (formerly SDS Biotech Corporation) proposes a tolerance be established for the residues of the fungicide 2,4,5,6-tetrachlorophthalonitrile (chlorothalonil, SDS-2787) and its metabolite, 4-hydroxy-2,5,6-trichlorophthalonitrile (SDS-3701), in/on pecans at 0.02 ppm. Tolerances are established for residues of chlorothalonil and its metabolite SDS-3701, in/on various r.a.c.'s ranging from 0.05 to 15 ppm (40 CFR 180.275).

A letter from Fermenta Plant Protection Company requests that EPA use pertinent chlorothalonil data in previously submitted petitions in addition to the residue data submitted in this petition (PP#7F3471) for RCB review. A registration standard for chlorothalonil has been issued (9/30/84, Acc#258778).

Conclusions:

- 1a. The nature of chlorothalonil residues is adequately understood for the proposed use in/on pecans.
- 1b. Chlorothalonil, SDS-3701 (4-hydroxy metabolite), impurities Hexachlorobenzene (HCB) and pentachlorobenzonitrile (PCBN) are the residues of concern.
- 1c. If additional metabolic studies show significant toxic components other than the parent and its metabolite, SDS-3701, then additional residue will be needed, with validated analytical methodology. Such components must be included in the tolerance expression.
- 2a. Analytical methodology is available for enforcement of the proposed tolerances (PAM II, Method I) for residues of chlorothalonil and metabolite SDS-3701.
- 2b. If the Agency determines that the impurities, HCB and PCBN, must be included in the tolerance expression, then adequate analytical methodology for enforcement will be needed. Protocol I of the FDA multiresidue methods gives marginal recovery (50-80%), but can provide adequate evaluation of any residues of HCB or PCBN in/on pecan nutmeats.
- 3a. Section B must be amended to restrict application to ground only. The submitted labels allow both; the labels do not preclude aerial applications. Supplemental labels for BRAVO®500, BRAVO®720, and BRAVO®90DG which cover only the limited application (ground equipment only) are needed. As an alternative, the petitioner can submit additional residue data to support aerial applications.
- 3b. Section B must be amended to support a PHI of no less than 36 days. Residue data to support the proposed 30 day PHI were not submitted by petitioner: the PHI's ranged from 36 to 146 days. As an alternative the petitioner can submit additional residue data to support the proposed PHI.
- 4a. Residue data is submitted from GA, Al, TX, Ms, FL, SC, and AR. These states represent 97% of the major growing areas for pecans in the annual US production. No detectable residues (<0.01 ppm) of chlorothalonil, or metabolite SDS-3701, were found in/on pecan nutmeats from crops treated with BRAVO®500 formulations at the maximum proposed rate, 6 pt. (3.1 lb a.i./A; 9 application total 28 lb a.i. and a minimum PHI of 36 days; and 10 application total 31 lb a.i. and a minimum PHI of 37 days).
- 4b. No detectable residues of HCB (<0.003 ppm) or PCBN (<0.005 ppm) were found in/on pecan nutmeats from crops treated with BRAVO®500 formulations at the maximum proposed rate, 6 pt. (3.1 lb a.i./A; 9 application total 28 lb a.i. and a minimum PHI of 36 days; and 10 application total 31 lb a.i. and a minimum PHI of 37 days).

5. No animal feed items are involved with this proposed use. Therefore, there are no concerns with respect to secondary residues in meat, milk, poultry, and eggs.
6. There are no Codex proposals, Canadian limits, or Mexican limits for chlorothalonil and/or its metabolite, 4-hydroxy-2,5,6-trichlorophthalonitrile (SDS-3701).

Recommendation:

RCB recommends against the proposed 0.02 ppm tolerance for residues of chlorothalonil and metabolite SDS-3701 in/on pecans because of deficiencies 3a and 3b.

Manufacture and Formulation:

The manufacture of chlorothalonil (TGAI) and a discussion of its impurities, including HCB and PCBN, has been previously reported. (See Confidential Appendix, memo of 9/10/85, M. Firestone.)

The proposed formulations of chlorothalonil are BRAVO®500 (EPA Reg. No. 50534-8), BRAVO®720 (EPA Reg. No. 50534-188), and BRAVO®90DG (EPA Reg. No. 50534-157). BRAVO®500 and BRAVO®720 formulations are liquid concentrates which contain 4.17 lb a.i./gal (40.4% a.i., 59.6% inerts) and 6.0 lb a.i./gal (54.0% a.i., 46.0% inerts), respectively. BRAVO®90DG is a water-disperable granular formulation which contains 90.0% a.i. and 10.0% inerts. All inerts have been cleared according to §40 CFR 180.1001.

Proposed Use:

Supplemental labels submitted in Section B of the petition calls for application of chlorothalonil, after budbreak, and repeated at intervals not exceeding 14 days, at a maximum rate of 3.1 lb/A with a maximum of 10 applications per season. (31 lb a.i. total). Chlorothalonil is not to be applied after shuck split. Minimum PHI is 30 days. In regard to the proposed formulations, BRAVO® 500 (40.4% a.i.) allows the application of 4.5 to 6.0 pt/A (2.25 to 3 pt/100 gal, 2.3 to 3.1 lb a.i./A), BRAVO® 720 (54.0% a.i.) allows the application of 3 to 4 pt/A (1.5 to 2 pt/100 gal, 2.2 to 3.0 lb a.i./A), and BRAVO® 90DG (90.0% a.i.) allows the application of 2.5 to 3.5 lb/A (1.25 to 1.75 lb/100 gal, 2.25 to 3.15 lb a.i./A). Label allows dilute volume of 200 gal/A for dilute spray and 20 to 150 gal/A (ground equipment only) for concentrate spray. The supplemental label suggest ground application in preference to aerial application. The formulations may be applied with aircraft using a minimum of 20 gal/A. Labels recommend the lower rates when concentrated sprays are used or when treating non-bearing or immature trees. A restriction against livestock grazing in treated areas is on the label for each formulation.

Nature of the Residue:

Several previously submitted metabolic studies (See PP#7F0599, PP#1F1024, and PP#6F1749) showed no translocation of chlorothalonil residues after foliar or soil-treatment applications with chlorothalonil (mixed with ^{14}C -chlorothalonil). Corn, cucumber, bean, and tomato (either direct-seeded or transplanted) were exposed to ^{14}C -chlorothalonil, and the resulting crops were analyzed for ^{14}C -residues (using autoradiographic imagery) after 16-23 days. In another study ^{14}C -residues were translocated into the foliar plant parts of corn and cucumber seedlings after soil treatment with ^{14}C -SDS-3701. At the time of harvest (58-69 days; total exposure time, 55 days), the greatest concentration of ^{14}C -residues were present in the plant leaves. The root tissues did not indicate the presence of ^{14}C -residues (using autoradiographic imagery). Accumulation of ^{14}C -residues increased as the exposure periods were extended. Similar results were found with radishes. Translocation of ^{14}C -residues (using ^{14}C -SDS-3701) occurred in the leafy tissues after exposure times of 19, 42, and 51 days. As the radish plants matured, the ^{14}C -residue levels concentrated in the leafy tissues.

In the above studies, only autoradiography was used to detect ^{14}C -residues and no chemical structural determinations were made of any compounds. It was apparently assumed that ^{14}C -SDS-3701 was adsorbed and transported intact without further metabolism or degradation. However, in a soil metabolic study (Acc#099248) three additional water-soluble metabolites (3-carboxytrichlorobenzamide, 3-cyanotrichlorohydroxybenzamide, and 3-cyanotrichlorobenzamide: 3.2-4.3% of the total applied chlorothalonil) were found along with chlorothalonil, metabolite SDS-3701, and 3-cyano-2,4,5,6-tetrachlorobenzamide (SDS-19221). Structural data was insufficient for positional assignment of the chlorines on the aromatic ring of these three water-soluble metabolites.

The feasibility of adsorption and translocation of soil metabolites were evaluated in a laboratory rotational crop study (Acc#099248). Soil was pretreated with ^{14}C -chlorothalonil and aged for 90 days. After aging, approximately 3% of the applied ^{14}C -chlorothalonil remained in the soil while the other ^{14}C -residues were distributed as follows: 22% metabolite SDS-3701, <2% metabolite SDS-19221, 38% unidentified water-soluble compounds, and 44% unextracted ^{14}C -residues. Three crops were direct-seeded into the treated soil: lettuce (leafy), carrot (root), and beans (fruiting). In all cases the total ^{14}C -residues were found to accumulate in the aerial plant parts as the exposure time increased (30-90 days). The greatest amount were present in the leafy plant parts. Metabolite SDS-3701 was identified in carrot roots and tops after 90 days, in bean plants after 30 and 63 days, and in bean pods and seeds after 45 and 63 days. Chlorothalonil and metabolite SDS-19221 were detected in plant samples, but at low levels. Chlorothalonil, and metabolites SD-3701 and SDS-19221 were identified by thin layer chromatography and quantitated by liquid scintillation counting. The water-soluble metabolites were characterized and quantitated by liquid scintillation counting as a single pool of residues. Although neither the identities

nor the chromatographic properties of the water-soluble metabolites were discussed, presumably these unknowns are the same as those partially identified above. Unextracted ^{14}C -residues were quantitated indirectly ($^{14}\text{CO}_2$) by total combustion analysis.

Foliar application of chlorothalonil to lettuce leaves (See Acc#257517) showed that the major terminal residue was the parent chlorothalonil (>87% up to 21 days post application). In addition, the relative amount of metabolite SDS-3701 increased with time (0.9 to 2.0%), similar to that observed in previous plant studies. No detectable residues of five known soil metabolites of chlorothalonil (See memo of 9/10/85, M. Firestone) were found in the treated lettuce. Up to 11% of the total ^{14}C -residues remained unidentified.

Although a majority of chlorothalonil tolerances were established before the results of the ^{14}C -chlorothalonil soil metabolism and translocation studies were reported, the Chlorothalonil Reregistration Standard (9/30/84) has addressed the need for additional data to support the plant metabolism of the parent compound. Because previous experiments with chlorothalonil revealed that the ^{14}C -residual translocation increased with plant maturity and longer PHI's, the lack of sufficient residue data for these additional metabolites and other unidentified metabolites, and the possible uptake and translocation of these metabolites, then the nature of chlorothalonil residues in plants is not adequately defined.

However, for this petition only, since the proposed use in/on pecans includes a label restriction that prohibits application after shuck-split, and a 30 day HPI, then the nature of the residue is adequately understood. The residues of concern for the proposed use are chlorothalonil, metabolite SDS-3701, and the impurities, HCB and PCBN. If additional metabolic studies show significant toxic components other than the parent and its metabolite, SDS-3701, then such components must be included in the tolerance expression.

Analytical Method:

The analytical methodology in this petition (PP#7F3471) is not identical to the PAM II (Method I) enforcement method. Residue data were collected by a similar procedure, but with some major changes in extraction procedures and compositions of elution solvents. The pecan nutmeats are blended with dry ice, then extracted at room temperature with acetonitrile after evaporation of dry ice. The acetonitrile extract is acidified (pH 4.5) and evaporated. The residue is applied to a Florisil column cleanup, and chlorothalonil and metabolite SDS-3701 are separated. The chlorothalonil fraction also contains the impurities HCB and PCBN. Samples are analyzed by EC chromatography. Metabolite SDS-3701 must be methylated before glc analysis.

This method is acceptable for valid data collection for residues of chlorothalonil, metabolite SDS-3701, HCB, and PCBN residues. Validation data gave adequate recovery of spiked samples: chlorothalonil (0.03-5.16 ppm, 65-100%), SDS-3701 (0.03-0.49 ppm,

67-110%), and impurities, HCB (0.010-0.052 ppm, 64-100%) and PCBN (0.023-0.123 ppm, 67-110%). This method has not been evaluated in an EPA laboratory. Future establishment of a tolerance in/on pecans residues of chlorothalonil and metabolite SDS-3701 will require use of the PAM II method for enforcement purposes. The PAM II, Method I, has a sensitivity of 0.01 ppm, which is within the proposed tolerance of 0.02 ppm. However, possibly the petitioner's validation method should be submitted to FDA for inclusion in PAM II as a lettered method as similar methods have been used in previously submitted petitions by Fermenta Plant Protection Company. This method can also be used to determine HCB and PCBN residues. Protocol I of the FDA multiresidue methods gives marginal recovery (50-80%), but can provide adequate evaluation of residues of HCB or PCBN in/on pecan nutmeats.

Residue Data:

Residue data are submitted from total of nine field experiments located in 7 growing areas, i.e., GA, AL, TX, MS, FL, SC, and AR. These states represent 97% of the major growing areas for the annual US pecan production. Crops were treated by ground equipment only with BRAVO[®]500 formulations (40.9-41.9% a.i.) at rates ranging from 2.5 to 6.5 pt/A (1.3 to 3.1 lb a.i./A), at intervals not exceeding 14 days. The number of applications ranged from 4 to 10 and PHI's varied from 36 to 146 days. (Applied 31 lb a.i./A total which conformed to maximum allowable on the supplemental label). Although no exaggerated rates above the label limits were reported, processing of chlorothalonil-treated pecans will not yield a concentration of residues. In addition, pecan shells are not used as a livestock feed item.

No detectable residues (<0.01 ppm) of chlorothalonil, or metabolite SDS-3701 were found in/on any pecan crop treated with the BRAVO[®]500 formulation at the maximum proposed rate (3.1 lb a.i./A) and a minimum PHI of 36 days. Likewise, no detectable residues of HCB (<0.003 ppm) or PCBN (<0.005 ppm) were found at the maximum rate and a 36 day PHI.

Samples collected after recorded PHI's were either frozen and shipped to lab for frozen storage and analyses, or stored dry, then shipped to lab for frozen storage and analyses. In general, samples should be frozen immediately upon sampling so as to provide reliable residue data. However, in this case since the nutmeat is the only plant part defined as edible, the residue data for all samples, whether immediately frozen, or stored dry and then frozen, will be acceptable only for the purposes of this petition (PP#7F3471).

Because no detectable residues (>0.01 ppm) were found in/on treated crops, and applications were before shuck-split, RCB can accept not holding up this tolerance for additional metabolic studies. However, if additional metabolic studies show significant toxic components other than the parent and its metabolite, SDS-3701, then additional residue data will be needed, with validated analytical methodology, and such components must be included in the tolerance expression. A method trial on any additional analytical methodology may also be needed.

Contrary to a statement included in the introduction to the submitted Section B, "Note that the use of chlorothalonil on pecans is limited to ground application equipment only", the petitioner has submitted labels which allows aerial application if ground application is not feasible. If it is the intent of the petitioner to limit the application method, then the reference to aerial application must be removed from the labels and a Revised Section B should be submitted. As an alternative, the petitioner can submit additional residue data to support aerial applications.

Meats, Milk, Poultry, and Eggs:

No animal feed items are involved with this proposed use. Therefore there are no concerns with respect to secondary residues in meat, milk, poultry, and eggs.

Other considerations:

There are no Codex proposals, Canadian limits, or Mexican limits for chlorothalonil and/or its metabolite, 4-hydroxy-2,5,6-trichlorophthalonitrile (SDS-3701).

cc: R.F.; PMSD/ISB; PM-21; J. Stokes (2 copies); PP #7F3471;
S.F.; Circu
RDI: JGarbus:7/21/87:PErrico:8/10/87:RSchmitt:8/11/87
TS-769:RCB:J. Stokes:js:Rm 805:CM#2:8/12/87

-8-

INTERNATIONAL RESIDUE LIMIT STATUS

F. Ives
7/24/87

CHEMICAL Chlorothalonil

CODEX NO. 81

CODEX STATUS:

No Codex Proposal
Step 6 or above (on pecans)

Residue (if Step 8): _____

Chlorothalonil

<u>Crop(s)</u>	<u>Limit</u> <u>(mg/kg)</u>
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PROPOSED U.S. TOLERANCES:

Petition No. 7F3471

RCB Reviewer Jerry Stokes

Residue: Chlorothalonil and

4-hydroxy-2,5,6-trichlorophthalonitrile

<u>Crop(s)</u>	<u>Limit</u> <u>(mg/kg)</u>
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pecans 0.02

CANADIAN LIMITS:

No Canadian limit (on pecans)

Residue: Chlorothalonil

<u>Crop(s)</u>	<u>Limit</u> <u>(mg/kg)</u>
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MEXICAN LIMITS:

No Mexican limit (on pecans)

Residue: Chlorothalonil

<u>Crop(s)</u>	<u>Limit</u> <u>(mg/kg)</u>
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NOTES: