

3-7-85



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

MAR 7 1985

OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP#5F3183 (RCB No. 371). Chlorothalonil on Cherries.
Evaluation of Analytical Methods and Residue Data
(Accession Numbers 073106, 073107, 073108, 073109).

FROM: Michael P. Firestone, Ph.D., Chemist
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THRU: Charles L. Trichilo, Ph.D., Chief
Residue Chemistry Branch
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TO: Henry Jacoby, Product Manager No. 21
Registration Division (TS-767)

and

Toxicology Branch
Hazard Evaluation Division (TS-769)

SDS Biotech Corporation proposes to establish a temporary tolerance for the fungicide chlorothalonil (2,4,5,6-tetrachloroisophthalonitrile) and its metabolite 4-hydroxy-chlorothalonil (4-hydroxy-2,5,6-trichloroisophthalonitrile) in or on the raw agricultural commodity (rac) cherries (sweet and tart) at 3.0 ppm.

Regarding the definition of the rac cherries, the petitioner proposes the following:

"In order to monitor residues of chlorothalonil occurring on the RAC, and for the sake of establishing tolerances on the RAC cherries, the RAC should be considered to be harvested cherries as they leave the farm. In the case of cherries harvested dry (primarily sweet cherries), the RAC would be cherry fruits as they are picked from the tree. For mechanically harvested cherries, the RAC would be cherries taken from water vats as they arrive at the processing plant. ..."

However, for the purposes of collecting residue data and establishing a tolerance, RCB considers the rac to be unwashed cherries as they are picked from the tree, since cherries can be harvested dry.

The petitioner also states that the present petition has been submitted in order to amend the previously established 0.5 ppm chlorothalonil tolerance on cherries (sweet and sour) (see PP#2F2602).

Note: The tolerance proposal as stated above is contradictory, and is presumably intended as a request for a permanent tolerance, not a temporary tolerance as stated in Section F. The petitioner should be informed that a revised Section F proposing a permanent tolerance will need to be submitted in a future amendment.

Chlorothalonil tolerances are established on several rac's ranging from 0.05 ppm to 15 ppm (see 40 CFR 180.275).

Tolerances are pending for chlorothalonil on several rac's including peaches and cherries at 25 ppm (PP#6F1749), peaches at 3 ppm (PP#3E2939), apples at 0.1 ppm (PP#4F3025) and almonds/almond hulls at 0.05 ppm and 0.2 ppm, respectively.

peach 25 } 6 ppm
cherries 25 }

Conclusions

- 1a. The petitioner will need to submit a revised Section F in which a permanent tolerance is proposed.
- 1b. The petitioner should be informed that RCB considers the rac to be unwashed cherries as they are picked from the tree, since cherries can be harvested dry.
- 2a. The petitioner will need to submit a revised Section B/label in which a restriction is included which will limit the number of post-shuck-split applications allowed. The petitioner should be informed that the proposed use must be supported by the submitted residue data.
- 2b. RCB does not consider split PHIs (i.e., 7 days for cherries harvested into water and 30 days for cherries not harvested into water) acceptable (see also Conclusion 1b above). Furthermore, water can not remove any systemic residues. The petitioner will need to propose only a single PHI in a revised Section B/label.
- 2c. The revised Section B/label should contain both a restriction against grazing treated orchards/groves and cutting cover crops for feed.
- 3a. In RCB's review of PP#4F3025, the petitioner was advised of the need for a ring-labeled ¹⁴C-chlorothalonil foliar-applied apple metabolism study (see M. Kovacs, Jr. memo of 5/30/84).

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RCB reiterates the need for such a plant metabolism study in support of the proposed post-shuck-split chlorothalonil use on cherries. Thus, the nature of the residue in plants is not adequately understood.

- 3b. Although the nature of the residue in animals is not adequately understood, since there are no feed items involved in this petition, this deficiency has no bearing on the establishment of an amended tolerance for chlorothalonil on the rac cherries.
- 4. RCB can not conclude at this time that adequate analytical methodology is available to enforce the proposed tolerance on cherries until the nature of the residue in plants has been adequately resolved (see Conclusion 3a).
- 5a. RCB considers the residue data inadequate to support the proposed 3 ppm chlorothalonil tolerance on cherries.
- 5b. Since RCB considers the rac to include dry harvested cherries (see Conclusion 1b), residue data generated on washed tart cherries are not considered adequate to support the establishment of an amended chlorothalonil tolerance on cherries.
- 5c. Residue data generated on dry harvested cherries from only one field trial are not considered adequate to support any proposed tolerance. Therefore, the petitioner will need to submit additional residue data generated on cherries (sweet and tart) harvested dry and reflective of the proposed use (i.e., maximum number of post-shuck-split treatments, maximum application rate, etc.). These residue data must be geographically representative of the major cherry growing regions of the country. Thus, the petitioner will need to generate the additional residue data on field-treated cherries grown in the states of CA, OR or WA, MI, and NY or PA (note: if these treated samples are stored more than 6 months prior to analysis, additional storage stability data will be required).
- 5d. Pending RCB's final conclusion concerning the nature of the residue in plants (see Conclusion 3a), the petitioner may need to submit residue data on components of the terminal residue other than chlorothalonil, 4-hydroxy-chlorothalonil, HCB, and PCBN.
- 6. Cherries are not considered an animal feed item. Thus, RCB does not expect any problem of secondary residues in meat, fat, milk, poultry or eggs from the proposed use.

7. An International Residue Limit Status sheet is attached to this review. There are no Canadian or Mexican tolerances/limits established for chlorothalonil on cherries. Codex has established a 10 ppm limit (parent compound only) which is considerably higher than the proposed 3 ppm (parent plus 4-hydroxy metabolite) tolerance. This incompatibility will be reevaluated in the future when the additional requested residue data on dry-harvested cherries have been submitted.

Recommendation

RCB recommends at this time against the establishment of the proposed amended tolerance of 3 ppm chlorothalonil on cherries because of the reasons cited in conclusions 1a, 1b, 2a, 2b, 2c, 3a, 4, and 5a-5d.

Detailed Considerations

Manufacture and Formulation

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

Hexachlorobenzene (HCB) and pentachlorobenzonitrile (PCBN) are impurities in the technical product.

The BRAVO 500 formulation proposed for use on cherries and utilized in the submitted cherry residue studies (Batch RMSTOLO) reportedly contained 41.8% chlorothalonil, HCB and PCBN. The levels of HCB and PCBN on treated cherries will be discussed in the Residue Data section of this review. BRAVO 500 contains 4.18 lb ai/gal (500 g/l). This formulation was described in RCB's review of PP#6F1799 (see P. Errico memo of 8/13/80). All inerts are cleared under 40 CFR 180.1001.

Proposed Use on Cherries

The established use on cherries allows one application of BRAVO 500 at popcorn stage (pink, red or early white bud), a second application at full bloom, and a third application at petal fall, all at a rate of 4 1/2 to 8 pints/A (2.3 to 4.2 lb ai/A) to control blossom blight and brown rot. To control cherry leafspot, a fourth application is allowed at shuck-split and post-harvest applications are allowed within 7 days after fruit is removed and also at 10 to 14 days later, all at reduced rates of 4 1/2 to 6 pints/A.

IMPURITY INFO IS NOT INCLUDED

2 pints/A = 2.3 lb ai/A

The proposed amended use to control cherry leafspot, brown rot and Coryneum blight (shot hole) would increase the shuck-split and post-harvest application rates to 4 1/2 to 8 pints/A, and allow additional applications at 10 to 14 days after shuck-split (no limitation as to the number of post-shuck-split applications). A PHI of 30 days is proposed except on cherries which are machine-harvested into water, for which a 7-day PHI would be allowed.

The proposed supplemental label specifies mixing 1 1/2 to 2 pt BRAVO 500/100 gal of dilute spray, and applying 300 gal (tart cherry) or 400 gal (sweet cherry) of dilute spray per acre.

The proposed supplemental labeling allows application by ground or aerial equipment, but contains a restriction against allowing livestock to graze in treated areas.

RCB's Comments/Conclusions re: Proposed Use on Cherries

The petitioner will need to submit a revised Section B/label in which a restriction is included which will limit the number of post-shuck-split applications allowed. The petitioner should be informed that the proposed use must be supported by the submitted residue data.

RCB does not consider split PHIs (i.e., 7 days for cherries harvested into water and 30 days for cherries not harvested into water) acceptable. The petitioner will need to propose only a single PHI in a revised Section B/label (note: as stated previously, RCB considers the rac to be unwashed cherries as they are picked from the tree).

The revised Section B/label should contain both a restriction against grazing treated orchards/groves as well as a restriction against cutting cover crops for feeds.

Nature of the Residue

No new plant or animal metabolism studies were submitted in the current petition. The metabolism of chlorothalonil in plants and animals has been reviewed in detail in the Residue Chemistry Chapter of the Chlorothalonil Registration Standard - dated 11/4/83.

With regard to the metabolism of chlorothalonil in plants, the following conclusions were reached in EPA's 11/4/83 Standard:

"The metabolism of chlorothalonil residues in plants is not adequately understood due to the lack of sufficient data on this topic. The following additional data are required:

1. Studies in which the unidentified water-soluble compounds, which constitute the major portion of the [^{14}C]chlorothalonil residues taken up from treated soil by plants, are characterized along with other possible metabolites of chlorothalonil.
2. Translocation studies involving the application of ring-labeled [^{14}C]chlorothalonil to foliar plant surfaces (one such study was submitted but involved immature plants).
3. Data on whether the impurities in technical chlorothalonil need to be included in the tolerance definition."

In RCB's review of PP#4F3025, the petitioner was advised of the need for a ring-labeled ^{14}C -chlorothalonil foliar-applied apple metabolism study (see M. Kovacs, Jr. memo of 5/30/84).

RCB reiterates the need for such a plant metabolism study in support of the proposed post-shuck-split chlorothalonil use on cherries. Thus, the nature of the residue in plants is not adequately understood.

The following was concluded in EPA's Chlorothalonil Registration Standard with regard to the nature of the residue in animals:

"Presently, tolerances for residues of chlorothalonil in feed items are expressed in terms of the parent (DAC 2787) and its 4-hydroxy metabolite (DAC 3701); however, the propriety of the currently established tolerance definition is currently in question due to the inadequacy of the available plant metabolism data (see Nature of Residue in Plants section of this standard). Further, the metabolism of chlorothalonil and DAC-3701 in food animals is not adequately understood. The available ruminant studies did not utilize labeled material (except in one of the rumen fluid studies) and did not identify or quantify residues in tissues (muscle, liver, kidney, and fat). The available rat and dog metabolism studies are useful for comparative purposes but cannot substitute for studies involving poultry and ruminants. The following additional data are required:

1. Studies which elucidate the metabolism, distribution, and accumulation of [^{14}C]chlorothalonil and of [^{14}C]DAC-3701 in poultry and ruminants, including eggs and milk, respectively. A non-ruminant (swine) metabolism study may be required if the ruminant metabolism study is found to differ significantly from that of the rat. Also, if the required plant metabolism data indicate that additional metabolites are residues of concern, additional animal metabolism studies utilizing these metabolites may be necessary.

2. Data are also required for the determination whether or not the impurities in technical chlorothalonil need to be included in the meat, milk, poultry and egg tolerances."

Although the nature of the residue in animals is not adequately understood, since there are no feed items involved in this petition, this deficiency has no bearing on the establishment of an amended tolerance for chlorothalonil on the rac cherries.

Analytical Methodology

The enforcement method for determination of residues of chlorothalonil and its 4-hydroxy metabolite has been published in the Pesticide Analytical Manual - Volume II.

The method used to generate the residue data for chlorothalonil, 4-hydroxy-chlorothalonil, HCB and PCBN presented in this petition is similar to the enforcement method, and has been previously discussed in RCB's review of PP#2F2602 - Chlorothalonil on Stone Fruits (see K. Arne memo of 5/3/82).

In brief, residues of chlorothalonil, 4-hydroxy-chlorothalonil, HCB and PCBN are extracted from cherries using acidified acetone and partitioned into ether. Residues of chlorothalonil, HCB and PCBN were separated by Florisil column chromatography. 4-Hydroxy-chlorothalonil residues were derivatized to corresponding methyl ether and cleaned up on a Florisil column. The residues were quantitated by gas-liquid chromatography using a ⁶³Ni-electron capture detector.

Control values for 4-hydroxy-chlorothalonil, HCB, and PCBN residues in untreated cherries were all below the reported method sensitivities of 0.01 ppm, 0.003 ppm, and 0.005 ppm, respectively. Control values for chlorothalonil reportedly ranged from <0.01 ppm (method sensitivity) to 0.21 ppm.

Fortification-recovery data generated on cherries (sweet and tart) are presented below:

Residue	Fortification (ppm)	Percent Recovery Range	Ave. of 10 Samples
chlorothalonil	0.03 - 10.00	67 - 133	101
4-hydroxy- chlorothalonil	0.03 - 0.50	88 - 127	103
HCB	0.007 - 0.05	65 - 75	71
PCBN	0.02 - 0.10	72 - 87	78

RCB can not conclude at this time that adequate analytical methodology is available to enforce the proposed tolerance on cherries until the nature of the residue in plants has been adequately resolved (see previous discussion in Nature of the Residue section of this review).

Residue Data

According to the Chlorothalonil Registration Standard, chlorothalonil residues are relatively stable in plant samples when stored at sub-freezing temperatures for 6-14 months. A storage stability study submitted in PP#5E1569 indicated that 85% and 71% of chlorothalonil residues (fortified at 0.1 pm) 78% and 83% of 4-hydroxy-chlorothalonil residues remained in the peel and pulp of passion fruit, respectively following 6 months of storage at -15°C. The 14 month study involved fortified mint hay (89% and 84% recoveries for fortifications of 1.0 mg and 5.0 mg, respectively). The above passion fruit study can be translated to cherries (i.e., residues stored frozen for up to 6 months will be considered stable).

Residue data on tart cherries were generated on samples grown in the states of New York (3 trials) and Michigan, (2 trials). Cherries were treated with chlorothalonil by ground application either 7 or 8 times (3 or 4 applications after shuck-split) at an application rate of 6 pt Bravo 500/A (maximum proposed use allows an unlimited number of applications at a rate of 8 pt BRAVO 500/A). The PHI was either 6 or 7 days. Residues of chlorothalonil, 4-hydroxy-chlorothalonil, HCB, and PCBN reportedly ranged from 0.15 - 1.66 ppm, <0.01 - 0.02 ppm, <0.003 - <0.003 ppm, and <0.005 - 0.016 ppm, respectively. However, since these data were generated on cherries which had been rinsed with water (i.e., not unwashed cherries as they are picked from the tree), RCB does not consider the above residue data adequate to support the establishment of an amended chlorothalonil tolerance on cherries (note: in PP#2F2602, the petitioner considered the rac to be unwashed cherries as they are picked from the tree).

The petitioner also submitted residue data from one field trial conducted in Michigan and generated on sweet cherries handpicked (dry harvested) 27 days following final chlorothalonil application. This sample had been treated 5 times at a rate of 8 pt BRAVO 500/A, although only once following shuck-split. Residues of chlorothalonil, 4-hydroxy-chlorothalonil, HCB, and PCBN were reported as 1.52/2.32 ppm, <0.01/0.01 ppm, <0.003/<0.003 ppm, and 0.018/0.011 ppm, respectively.

This one trial is not considered adequate to support the proposed use on cherries. The petitioner will need to submit additional residue data generated on cherries (sweet and tart) harvested dry and reflective of the proposed use (i.e., maximum number of post-shuck-split, maximum application rate, etc.).

The residue data must be geographically representative of the major cherry growing regions of the country. Thus, the petitioner will need to generate residue data on field-treated cherries grown in the states of CA, OR/WA, MI and NY/PA (note: if these treated samples are stored more than 6 months prior to analysis, additional storage stability data will be required).

RCB can reach no conclusion as to the adequacy of the proposed 3 ppm tolerance on cherries until deficiencies involving the proposed use, nature of the residue and lack of sufficient residue data have been resolved.

Pending RCB's final conclusion concerning the nature of the residue in plants, the petitioner may need to submit residue data on components of the terminal residue other than chlorothalonil, 4-hydroxy-chlorothalonil, HCB, and PCBN.

The petitioner has also submitted the results of a cherry processing study, which are presented below:

Commodity	Residue ^a (ppm)	- Range/(Average)
whole cherries	2.35 - 3.10	(2.74)
washed whole cherries ^b	0.49 - 0.55	(0.52)
washed pitted cherries	0.32 - 0.42	(0.38)
canned cherries^c	0.02 - 0.04	(0.03)
waste liquid from pitter	2.47 - 2.64	(2.55)
cherry pits	0.04 - 0.09	(0.06)

- a) Chlorothalonil residue levels only. 4-Hydroxy-chlorothalonil residue levels in all sample were reported as 0.01 ppm or <0.01 ppm.
- b) Cherries (35.75 lb) were placed in 30 gal container, soaked for 15 min. Then water was run through container for 2 hours (total water used = 200 gal).
- c) Results based on entire contents of the can.

Residue in Meat, Fat, Milk, Poultry and Eggs

Cherries are not considered an animal feed item. Thus, RCB does not expect any problem of secondary residues in meat, fat, milk, poultry or eggs.

Other Considerations

An International Residue Limit Status sheet is attached to this review. There are no Canadian or Mexican tolerances/limits established for chlorothalonil on cherries. Codex has established a 10 ppm limit (parent compound only) which is considerably higher than the U.S. proposed 3 ppm (parent plus 4-hydroxy metabolite) tolerance. This incompatibility will be reevaluated in the future when the additional requested residue data on dry-harvested cherries have been submitted.

cc:R.F., Circu, Reviewer, TOX, EAB, EEB, PP#5F3183 (RCB#371)
Robert Thompson, FDA
RDI:JHOnley:2/11/85:RDSchmitt:2/11/85
TS-769:RCB:CM#2:RM810:X7484:MPFirestone:wh:3/5/85

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL: Chlorthalonil

CCPR NO.: 81

PETITION NO.: 5F3183

REVIEWER: Michael P. Firestone

7. Dec 12/6/84

Codex Status

☐

No Codex Proposal Step
6 or above

Residue (if Step 9):

chlorthalonil

Proposed U.S. Tolerances

Residue: 2,4,5,6-tetrachloroisophthalonitrile
(chlorthalonil) and its metabolite
4-hydroxy-2,5,6-trichloroisophthalonitrile

Crop(s)

Limit (mg/kg)

cherries

10

Crop(s)

Tol. (ppm)

cherries (sweet and tart)

3.0

CANADIAN LIMIT

Residue:

MEXICAN TOLERANCIA

Residue:

Crop(s)

Limit (ppm)

none (on cherries)

Crop(s)

Tolerancia (ppm)

none (on cherries)

Notes: