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PP# 8E2065. Chlorothalonil on dry beans. Evaluation of analytical method and residue data.

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Minor Uses (C. Fletcher), Emergency Response (TS-767) and Toxicology Branch (TS-769)

THRU. Chief, Residue Chemistry Branch

Interregional Research Project No. 4, State Agricultural Experiment Station, Rutgers University, G. M. Markle, Assistant Coordinator, on behalf of the IR-4 Technical Committee and the Agricultural Experiment Stations of AR., FL., GA., KY., MI., NY., TN., and the USDA requests the establishment of a 0.3 ppm tolerance for combined residues of the fungicide chlorothalonil (tetrachloroisophthalonitrile) and its metabolite (4-hydroxy-2,5,6-trichloroisophthalonitrile) in or on dry beans.

Permanent tolerances for chlorothalonil have previously established on a variety of crops. These tolerances range from 0.1 to 15 ppm (40 CFR 180.275).

Conclusions

1. The nature of the residue is adequately understood from the data on other crops.

2. Analytical methods are available for enforcement of the proposed tolerance on dry beans.

3. The residue data submitted by the petitioner are adequate to demonstrate that residues resulting from the proposed use will not exceed the proposed tolerance.

4.(a) The proposed use restricts grazing of treated fields as well as the feeding of treated plant parts to livestock, thus we expect no residues to occur in meat and milk from this source.

(b) According to the Harris Guide, dry beans are a livestock and poultry feed item. Since residues of chlorothalonil have been detected on dry beans up to 41 days after application, there appears to be a direct possibility of transfer of residues to meat, milk, poultry, and eggs. The amount of residues of chlorothalonil from this source, added to the possible residues from the feeding of other crops with established tolerances for chlorothalonil, indicates the need for the establishment of a tolerance for residues of chlorothalonil and its 4-hydroxy metabolite in meat, milk, poultry, and eggs.

IMPURITY INFO IS NOT INCLUDED

INERT INGREDIENT INFORMATION IS NOT INCLUDED
MANUFACTURING PROCESS INFORMATION IS NOT INCLUDED

Recommendation

We recommend against the establishment of the proposed tolerance due to the deficiency outlined in Conclusion 4(b).

A recent communication from Dr. J. Blanchard (to J. G. Cummings. 10/27/78) points out that an NCI report has just issued which finds chlorothalonil to be carcinogenic in the rat. Before the petitioner (IR-4) or the producer (Diamond Shamrock) are asked to provide a poultry feeding study and propose appropriate meat, milk, poultry and egg tolerances, any problems regarding the carcinogenicity study should be resolved. By copy of this memo TOX is requested to determine whether chlorothalonil should be referred to SPRD for RPAR consideration.

Detailed Considerations

Formulation

Chlorothalonil is produced [redacted] Technical chlorothalonil is 95.6-98.6% pure, impurities in the product include [redacted]

Analysis of 308 batches of technical chlorothalonil showed no detectable HCB in 283 (92%) of the batches and an average of [redacted] ppm in the remaining 8% of the batches.

The formulation to be used is Diamond Shamrock Corporation's Bravo® 6F (EPA Reg. No. 677-313) containing 6.0 lb of chlorothalonil/gal. This formulation contains 54% active ingredient with the following inerts: [redacted] All inerts are cleared under Section 180.1001 (PP# 6F1700, W.S. Cox, 11/17/76).

The possibility of dioxins being present in the technical material was addressed in our review of PP# 1F1024 (W.S. Cox, 1/6/71). Chlorothalonil, as its hydroxy metabolite, is theoretically a precursor of a dioxin moiety. However, we feel that due to the route of synthesis of the parent compound (dicarboxylic acid to diamide and to dicyano, followed by chlorination), dioxins would not constitute a problem.

Proposed Use

For control of rust on dry beans, apply 2 to 3 pints per acre in sufficient water to obtain adequate coverage. Begin applications at early bloom stage or when disease first threatens and repeat at 7 to 10 day intervals. Under severe conditions, use the higher rate and shorten interval.

Do not apply within 14 days of harvest. Do not graze treated areas or feed treated plant parts to livestock.

Total dosage/acre and total number of applications/season: 6/75 lbs a.i./acre for three applications at 2.25 lbs a.i./acre or 6 lbs a.i./acre for four applications at 1.5 lbs a.i./acre.

Nature of the Residue

No new metabolism studies were submitted with this petition. The metabolism of chlorothalonil in plants and animals has been reviewed in detail in earlier petitions (PP#'s 7F0599, 1F1024, 2F1230, 4E1502, 6F1799, and 6G1871). Based on the available studies for several species of plants (corn, tomatoes, potatoes) and animals (dogs, rats, cows), we conclude that the nature of the residue is adequately understood and can be translated to dry beans.

The parent compound and the 4-hydroxy metabolite constitute the residue of concern in plants and animals. The 4-hydroxy metabolite is a minor component of the residue; however, it is of concern because of its transfer potential to meat and milk. The transfer rate for the metabolite is over 100X that for the parent compound.

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. Residues on dry beans are expected to result from foliage contamination of the beans during harvesting.

Two minor metabolites were isolated from feces of dogs fed chlorothalonil and identified as trichlorodicyanoaniline (probably present in conjugated form) and 2,4,5-trichloroisophthalonitrile (PP# 7F0599, B. Malone, 8/28/67).

Analytical Method

The method of enforcement for determination of residues of chlorothalonil and its 4-hydroxy 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, recoveries of chlorothalonil from dry beans fortified at 0.05 to 0.5 ppm ranged from 87% to 100%, recoveries of the 4-hydroxy metabolite fortified at 0.04 to 0.5 ppm ranged from 60% to 105%.

Since the analytical method used to produce residue data involves a dry-grinding of the beans prior to extraction, there is concern that some of the chlorothalonil could be lost through volatilization due to the heat generated during the grinding. This question was resolved in our review of PP# 6F1799 (amendment of 11/19/76; R. B. Perfetti) concerning chlorothalonil on soybeans. Two experiments demonstrated that the dry-grinding of soybeans bearing surface residues of chlorothalonil prior to extraction does not result in significant losses of the pesticide. We conclude that the dry-grinding of dry beans also will not result in significant losses of chlorothalonil through volatilization.

Residue Data

The residue data presented represents 3 prominent varieties of field beans (Great Northern, Seafarer., and Pinto) from various geographical locations. The normal application of Bravo 6F for control of fungal diseases in field beans resulted in PHI's of 32-69 days. Samples analyzed after application of chlorothalonil at a rate of either 1.5 or 2.25 lbs. a.i./acre per each application with a PHI in the above normal range of between 32-69 days showed combined residues (sum of parent and its 4-hydroxy metabolite) to be less than 0.1 ppm.

The proposed use calls for a maximum of three applications at 2.25 lbs a.i./acre coupled with a PHI of 14 days. Representative samples of dry beans treated at the above rate and harvested 14 days after the last application showed a maximum combined residue value of 0.2 ppm.

Some samples showed a particularly high value for the 4-hydroxy metabolite compared to the corresponding value for the parent, especially for those samples harvested at 0 days after the last application. These samples were treated with a different formulation, Bravo W-75. Even with this different formulation, we can see that there is rapid degradation of both the parent and metabolite; for samples with 7 day PHI's, the combined residue total is less than 0.3 ppm.

The data indicate that residues on treated dry beans occur from the transferof surface residues on the pods to the beans during the threshing process. The data support a conclusion that the proposed tolerance of 0.3 ppm for the combined residue is adequate.

Meat, Milk, Poultry, and Eggs

In a milk-out study reported in PP# 1F1024 (W.S. Cox, 1/8/71), cold chlorothalonil was fed to lactating cows for 30 days at rates of 25, 75, and 250 ppm in the total diet. By a method sensitive to 0.02 ppm, ca. 5% of the milk samples in the 30-day study showed apparent residues of 0.03 or 0.04 ppm but these were scattered among the test groups. No tests were made for the 4-hydroxy metabolite; however, two other postulated metabolites were looked for and were found to be absent.

In a second study, lactating cows were again fed chlorothalonil (30 days) at the above rates, but with 0.2, 016, and 2.0 ppm of the 4-hydroxy metabolite added respectively. In this study, dose responsive residues of the 4-hydroxy metabolite were found in the milk with maxima ranging from 0.30 ppm at the low level to 1.34 ppm at the high level. Residues of chlorothalonil, per se, were not detected (<0.05 ppm).

The second cow feeding study (above) shows that detectable residues of the 4-hydroxy metabolite transfer to all tissues at feeding levels of 0.6 ppm or higher (cattle sacrificed at 30 days). These residues are dose responsive and tend to be higher in the transport and excretory organs (liver and kidney).

An additional milk-out study was presented in PP# 2F1230 (W.S. Cox, 5/24/72). One cow was fed the parent compound at 250 ppm, a second cow was fed 2 ppm of the 4-hydroxy metabolite, and a third served as a control. The two cows were fed the chemicals for 44 days with milk samples taken at intervals of 2 to 6 days (average 3.1 days) and during a 15-day withdrawal period. The study shows that the parent compound has relatively little tendency to transfer to milk; 0.2% of the ingested fungicide appeared in the milk as the 4-hydroxy metabolite (1.3 ppm appeared in the milk as a result of ingesting 250 ppm chlorothalonil in the daily ration). The results for feeding of the parent compound are in strong contrast to those for the 4-hydroxy metabolite as the transfer rate for the metabolite is over 100X that for the parent. From a daily feeding of 2.0 ppm of 4-hydroxy chlorothalonil, maximum residues of 1.54 ppm of the hydroxy metabolite are reported in the milk.

We conclude that chlorothalonil per se has little tendency to transfer to milk, but the 4-hydroxy metabolite is stored in meat, fat, and milk.

The proposed use in the subject petition restricts grazing of treated fields as well as the feeding of treated plant parts to livestock. If the beans are combined directly, the pods would be left in the field; this would eliminate any concern over use of "bean cannery waste" as a livestock feed item. We expect no residues to occur in meat and milk from the feeding of treated plant parts.

According to The Harris Guide, dry beans are cattle and poultry feed items. Since residues of chlorothalonil have been detected on dry beans up to 41 days after application, there appears to be a direct possibility of transfer of residues to meat, milk, poultry, and eggs from the feeding of dry beans to livestock.

Other crops that have established tolerances for combined residues of chlorothalonil and its 4-hydroxy metabolite can also be used as livestock feed items. These include brussel sprouts, cabbage, cauliflower, and tomatoes, all at 5 ppm, plus sweet corn at 1 ppm, and peanuts at 0.3 ppm.

The high transfer rate of the 4-hydroxy metabolite indicates the need for the establishment of a tolerance for residues in meat, milk, poultry, and eggs.

A recent communication from Dr. J. Blanchard (to J. G. Cummings, 10/27/78) points out that an NCI report has just issued (NIH 78-41) which finds chlorothalonil to be carcinogenic in the rat. Before the petitioner (IR-4) and Diamond Shamrock are asked to provide a poultry feeding study and propose appropriate meat, milk, poultry, and egg tolerances, any problems regarding this carcinogenicity study should be resolved.

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cc: EFB, TOX, FDA, CHM (3)
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