

US EPA ARCHIVE DOCUMENT



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

NOV 13 1992

MEMORANDUM

SUBJECT: PP#2E04042. Chlorothalonil (Bravo® 500 and Bravo® 720 Agricultural Fungicide, EPA Reg. No. 50534-8 and 50534-188) in or on Asparagus. Evaluation of analytical method and magnitude of residue data.
MRID No. 420739-01; CBTS No. 8902; DP Barcode: D171181.

FROM: William D. Wassell, Chemist *W.D. Wassell 11/12/92*
Tolerance Petition Section I
Chemistry Branch I - Tolerance Support
Health Effects Division (H7509C)

THROUGH: Robert S. Quick, Section Head *RW Cook for RSQ*
Tolerance Petition Section I
Chemistry Branch I - Tolerance Support
Health Effects Division (H7509C)

TO: Hoyt L. Jamerson, PM - 43
Emergency Response and Minor Use Section
Registration Division (H7505C)

and

Toxicology Branch II
Fungicide/Herbicide Support
Health Effects Division (H7509C)

W.L. Biehn, Ph.D., Associate Coordinator, Interregional Research Project No. 4 (IR-4), State Agricultural Experiment Station, Rutgers University, New Brunswick, New Jersey on behalf of the IR-4 Project and the Agricultural Experiment Stations of Kentucky, North Carolina, Oklahoma, Virginia and Washington requests the establishment of a tolerance for the combined residues of the fungicide chlorothalonil, [tetrachloroisophthalonitrile] and its metabolite 4-hydroxy-2,5,6-trichloroisophthalonitrile (SDS-3701) in or on the raw agricultural commodity (RAC) asparagus at 0.10 ppm.

Chlorothalonil is a FIFRA '88 List A pesticide active ingredient and the Chemistry Chapters of the Chlorothalonil Final Registration Standard and Tolerance Reassessment (FRSTR) have been completed (3/11/88).

Tolerances are established (40 CFR §180.275(a)) for the combined residues of the fungicide chlorothalonil and its metabolite 4-hydroxy-2,5,6-trichloroisophthalonitrile in or on various RAC's ranging from 0.05 to 15 ppm. A tolerance with regional registration is established (40 CFR §180.275(b)) for

the combined residues of this fungicide and its metabolite at 2 ppm in or on mint hay.

A letter (dated 4/12/91) from Ralph P. Burton, Manager, Product Registrations, ISK Biotech Corporation to Mr. Hoyt L. Jamerson, Registration Division, authorizes the Agency to review and rely on all test data owned or submitted to the EPA by ISK Biotech for chlorothalonil, which may be necessary to support the proposed tolerance.

Conclusions:

1. The manufacturing process of chlorothalonil (technical product) has been adequately discussed in the Product Chemistry Chapter of the FRSTR (3/11/88). We have determined that the impurity hexachlorobenzene (HCB) is of concern.
2. CBTS concludes the proposed directions for use of the product on asparagus are not adequate. We request a revised Section B that includes a maximum seasonal use rate and a pre-harvest interval that reflects the residue data (see discussion in the Magnitude of Residue section of this review).
- 3a. Plant metabolism data were not submitted with this petition. For the purpose of this minor crop petition for asparagus only, we conclude the nature of the residue is adequately understood and the regulated residues are chlorothalonil and its 4-hydroxy metabolite.
- 3b. The impurity HCB is not included in the tolerance expression. HCB can occur as a residue in chlorothalonil treated commodities. The HCB residue levels are used in calculating dietary risk considerations associated with HCB for chlorothalonil treated commodities.
4. Animal metabolism data were not submitted with this petition. Animal feed items are not derived from asparagus. Therefore, there is no concern for animal metabolism and secondary residues of chlorothalonil in animal commodities resulting from the proposed use.
5. For the purpose of this minor crop petition only, CBTS concludes adequate methodology for the enforcement of residues resulting from the proposed use of chlorothalonil on asparagus does exist.
6. The description of the analytical procedures utilized in the submitted studies are not adequate and the deficiencies cited in the Analytical Methods - Data Collection section of this review must be addressed.
 - 7a. CBTS concludes the residue data does not support the proposed use and we can draw no conclusions regarding the requested tolerance level of 0.1 ppm for the combined residues of chlorothalonil and its 4-hydroxy metabolite in or on asparagus.
 - 7b. The GLP Compliance Statement contained on page 3 of MRID No. 420739-01 covers only the analytical portion of the submitted study and does not cover the field portion of the study. The registrant should submit a GLP Compliance or

Non-compliance Statement that refers to all aspects of the study as is required under 40 CFR §160.12.

8. Storage stability data for chlorothalonil on asparagus were not included in the current submission, but references to previously submitted studies are contained in the submission. We can draw no conclusions on the adequacy of the storage stability data for chlorothalonil, its 4-hydroxy metabolite and HCB because the length and conditions of storage for the residue samples were not included in the submission.

9. The International Residue Limit Status sheet is attached and there are no established Codex, Mexican or Canadian tolerances for chlorothalonil and its metabolite 4-hydroxy-2,5,6-trichloroisophthalonitrile in or on asparagus. Therefore, the establishment of the proposed tolerance on this commodity will not create compatibility problems.

Recommendations:

For reasons 2, 6, 7 and 8, stated above, CBTS can not at this time recommend for the establishment of the proposed tolerance limit of 0.1 ppm for the combined residues of chlorothalonil and its 4-hydroxy metabolite in or on the raw agricultural commodity asparagus.

Note to PM: CBTS requests submission of this review in its entirety to the petitioner.

Note to Registrant and PM: The GLP Compliance Statement contained on page 3 of MRID No. 420739-01 covers only the analytical portion of the submitted study and does not cover the field portion of the study. The registrant should submit a GLP Compliance or Non-compliance Statement that refers to all aspects of the study as is required under 40 CFR §160.12.

Detailed Considerations

Manufacture and Formulation:

The manufacturing process of chlorothalonil (technical product) has been adequately discussed in the Product Chemistry Chapter of the FRSTR (3/11/88). We have determined that the impurity hexachlorobenzene (HCB) is of concern.

The formulations to be used are Bravo® 500 and Bravo® 720 Agricultural Fungicide (EPA Reg. No. 50534-8 and 50584-188, respectively); these are products of ISK Biotech Corporation of Mentor, Ohio. Bravo® 500 and Bravo® 720 are broad spectrum fungicides containing 4.17 or 6.0 lbs active ingredient per gallon, respectively.

Proposed use:

Apply Bravo® 500 or Bravo® 720 to control rust, purple spot and Cercospora leaf blight on asparagus at a rate of 3 to 5.75 pints per acre or 2 to 4 pints per acre, respectively (1.5 to 3.0 lbs ai/A) in at least 25 to 50 gallons per acre.

Begin applications after harvest of spears and when conditions favor disease development on the ferns, generally when leaf wetness occurs. Repeat applications at 2 to 4 week intervals until the ferns are no longer productive. Use the high rate and shortest retreatment interval when conditions favor disease. Do not apply within 100 days of anticipated harvest of spears during the subsequent growing season. A maximum seasonal use rate is not specified.

CBTS concludes the proposed directions for use of the product on asparagus are not adequate. We request a revised Section B that includes a maximum seasonal use rate and a pre-harvest interval that reflects the residue data (see discussion in the Magnitude of Residue section of this review).

Nature of the Residue - Plants:

Plant metabolism data were not submitted with this petition. The available plant metabolism data for chlorothalonil has been extensively reviewed in the Residue Chemistry Chapter of the FRSTR (dated: 3/11/88), PP#5F3183 (see memo of S.H. Willett, 11/3/88) and PP#6E3410 (see memo of S.H. Willett, 6/22/89). In PP#6E3410, we concluded that the nature of the residue in plants is not adequately understood. We are requiring at least one additional metabolism study in order to adequately delineate the nature of the residue in plants (see memo of S.H. Willett, 9/8/89).

A metabolism study on tomatoes with ¹⁴C-chlorothalonil was submitted and reviewed in conjunction with PP5F3183 (see our memo of 11/3/88, S.H. Willett). This study suggests that the residues are primarily comprised of chlorothalonil and 4-hydroxy-2,5,6-trichloroisophthalonitrile (SDS-3701). Some translocation of residues occurs from the foliage, root and possibly the fruit skin, but the residues appear to be primarily surface in nature. For the purpose of this minor crop petition for asparagus only, we conclude the nature of the residue is adequately understood and the residues of toxicological concern are chlorothalonil and its 4-hydroxy metabolite (SDS-3701) along with the impurity HCB.

Chlorothalonil and its 4-hydroxy metabolite are included in the tolerance expression for residues resulting from the use of chlorothalonil, but residue levels of HCB are considered separately. Currently, CB estimates residue levels of HCB at 0.5% of the chlorothalonil tolerance level for individual commodities. This value is utilized to estimate dietary risk associated with HCB, but additional data on HCB levels has been requested for reregistration of chlorothalonil (see our memo of 4/11/89, D.F. Edwards, Ph.D., DEB No. 4892). HCB residue data has not been requested for all commodities for which chlorothalonil is registered.

Nature of the Residue - Animal:

Animal metabolism data were not submitted with this petition. Animal feed items are not derived from asparagus. Therefore, there is no concern for animal metabolism and secondary residues of chlorothalonil in animal commodities resulting from the proposed use.

Analytical Methods - Enforcement:

Recovery of chlorothalonil via FDA Multiresidue Protocol E (PAM I 211.1 and 212.1) is complete (Pesttrak data base (11/6/90)). The 4-hydroxy metabolite of chlorothalonil (SDS-3701) is not recoverable via FDA Multiresidue Protocols (Pesttrak data base (11/6/90)). Recovery of the impurity HCB via FDA Multiresidue Protocols E and D (PAM I, 211.1 and 232.4) is complete.

An enforcement method for the determination of residues of chlorothalonil and its 4-hydroxy metabolite has been published in PAM II (Pesticide Reg. Sec. 180.275) as Method I. Additionally, we have recommended for a method entitled "General Analytical Procedure for the Determination of Residues of Chlorothalonil (SDS-2787), SDS-3701, SDS-46851, HCB and PCBN on Selected Crops" to be published in PAM II as this appears to be a better methodology than the currently published method (see memo of W.T. Chin, Ph.D., 2/22/91). This method has not yet appeared in PAM II.

For the purpose of this minor crop petition only, CBTS concludes adequate methodology for the enforcement of residues resulting from the proposed use of chlorothalonil on asparagus does exist.

Analytical Methods - Data Collection: (MRID No. 420739-01)

The analytical portions of the residue studies were conducted at Hazelton Laboratories of Madison, WI. The analytical method utilized for residue determinations in the submitted study is entitled: "General Analytical Procedure for the Determination of Residues of Tetrachloroisophthalonitrile (Chlorothalonil, SDS-2787), SDS-3701, SDS-46851, HCB and PCBN on Selected Crops," Document Number 316-88-0138-MD-001. Briefly, the residues are extracted by blending the samples with acidic acetone and selectively partitioned into an appropriate organic solvent. The extract containing the residues of chlorothalonil, HCB, and PCBN is subjected to liquid/solid column chromatography in order to separate the residues into individual fractions. The residues of SDS-3701 and SDS-46851 are methylated and subsequently separated by liquid/solid column chromatography. The residues in all fractions are quantified by gas chromatographic analysis utilizing a ⁶³Ni electron capture detector. Method quantification limits of 0.03 ppm for chlorothalonil and 0.03 ppm for its 4-hydroxy metabolite and 0.01 ppm for HCB are specified.

The description of the analytical procedures are not adequate and the following deficiencies must be addressed:

- a. Chromatograms for samples fortified at the quantification limit should be provided along with the chromatograms for analytical standards equivalent to these fortification levels.
- b. The description of the sample homogenization procedures are not adequate and the registrant must provide a more detailed description of the procedure. The registrant must address how the duplicate samples were prepared from the field samples and list the conditions of the samples during the homogenization

procedure (ie. thawed, partially frozen or completely frozen and blended in the presence of dry ice).

c. Several options are listed in the extraction procedure, yet the analytical facility does not indicate which options were utilized in the submitted study.

d. Additional information on the standards is requested. This information is to include, but not limited to: (i) dates of receipt for the analytical grade standards; (ii) dates of preparation for the standard solutions; (iii) preparation method(s) for the standard solutions including the derivatization procedures for the SDS-3701 standard.

e. A complete list of all instrument operating parameters are requested.

f. An example calculation that can be traced back to the raw data must be submitted.

g. Please explain further and briefly discuss the scientific impact on the study of the one of the protocol deviations (found on Page 48): "Due to method problems, some final validation data were generated after the initiation of field samples."

h. A complete sample history must be submitted for all samples used to support the proposed tolerance levels. The information should include but not be limited to: (i) dates of harvest, shipment, receipt, homogenization, extraction and analysis for all sample including fortifications, controls and reagent blanks; (ii) sample storage conditions from harvest through analysis also to include conditions of samples upon receipt by the various facilities.

i. Please define the meaning of the term "Amended Level (ppm)" as used in Tables 1 and 3.

Note to IR-4: Analyses for chlorothalonil metabolite SDS-46851 (3-carboxytrichlorobenzamide) and the impurity PCBN (pentachlorobenzonitrile) are not necessary for future chlorothalonil submissions.

Magnitude of Residue: (MRID No. 419882-01)

Field trials were conducted in Michigan (2), Oklahoma (4), California (2) and Washington (1) during the years 1983 through 1988 with chlorothalonil on asparagus in order to produce treated crop samples for residue analysis. Residues of chlorothalonil, its 4-hydroxy metabolite and HCB above the method quantification limits were not found in any of the treated samples. A summary of the details of each of the trials is provided in Table 1, below.

Table 1. Summary of Chlorothalonil Field Trial Data Submitted in support of the Proposed Tolerance in/on Asparagus.

Location (Year)	No. of Applications (Formulation)	Application Rate (lbs ai/A)	Total Rate (lbs ai/A)	PHI (days)	Application Interval
E. Lansing, MI (1986)	5 (Bravo® 500)	2.1	8.3	262	14 days
E. Lansing, MI (1987)	5 (Bravo® 720)	2.1	10.3	233	14 days
	5 (Bravo® 500)	2.1	10.3	233	14 days
Bixby, OK (1983)	8 (Bravo® 500)	1.6	12.5	215	10 - 15 days
	8 (Bravo® 500)	3.1	25	215	10 - 15 days
Bixby, OK (1987)	3 (Bravo® 720)	1.6	4.7	248	15 - 19 days
Bixby, OK (1988)	4 (Bravo® 720)	1.6	6.25	235	16 - 25 days
	4 (Bravo® 720)	1.6	6.25	193	16 - 25 days
	4 (Bravo® 720)	1.6	6.25	235	16 - 25 days
	4 (Bravo® 720)	1.6	6.25	193	16 - 25 days
Stockton, CA (1987)	6 (Bravo® 720)	2.25	13.5	97	14 days
	3 (Bravo® 720)	3	9	107	28 days
Sunnyside, WA (1987)	3 (Bravo® 720)	1.13	3.4	223	unknown
	3 (Bravo® 720)	2.25	6.75	223	unknown

CBTS concludes the residue data does not support the proposed use and we can draw no conclusions regarding the requested tolerance level of 0.1 ppm for the combined residues of chlorothalonil and its 4-hydroxy metabolite in or on asparagus. Under the proposed use and in a worst-case scenario, a maximum of approximately 11 applications at a rate of 3 lbs ai/A (33 lbs ai/A/season) may be made with a preharvest interval of 100 days.

The registrant should revise the use pattern to match the application rate and pre-harvest interval reflected in the majority of the submitted residue studies; none of the existing residue data reflect the proposed use in a worst case scenario. The petitioner should also conduct at least one additional residue

trial in California and Washington to reflect the majority of the residue data in this petition - presumably this will be reflective of the revised use pattern that we are suggesting above.

Note to the Registrant and the PM: The GLP Compliance Statement contained on page 3 of MRID No. 420739-01 covers only the analytical portion of the submitted study and does not cover the field portion of the study. The registrant should submit a GLP Compliance or Non-compliance Statement that refers to all aspects of the study as is required under 40 CFR §160.12.

Storage Stability: (MRID Nos. 418087-01)

Storage stability data for chlorothalonil on asparagus were not included in the current submission. The submission contained references to a series of storage stability studies submitted to the agency for unknown reasons. These studies (MRID Nos. 415648-20 through -27) were not extensively reviewed in conjunction with this petition and our comments are meant only as guidance to the petitioner for future submissions in support of this petition. The volumes contain a description of storage stability studies conducted with field incurred residues of chlorothalonil in or on various commodities. The study is intended to last for approximately 6 years and the reports contain preliminary data from the first year of the study. In some cases it will be difficult at best to draw any conclusions from the submitted studies for the following reasons: (i) residue levels of chlorothalonil are variable throughout the study; (ii) in a majority of the studies, residue levels of the 4-hydroxy metabolite of chlorothalonil are variable and near the quantification limit of the analytical method; (iii) residue levels of HCB are generally below the quantification limit of the analytical method; (iv) some residue samples in the current submission may have been stored for up to 7 years prior to analysis.

CBTS can draw no conclusions on the adequacy of the available storage stability data for chlorothalonil, its 4-hydroxy metabolite and HCB because the storage length and conditions for the residue samples were not included in the submission.

Meat, Milk, Poultry and Eggs:

Animal feed items are not derived from asparagus. Therefore, there is no concern for animal metabolism and secondary residues of chlorothalonil in animal commodities resulting from the proposed use.

Other Considerations:

The International Residue Limit Status sheet is attached and there are no established Codex, Mexican or Canadian tolerances for chlorothalonil and its metabolite 4-hydroxy-2,5,6-trichloroisophthalonitrile in or on asparagus. Therefore, the establishment of the proposed tolerance on this commodity will not create compatibility problems.

Attachment: IRL Status Sheet

cc: WDWassell, RF, Circ., PP#2E042, chlorothalonil SF, chlorothalonil Rereg. File

RDI: R.W. Cook: 11/10/92; D.E. Edwards 11/12/92.

H7509C:CBTS:WDWassell:wdw:CM#2:Rm 804U:(703)305-6135:10/27/92.

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INTERNATIONAL RESIDUE LIMIT STATUS

-10-

J. Wass
10/28/92

CHEMICAL Chlorothalonil

CODEX NO. 91

CODEX STATUS:

No Codex Proposal
Step 6 or above (on asparagus)

Residue(if Step 8): _____

Chlorothalonil

PROPOSED U.S. TOLERANCES:

Petition No. 2E4042

RCB Reviewer W.D. Wassell

Residue: Chlorothalonil & its 4-hydroxy

Metabolite

Crop(s) Limit (mg/kg)

Crop(s) Limit (mg/kg)

Asparagus 0.1 ppm

CANADIAN LIMITS:

No Canadian limit (on asparagus)

Residue: _____

Chlorothalonil

Crop(s) Limit (mg/kg)

MEXICAN LIMITS:

No Mexican limit (on asparagus)

Residue: _____

Crop(s) Limit (mg/kg)

NOTES: