UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: NOV 17 1976

SUBJECT: PP# 6F1799 as amended. Chlorothalonil on soybeans. Evaluation of analytical methods and residue data.

FROM: William S. Cox, Chemist, Chemistry Branch, RD (WH-567)

TO: PM No. 21 (Dr. E. Wilson) and Toxicology Branch

THRU: Chief, Chemistry Branch EHG for J. G. Cummings

Diamond Shamrock Corporation is proposing that a tolerance of 0.2 ppm be established for residues of the fungicide, chlorothalonil (tetrachloroisophthalonitrile) and its metabolite, 4-hydroxy-2,5,6-trichloroisopthalonitrile) in or on soybeans.

Tolerances for chlorothalonil have been established (CFR 40, Section 180.275) on a number of raw agricultural commodities at levels ranging from 0.1 to 15 ppm. Co-pending PPs #6E1749 and 6E1841 (which are in reject status) are proposing tolerances for cherries, peaches and certain leafy vegetables.

Conclusions

1. By translation of tracer studies on other plants, we consider the fate of chlorothalonil on soybeans to be adequately understood.

2. The available analytical methods are adequate for enforcement of the proposed tolerance.

3. We are unable to make any conclusions as to the adequacy of the proposed tolerance. This situation derives from the fact that the analytical procedure used for the residue data involved a dry grinding of the soybeans prior to extraction which could have resulted in losses of chlorothalonil via volatility due to the heat generated during the grinding.

4. There are no data reflecting the fate of chlorothalonil during the processing of treated soybeans into soybean oil, meal and soapstock.

5. Until the deficiencies implicit in Conclusions 3 and 4 have been resolved, we can make no conclusions with respect to Section 180.6(a). There are restrictions which preclude the feed uses of soybean forage and soybean vine hay.

Recommendation

Because of Conclusions 3, 4, and 5, we recommend against the proposed tolerance. For further consideration of the proposed tolerance, we will need the following:

(I) Residue data generated by a procedure which does not involve the dry grinding of the beans prior to extraction. Alternatively, data demonstrating that the dry grinding of soybeans bearing surface residues does not result in significant losses of chlorthalonil.

(II) Data reflecting the processing the field-treated soybeans into soybean meal, oil and soapstock; alternatively, data which clearly demonstrate that residues of chlorothalonil are not present (<0.01 ppm) at the time the beans enter the processing step which involves the extraction of the oil from the crushed beans.

(III) Should the data from studies conducted to satisfy I and II (above) indicate that significant residues of chlorothalonil occur on the beans or in any of its feed byproducts, tolerance proposals for residues in the meat, fat, and meat byproducts of livestock (and poultry) may be appropriate. If so, adequately validated methodology for the enforcement of such tolerances would also be required.

Note: We have previously deferred to EEE (in connection with PP #6E1841) as to appropriate crop rotation restrictions for the uses of chlorothalonil.

Detailed Considerations

Formulation

Chlorothalonil is formulated as Bravo 6F containing 6 lbs. of chlorothalonil/gal. All the inerts are cleared.

IMPURITY INFO IS NOT INCLUDED

Technical chlorothalonil is 95.6-98.5% pure. Impurities consist of [redacted] A description of the manufacturing process was submitted in connection with PP# 4E1502 and discussed in the Dr. R. Schmitt memo of 11/27/74.

The possibility of HCB in the technical product and as a residue was discussed in the Dr. R. Schmitt, 10/27/74 review of PP# 4E1502. It was concluded at that time, and we now concur, that no problem of HCB residues exists from the use of chlorothalonil.

Proposed Use

Soybeans: Anthracnose, Diaporthe pod and stem blight, frogeye leaf spot (Cercospora sojina), purple seed stain, and Septoria brown spot--Use BRAVO 6F at 1 1/2 to 2 1/2 pints per acre if two applications are scheduled, or 1 to 2 pints per acre if three applications are scheduled. Apply in sufficient water to obtain complete coverage. A minimum of five gallons of water per acre should be used for aerial application. Applications should be made at 14 day intervals. Three applications should be scheduled in areas having a history of moderate to severe disease, as disease control is generally improved with the three application program. The time of first application should be determined as follows:

Determinant (Southern) Soybean Varieties

Two application program: Make first application at early pod set (majority of pods are 1/8 to 3/8 inch in length), and the second application 14 days later. Use 1 1/2 to 2 1/2 pints per acre (1.13 to 1.88 lbs act/A).

Three application program: BRAVO 6F should be applied at 14 day intervals starting at early to mid flowering. Use 1 to 2 pints per acre (0.75 to 1.5 lbs act/A).

Indeterminant (Northern) Soybean Varieties

Two application program: Make first application two to three weeks after first flowering when the largest pods are from 1 to 1 1/2 inch in length, and the second application 14 days later. Use 1 1/2 to 2 1/2 pints per acre.

Three application program: BRAVO 6F should be applied at 14 day intervals starting one week after first flowering. Use 1 to 2 pints per acre.

The following restrictions apply:

DO NOT apply within 6 weeks of harvest.*
DO NOT allow livestock to graze treated areas.
DO NOT feed soybean hay or threshings from treated fields to livestock.

*The petitioner originally proposed a PHI of 30 days. This was changed to 6 weeks in the amendment letter of 9/8/76.

Nature of the Residue

The metabolism of chlorothalonil has been discussed most recently in connection with PP# 4E1502 (Dr. R. Schmitt review dated 7/22/74). No additional metabolism data have been submitted with this petition.

The parent compound and small amounts of the 4-hydroxy metabolite constitute the residue of concern in plants. This conclusion is based on ^{14}C studies on corn and tomatoes and cold studies on potatoes in which other possible metabolites were not detected. The 4-hydroxy metabolite is the principal component of the residue in soils (70%) but on plants the 4-hydroxy metabolite is at most 10% of the residue. Foliar deposits of chlorothalonil do not translocate and there is no uptake from roots to aerial plant parts. By translation of the available studies for several species of plants and animals, we conclude that the fate of chlorothalonil on soybeans is adequately understood. The parent compound and the 4-hydroxy metabolite are the only components of concern in plant and animal residues.

In the specific case of soybeans, the residue data indicate that there will be only low-level surface contaminative residues on the harvested beans, at levels up to about 0.1 ppm of chlorothalonil per se. *Apparent* residues of 0.01 or 0.02 ppm of the 4-hydroxy metabolite were reported for both *treated* and *untreated* beans. We consider the proposed use to be essentially a "no-residue" situation for the *4-hydroxy metabolite*.

Overall, we conclude that the fate of chlorothalonil on soybeans has been adequately described.

Analytical Methods

A. Determination of chlorothalonil residues--The method of enforcement used in the determination of residues of chlorothalonil *per se* is outlined in PAM II; the basic procedure involves an acidified-acetone extraction, separation of the parent compound from the 4-hydroxy metabolite on a Florosil column, by elution using acetone-dichloromethane (5:95) for the parent compound and a 50:50 mixture of the same solvents for the more polar metabolite. After concentration of the residues, determinations are made by ECGC.

This procedure has been validated by AMS, CHM on peanuts at 0.3 and 0.6 ppm chlorothalonil and on broccoli at 2.5 and 5 ppm chlorothalonil. (Note: The validations by AMS, CHM were conducted using a microcoulometric detection system rather than the electron-capture detector normally used for enforcement.)

In the subject petition, the data were for chlorothalonil residues *per se* were generated by two different procedures; one used in the 1974 studies and one used in the 1975 studies. In both instances, the procedures used are modifications of the PAM II enforcement procedure, with the major modification involving a partitioning step prior to column cleanup which separates the acidic metabolite from the non-polar parent compound. The residues of chlorothalonil were subjected to column cleanup in both sets of studies; however, in the 1974 studies, the column was packed with activated alumina and the residues were eluted with 10:90 acetone/methylene chloride, whereasin the 1975 studies, chlorothalonil residues were eluted from a Florosil column using a mixture of methylene chloride/hexane/acetonitrile in the ratio of 50/49.65/0.35.

Another modification in the soybean procedure involved the addition of water to the acidified-acetone extraction solution plus an increase in the amount of sulfuric acid present in the extracting medium; that is, over the amount called for in the PAM II method.

None of the modifications described ~~is~~ are so drastic as to question the validity of the residue studies; the chemistry involved in the various changes are quite straightforward. However, there is one step in the procedure for soybeans which raises a question as to the validity of the recovery studies and, as a corollary, the residue studies. The procedure calls for the dry grinding of the soybeans prior to the introduction of any liquids. Such dry grinding would be expected to generate considerable heat and the various residue studies indicate that the rather rapid losses of chlorothalonil can be attributed, at least in significant part, to its volatility; thus, the possibility of losses during the dry grinding must be considered. By telecon of 9/9/76 (W.S. Cox/Don Stallard, Diamond Shamrock), we were informed that the soybeans used in the recovery studies were fortified after the samples were ground. Thus, in the absence of the data to the contrary, we must assume that the dry grinding prior to extraction could result in the losses of residues of chlorothalonil.

In spite of the above remarks, we can conclude that the available methods are adequate for the enforcement of the proposed tolerance. This is based on the fact that we consider the residues, if any, on soybeans to be trace contaminative surface residues and by a minor modification of the existing PAM II method, which has been successfully tried out on peanuts, such residues on soybeans can be determined. However, as indicated below under Residue Data, we cannot recommend for the proposed tolerance until the question of the validity of the fortification and residue studies has been resolved.

For further consideration of the proposed tolerance, the petitioner must resolve the question of possible losses of chlorothalonil during grinding or submit additional residue data reflecting an omission of the dry guiding procedure.

Residue Data

As indicated directly above under Analytical Methods, the validity of the available residue data are questionable because of the dry grinding of the soybeans prior to extraction. However, we will discuss the residue studies on the basis that the residues reported are representative of those to be expected from the proposed use with the understanding that they will be re-evaluated at the time additional recovery data are submitted.

The 1974 studies involved application rates of 0.6 to 1.5X the recommended maximums for either 2 or 3 applications per season. Fourteen pertinent studies mostly from the southeastern and deep south states were prsented. Four of these reflected PHIs of 42 days (the proposed PHI) or less and two others reflected PHIs reasonably close (i.e., 48 days). As a compensating factor, the four exaggerated rate studies (at 1.5X the proposed maximum for three applications) had PHIs ranging from 38 to 48 days. Only one of these four studies had finite residues reported--these were 0.08 ppm (at 48 days PHI) for chlorothalonil and non-detectable for the hydroxy metabolite. Only one other study (out of the 14 pertinent studies) had a reported finite residue for chlorothalonil--this value was also 0.08 ppm of chlorothalonil <u>per se</u> from samples taken at 28 days after the last of three 1X applications.

The 1975 studies (a total of six, but involving 2 application rates at each study site) reflect application rates of 0.75 to 2.0 the maximum recommended for 3 or 2 applications, respectively. Only one study reflected the proposed PHI of 42 days; all the others ranged from 59 to 76 days. However, the one study with the 42-PHI included the exaggerated (2X) rate and the rainfall in the PHI period was rather moderate. Finite residues of 0.05 ppm of chlorthalonil <u>per se</u> were reported from the 1X application rate at 42 days PHI, whereas the 2X study at the same PHI had reported residues of 0.03 ppm. In three of the other five studies, low level (0.01 to 0.03 ppm) residues of chlorothalonil were reported for samples taken 59 to 72 days post treatment. The results for residues of chlorothalonil per se do not seem to be either dose-dependent or time-related (with respect to the length of the PHI). All results for the 4-hydroxy metabolite were reported as "non-detectable" (<0.01 ppm).

Overall, the data indicate that residues, when present, on treated soybeans occur from the transfer of surfaces residues on the pods to the beans during the threshing process.* The data, if accepted at face value, support a conclusion that the proposed tolerance of 0.2 ppm is adequate. However, as indicated above, until the question of possible losses during the preliminary grinding step has been resolved, we can make no final conclusions as to the adequacy of the proposed tolerance.

*Note: Chlorothalonil is not systemic; furthermore, soybean pods are tightly closed throughout the growing season and at harvest, even after desiccation.

<u>Residues in the processed byproducts of soybeans</u>

In the absence of any data reflecting the processing of soybeans, and particularly in view of the question of the validity of the residue data for soybeans, we can make no conclusions as to the need for food additive tolerances in connection with the proposed use. Processing data for meal, oil and soapstock will be required unless additional data show no detectable chlorothalonil residues (<0.01 ppm) on soybeans intended for commercial processing.

<u>Residues in meat, milk, poultry and eggs</u>

Although feeding studies reviewed in connection with PP# 2F1230 (see review dated May 23, 1972) would indicate that the proposed use fall into category 3 of 180.6(a), we are not making any conclusions at this time because of the deficiencies in the residue data and the absence of residue data with respect to the processing fraction of treated soybeans.

Other considerations

There is an established tolerance for tomatoes at 5 ppm (PP #0F01024). At the time the tolerance was established, tomato pomace (including processing waste) was not considered a feed item. However, it is now so considered. The petitioner has presented, as an addendum (letter of 8/9/76), the results of a processing study which demonstrates that virtually all the residues (over 99%) of chlorothalonil are removed during the normal processing (alkaline detergent wash) of tomatoes. Thus, we need have no further concern as to the concentration of residues in processed tomato byproducts or the impact of treated tomatoes on secondary residues of chlorothalonil in meat or milk.

WSCox

W. S. Cox