Petition 1-11-77

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PP# 6G1871. Chlorothalonil in or on Oranges.
Evaluation of analytical methods and residue data.

M. J. Nelson, Chemist, CHM
RD (WH-567)

SRS (D. Stubbs)
and TOX

THRU: Chief, CHM

The Diamond Shamrock Corporation proposes the establishment of a temporary pesticide tolerance for residues of chlorothalonil (tetrachloroisophthalonitrile) in or on process oranges at 0.5 ppm for use of this chemical as a harvest aid in combination with abscission chemicals in the State of Florida.

Tolerances are established (40 CFR 180.275) for combined residues of chlorothalonil (formulated as BRAVO) and its 4-OH metabolite in or on a variety of r.a.c.'s at levels ranging from 0.1-15 ppm for a fungicidal use.

There are no currently established chlorothalonil tolerances reflecting a harvest aid use. We note the petitioner has not included the 4-OH metabolite in the proposed tolerance.

The proposed experimental program will entail the use of 250 gallons (4 lbs ai/gal) of SWEEP 4F formulation on approximately 750 acres of oranges in Florida. The SWEEP formulation is to be applied in combination with the abscission chemicals, RELEASE (5-chloro-3-methyl-4-nitro-1H-pyrazole; see PP# 5G1579) and/or ACTI-AID (Component A) (cycloheximide; see PP# 2F1252).

For oranges, there is a temporary tolerance of 0.1 ppm established for RELEASE (exp. date: 4/30/77) and a permanent tolerance of 0.1 ppm established (40 CFR 180.336) for cycloheximide.

In addition, residue studies will be run on fruit treated with chlorothalonil used both as a fungicide and as an abscission chemical to determine whether any potential residue problems might occur with double application. At present there are no established or proposed tolerances for the fungicidal use of chlorothalonil on oranges or other citrus.

There are several other petitions (e.g., PP's # 6F1749, 6E1761, 6F1799, 6G1813/6H5136, 6E1841) for chlorothalonil co-pending.

Conclusions

1. The nature of the residue is adequately understood. Chlorothalonil and its 4-OH metabolite are the residues of concern.

2. Adequate methodology is available for enforcement of the proposed tolerance.

3a. Residues in oranges are not considered likely to exceed the proposed tolerance level.

3b. Residues in processing by-products will be considerably less (except in the concentrated oil) than in the r.a.c.

3c. The proposed tolerance should be established in terms of combined residues of chlorothalonil and its 4-OH metabolite.

4. We categorize the proposed use in 40 CFR 180.6(a)(3) with respect to secondary residues in meat, milk, poultry, and eggs.

5. A label restriction to preclude grazing of cover crops in treated groves by livestock is needed.

6. We do not consider the use of RELEASE in a tank-mix combination with chlorothalonil to be acceptable for this experimental program since there are no permanent tolerances for residues of RELEASE on the subject crop.

Recommendations

TOX and EEE considerations still permitting, CHM could recommend favorably for a 0.5 ppm temporary tolerance on oranges provided: (1) the tolerance is proposed in terms of combined residues of chlorothalonil and its 4-OH metabolite (revised Sec. F); (2) a label restriction is added to preclude the grazing of cover crops in treated groves by livestock (revised Sect. B); and (3) the proposed tank mix uses with RELEASE are deleted from the proposed labeling (revised Sec. B).

The tolerance, if and when established, should be for the r.a.c. "oranges" rather than "process oranges" as the petitioner has proposed.

We note that TOX (D. Ritter, 11/18/76 review) and EEE (R. E. Ney, Jr. and N. Dodd, 10/26/76 review) have raised no objections to the proposed tolerance.

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For consideration of a future permanent tolerance request, we will require the following:

(1) Residue data from several varieties of oranges;
(2) Residue data reflecting the proposed use pattern;
(3) Residue data reflecting treatment to oranges destined for the fresh fruit market. (A label restriction prohibiting use on fresh market oranges will not be considered practical for a permanent tolerance);
(4) Residue data reflecting aerial application (or imposition of a label restriction limiting use to ground application equipment only);
(5) Residue data for the 4-OH metabolite and for chlorothalonil per se (measured as separate entities) on oranges (in addition to the limited amount of metabolite residue data submitted with the temporary tolerance request);
(6) Submission of raw data sheets;
(7) Submission of a representative number of gas chromatograms (for different substrates, parent and 4-OH metabolite, treated and control);
(8) Residue data for each of the active ingredients in the tank mix(es) used.

Detailed Considerations

Manufacture and Formulation

A description of the manufacturing process was submitted in conjunction with PP# 4E1502 and was discussed in our (R. Schmitt) 11/27/74 review thereof.

Technical chlorothalonil is 95.6-98.5% pure. Impurities consist of [redacted] none of these are anticipated to present a residue problem at the levels present in the formulation.

The possibility of HCB in technical chlorothalonil was also discussed in the aforecited R. Schmitt review. It was concluded at that time, and we concur, that no HCB residue problem exists from the use of chlorothalonil.

The possibility of dioxins being present in the technical material was addressed in the W. Cox review (1/6/71) of PP #1F1024. Chlorothalonil, as its hydroxy metabolite, is theoretically a precursor of a dioxin moiety. We concur with our previous conclusion that due to the route of synthesis of the parent compound [redacted] dioxins would not constitute a problem.

A new experimental chlorothalonil formulation, SWEEP, has been developed especially for harvest aid usage; it contains a lower average particle size (1.5 μm) than the present commercial chlorothalonil formulation (BRAVO, 3.3 μm).

SWEEP is formulated so as to contain 4 lbs. ai/gal. The composition of the formulation is as follows:

active ingredient

chlorothalonil	39.00%

inert ingredients

[redacted]

INERT INGREDIENT INFORMATION IS NOT INCLUDED

PRODUCT IMPURITY INFO NOT INCLUDED

All the adjuvants in the formulation are cleared under Sec. 180.1001.

Proposed Use

For fruit loosening, apply 0.5-2.0 qts. (i.e., 0.5-2.0 lbs ai) of SWEEP/500 gals. of water (i.e., ca 125-500 ppm) plus 0.25-2.5 qts (i.e., 1.7-16.7 oz. ai) of RELEASE/500 gals. of water (i.e., ca 25-250 ppm) and/or 0.12-0.75 qts. (i.e., 1.9-12.0 oz ai) of ACTI-AID (Component A)/500 gals. of water (i.e., ca 30-185 ppm) to oranges grown in Florida for processing.

~~Rate is dependent upon variety (early and midseason vs. Valencias), (Component A)/500 gals. of water (i.e., ca 30-185 ppm) to oranges grown in Florida for processing.~~

Rate is dependent upon variety (early and midseason vs. Valencias), temperature, and intended method of harvesting (hand vs. mechanical).

Make application 4-7 days prior to anticipated harvest. Apply 500-1000 gals. of spray mix/A, broadcast, to obtain uniform coverage of leaves and fruit. Gallonage per tree varies from 5-10 gallons depending on tree shape, size, foliage, and spacing. Use 2 qts. of Ortho X-77 per 500 gallons of spray mix as a sticker (cleared under Sec. 180.1001).

Limitations: For use in Florida only. Do not use on fresh market oranges. Do not apply more than once per season. Do not apply SWEEP in combination with ACTI-AID (Component A) on Valencias. Do not apply when rain is predicted within 24 hours, immediately following a heavy dew, within 2 weeks following a freeze, or in wind conditions which favor drift.

There is no label restriction to preclude grazing of cover crops by livestock in treated groves; such a restriction is needed.

The petitioner should be advised the label restriction limiting use to process oranges only will not be considered practical for a permanent tolerance. Residue data from treated oranges destined for the fresh fruit market will be needed.

We do not consider the use of RELEASE in a tank-mix combination with chlorothalonil to be acceptable for this experimental program since there are only temporary tolerances for residues of RELEASE on the subject crop. At such time as the RELEASE tolerances become permanent, we would have no objectsions to a tank-mix of chlorothalonil with RELEASE in an experimental permit but at present we do not consider it acceptable. (Cf PP #6G1690).

Nature of the Residue

The metabolism of chlorothalonil has been reviewed several times in conjunction with previous petitions (e.g., W. S. Cox, 11/17/76, PP #6F1799).

No new metabolism studies were submitted with this petition. Based on the available studies for several species of plants (e.g., corn, tomatoes, potatoes) and animals (dogs, rats, cows), we conclude that the fate of chlorothalonil is adequately understood, and can be translated to oranges.

The parent compound and the 4-hydroxy metabolite constitute the residue of concern in plants and animals. The 4-hydroxy metabolite constitutes a minor portion of the residue; in plants it comprises, at most, 10% of the residue; in animals, although a minor portion of the residue, it is the principal residue of concern because of its transfer (to meat and milk) potential.

The residue in plants is mainly surface in nature; foliar deposits of chlorothalonil do not translocate and there is no uptake from roots to aerial plant parts.

Analytical Methods

The method of enforcement for determination of residues of chlorothalonil and its 4-OH metabolite is outlined in PAM II; in essence it entails the simultaneous extraction of the parent and metabolite from the crop using acidified acetone, separation of the two on a Florisil column, conversion of the metabolite to its methyl ester, and determination of the derivative and parent compound via MC- or EC-GLC.

This procedure has been validated by AMS on peanuts and potatoes in conjunction with PP# 1F1024; adequate recoveries were obtained following fortification with parent and metabolite at levels ranging between 0.3-5.0 ppm.

In this subject petition, three variously modified and/or abbreviated versions of the enforcement methodology were utilized for obtaining residue data, as follows:

(1) chlorothalonil residues were extracted from the crop sample (specifically, field-treated whole oranges in this case) with methylene chloride, the residue concentrated, and quantitated by EC-GLC.

Residues (if any) of the 4-OH metabolite would not be measured by this procedure. No clean-up (column or partitioning) was employed.

Recovery data from oranges fortified with chlorothalonil (0.14-0.19 ppm) and measured by this analytical procedure were submitted to validate the methodology; reported recoveries were 83-119%. Method sensitivity, 0.01 ppm.

(2) Chlorothalonil and 4-OH metabolite residues were extracted simultaneously from the crop sample (certain of the processing fractions: juice, peel liquor, emulsion water, molasses, oil) with acidified solvent (acetone or isopropyl ether), and selectively liquid-liquid partitioned to separate the acidic polar metabolite from the non-polar parent compound. The chlorothalonil-containing fraction was then subjected to alumina column clean-up and was quantitated by EG-GLC; the 4-OH metabolite-containing fraction was converted to its n-propyl ether derivative, subjected to alumina or Florisil column clean-up (when molasses or citrus oil was the crop substrate), and quantitated by EG-GLC.

Recovery data from processing fractions (as listed above) fortified with chlorothalonil (0.12-2.0 ppm) and the 4-OH metabolite (0.12-2.0 ppm) indicated adequate (63-137%) recoveries by this procedure. Method sensitivity, 0.01-0.02 ppm.

(3) chlorothalonil and 4-OH metabolite residues were extracted separately from the crop sample (whole fruit subjected to processing and certain fractions thereof: chopped peels, peel frits, finisher pulp, dry pulp and peel). Chlorothalonil residues were extracted with methylene chloride, subjected to alumina column clean-up, liquid-liquid partitioned for further clean-up (for the oily substrates chopped peel, dry pulp and peel), and measured by EC-GLC. The 4-OH metabolite residues were extracted and carried stepwise through the procedure described in (2) above, with only that portion containing the metabolite being analyzed. No column clean-ups were required for these samples.

Recovery data for these substrates (as listed above) fortified with chlorothalonil and the 4-OH metabolite (ca 0.12 ppm of each) indicated adequate (77-123%) recoveries by these procedures. Method sensitivity, 0.01-0.02 ppm.

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Based on the submitted validation data, we conclude that each of the above procedures was adequate for obtaining the residue data. For enforcement purposes and in generating the additional residue data for the permanent tolerance, however, we request that methodology which measures residues of both chlorothalonil and the 4-OH metabolite be utilized in all cases (albeit this metabolite comprises only a small portion of the overall residue) since such methodology is available and since the Regulation is established in terms of combined residues of these two compounds.

We note that no gas chromatograms were submitted with this petition; for a permanent tolerance petition, a representative number of these (for different substrates) for the parent and metabolite, treated and control, will be required along with the raw data.

We conclude that adequate methodology is available to enforce the proposed tolerance. [Enforcement methodology is also available for RELEASE and ACTI-AID (Component A); see PP's # 5G1579 and 2F1252, respectively.]

Residue Data

Only a minimum of residue data were submitted: 3 field tests with Valencia variety oranges grown in Florida for processing and a processing study.

Two of the three field tests involved tank mix combinations of SWEEP with ACTI-AID (Component A). [Note: the proposed use directions recommend against ths combination on Valencias.] Chlorothalonil was applied as a 1000-1500 ppm spray (4-6X the maximum rate for Valencias; 2-3X the maximum recommended rate for other varieties) via ground application equipment. Fruit was harvested 0, 5, and 7 days later.

At 0-day PHI, residues of chlorothalonil ranged from 0.15-0.86 ppm at the 4X rate, and at 5-7 day PHI's, 0.04-0.63 ppm. Corresponding residues from the 6X rate were somewhat higher. Residues of chlorothalonil in control samples were all ND (<0.01 ppm). The 4OH-metabolite was not analyzed for.

The third field test involved a tank-mix combination of SWEEP plus ACTI-AID (Component A) plus RELEASE, with the concentration of chlorothalonil being 500 ppm (2X the maximum recommended rate for Valencias; 1X the maximum recommended rate for other varieties). Spraying was via ground application equipment and harvest was 0 and 6 days later. Residues of chlorothalonil at 0-day ranged from 0.05-0.57 ppm and, at a 6-day PHI, 0.03-0.16 ppm. Checks were all ND (<0.01 ppm). The 4OH-metabolite was not analyzed for.

No residue data were submitted reflecting aerial application. We are not raising a question re this for purposes of the temporary tolerance since data are available reflecting application via ground equipment at exaggerated rates. Either residue data reflecting aerial application or a prohibitive label restriction will be needed for a permanent tolerance.

Neither were residue data submitted for RELEASE or ACTI-AID (Component A). As stated in the Proposed Use section, we request the proposed tank mixes with RELEASE be deleted from the labeling. We are not raising a question re the absence of residue data for ACTI-AID for purposes of the temporary tolerance since its proposed use here is compatible with the rates, PHI's, etc., of the use patterns upon which the ACTI-AID (cycloheximide) tolerance for oranges was established. For a permanent tolerance, however, residue data will be needed for each active ingredient of the tank mix(es).

By-Products. In the fractionation study, oranges which had been treated at highly exaggerated rates with multiple applications of chlorothalonil (as Bravo 6F) to achieve high residues were used to facilitate delineation of the distribution of chlorothalonil (and metabolite) residues amongst the various by-products.

The initial processing step, washing, was shown to remove ca 95% of the initial residues (chlorothalonil is a non-systemic, surface-deposit residue). Residues of chlorothalonil in the further processed by-product fractions (dried citrus pulp, molasses, juice,) were less-than-to-approximately-the-same as in the washed fruit from which they were derived; ca a 3X concentration of residues (compared to the rac, un-washed oranges) was found in the oil, but as this fraction is diluted many-fold prior to use (flavoring agent), we have traditionally not considered a food additive tolerance necessary. Residues of the 4-OH metabolite comprised $\leq$ ca 10% of the total residue.

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Based on data reflecting exaggerated use conditions, we conclude that under the proposed conditions of use combined residues of chlorothalonil and its 4-OH metabolite in or on the r.a.c. oranges are not likely to exceed the proposed temporary tolerance level (0.5 ppm).

Total residues in the processing fractions will be considerably less (except in concentrated citrus oil) than in the r.a.c. per se (since $\sim$ 95% of the deposited residue is removed from the r.a.c. by washing). The 4-OH metabolite comprises a minor ($\leq$ ca 10%) portion of the total residue.

For the sake of consistency with the established Regulation, we request that the petitioner proposes the tolerance in terms of combined residues of chlorothalonil and its 4-OH metabolite.

For purposes of a future permanent tolerance request we require the following:

(1) Residue data from several varieties of oranges;
(2) Residue data reflecting the proposed use pattern;
(3) Residue data reflecting treatment to oranges destined for the fresh fruit market;
(4) Residue data reflecting aerial application (or imposition of a label restriction limiting use to ground application equipment only);
(5) Residue data for the 4-OH metabolite as well as chlorothalonil per se on oranges;
(6) Submission of raw data sheets;
(7) Residue data for each of the active ingredients in the tank mix(es) used.

Residues in Meat, Milk, Poultry, and Eggs

According to The Harris Guide, neither oranges nor their by-products are items of poultry feed. Therefore we classify the proposed use within 40 CFR 180.6 (a)(3) with respect to secondary residues in poultry tissues and eggs.

Cull citrus, cannery wastes, and various of the processing fractions (e.g., dried pulp, molasses) are livestock feed items, and may comprise up to 30% of the animal diet.

As discussed in the Residue Data section, residues in washed oranges and their feed by-products were shown to be $\leq$ 5% of the initial residue in unwashed fruit; based on the proposed 0.5 ppm tolerance level, this would correspond to $\leq$ 0.025 ppm. At a maximum of 30% of the daily diet, this reduces to an ingestion level of $<$ 0.0075 ppm, approximately $\leq$ 10% of which might be the 4-OH metabolite (i.e., $<$ 0.001 ppm). It is principally the 4-OH metabolite which is of concern in animals because of its demonstrated transfer potential to meat and milk (see W. S. Cox reviews of 1/6/71, PP # 1F1024, and 5/23/72, PP # 2F1230).

Since 4OH-metabolite residues would be fed at > 10X less than the limit of detection (0.01 ppm) of the metabolite, and since this metabolite has been shown not to bioaccumulate (i.e., residues reach a plateau during feeding and decrease following withdrawal; aforecited Cox reviews), we conclude that the proposed use would constitute a 40 CFR 180.6(a)(3) situation with respect to anticipated residues in meat and milk.

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