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Petitions Control Branch and Division of  
Pharmacology and Toxicology

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Petitions Review Branch, Division of  
Food Chemistry and Technology

AP 25-202

PP #99P0743 Daconil on potatoes. Evaluation of analytical methods and residue data.

The Diamond Shamrock Corp. (formerly Diamond Alkali Co.) proposes the establishment of a tolerance of 0.1 ppm for negligible residues of 2,4,5,6-tetrachloroisophthalonitrile (Daconil) and its metabolite, 4-hydroxy-2,5,6-trichloroisophthalonitrile in or on potatoes.

A petition for a temporary tolerance of 0.1 ppm Daconil on potatoes (PP #730316) was presented and we recommended for its establishment in September, 1966. The petitioner withdrew his petition in October, 1966, for unstated reasons. A petition for a permanent tolerance (PP #77P0599) for Daconil on a number of crops at several different levels was then presented. We recommend against the establishment of all the proposed tolerances (evaluation by B. Malone PS, DPC, 8/28/67), because of the need for information on the metabolism or degradation of Daconil on the plant, the possible presence of the 4-hydroxy soil metabolite in root crops and the persistence of this soil metabolite. The petition also lacked an adequate method for enforcement and sufficient evidence showing residues would not be transferred to meat or milk.

Additional data has been presented by the petitioner and the present submission has been redesignated PP #99P0743.

Conclusion

1. No residues would be incurred by route of translocation from foliage to tubers. Residues may be incurred by migration from the soil to the tubers or direct deposition on occasional exposed tubers. Residues of the parent compound plus the 4-hydroxy metabolite would not be likely to exceed 0.1 ppm. The latter finding is contingent upon the satisfactory resolution of the question of method sensitivity for the 4-hydroxy metabolite-Cencal 3(b) below.

2. No conclusions can be drawn regarding the presence of other metabolites in potatoes because the petitioner has not complied with our previous request for data on other possible degradation products, particularly trichlorodicyanoaniline and 2,4,5-trichloroisophthalonitrile which were found in the animal metabolism studies. We defer to DPT as to whether the need for data on these possible residues may be waived on toxicological grounds.

3. The petitioner has not resolved our previous objections to the analytical method (including its suitability for enforcement purposes), in that:

(a) The method does not determine the possible metabolites including trichlorodicyanovilene and 2,4,5-trichloroisophthalonitrile. (This deficiency may be disregarded if DFT waives the requirements as above in 2 or if it is otherwise shown that these are not terminal plant residues).

(b) The new (modified) method has not been validated for Daconil with the usual recovery experiments. The new method has been validated with respect to the 4-hydroxy metabolite but we would need some representative chromatograms to resolve questions on sensitivity for this compound.

(c) Specificity-- There is no confirmatory method. However, we believe the GLC method itself may be sufficiently specific if the petitioner can present a rationale or experimental evidence showing that other pesticides which have a tolerance on potatoes would be separated either on the Florisil column, in the GLC column, or excluded by virtue of the alternative electron capture-microcoulometric detectors, to the extent that they would not interfere with the determination of Daconil and metabolite(s).

4. The feeding of potatoes bearing the tolerance level of Daconil to livestock would not be likely to result in residues of Daconil or the 4-hydroxy metabolite in meat or milk ( $\pm$ 10.6 (e) 3).

5. Daconil per se is not appreciably persistent in soils. However, the 4-hydroxy metabolite has a half-life which is  $> 7$  mos. in some soils. It is recommended that the USDA be consulted as to whether a label warning is indicated with respect to rotation of crops.

#### Recommendations

We recommend against establishing the proposed tolerance. The petitioner should be informed that for further consideration, points raised in conclusions 2 and 3 must be resolved.

#### Detailed Considerations

##### Proposed Use

Daconil is formulated as a 75% wettable powder. It is applied as a spray in enough water to provide thorough, uniform coverage. The rate of application is 1-1.5 lbs/A (0.75-1.2 lbs act/A), beginning when plants are six inches high or when disease threatens. Repeat applications may be made at seven to ten day intervals or as needed. There is no PHI specified.

Nature of the Residue

**Soil metabolism:** The major degradation product of Daconil in soil is the 4-hydroxy metabolite. This compound can comprise as much as 80% of the residue in soils treated with Daconil. A second minor metabolite has not been identified. Contamination of soil with Daconil from the foliar applications accounts for our concern for possible residues in root crops.

**Animal metabolism:** Studies submitted in PP #7F0599 show two minor metabolites isolated from feces which were identified as trichlorodicyanomilline and 2,4,5-trichloroisophthalonitrile. The petitioner characterized the remaining metabolite(s) as highly polar and strongly hydrophilic but these compounds have not been identified.

In this present submission, tissues from animals (rats and dogs) fed from 1500-30,000 ppm Daconil were analyzed for DAC-3701. Small amounts of DAC-3701 were detected in the liver, kidney and urine.

**Plant metabolism:** The evaluation of PP #7F0599 (by S. Malone 8/28/67) pointed out that no significant studies of metabolism or degradation on plants had been presented. It has been shown by C<sup>14</sup> studies that no radioactivity translocates from aerial portions of plants to roots or from the roots to aerial portions. These studies were performed with crops other than root crops. However, there was absorption from treated soil into roots of corn and tomato plants.

No conclusions can be drawn regarding the presence of other metabolites in potatoes because the petitioner has not complied with our previous requests for data on other possible degradation products, particularly trichlorodicyanomilline and 2,4,5-trichloroisophthalonitrile. We defer to BPT as to whether the need for data on these possible residues may be waived on toxicological grounds.

Analytical Method

A method tryout was performed on the gas chromatographic procedure (electron capture or microcalorimetric detectors can be used) in connection with PP #7F0599. Only Daconil (the parent compound) was used to fortify the crops for validation of the method. In the evaluation of 8/28/67 (by S. Malone) and in the memo on the method tryout (by F.R. Fazzari, 10/24/67) we noted that the method, although validated for Daconil per se, was not adequate for enforcement for the following reasons:

- 1) No confirmatory method was presented.

2) Metabolites (if present) would not be determined by the method. A question was also raised on the ability of the extracting solvent (dichloromethane) to extract the total residue.

The petitioner has now submitted a modification of the original method [Identified as Analysis of DAC-3701 (4-hydroxy 2,5,6-trichlorocephthalonitrile) in Food Crops and Soil] involving a change in the extracting solvent and the cleanup. The petitioner claims that both Daconil and DAC-3701 can be determined by this method. However, no validation data for Daconil, using this modification, have been presented. It may be that the use of the Florisil column imparts a sufficient degree of specificity to the modification; however, here again because of the lack of data we can make no conclusion on this point. With regard to the ability of the method to detect residues of DAC-3701, the data show recoveries of 63-96% at fortifications of 0.1-0.25 ppm, with blank values reported to be <0.05 ppm. We can only state the method sensitivity is probably better than 0.1 ppm for DAC-3701. However, we need some representative chromatograms to resolve the question on sensitivity.

The method does not determine all the possible metabolites including trichlorodicyanoguanine or 2,4,5-trichlorocephthalonitrile.

#### Residue Data

In the evaluation of PP 67F0399 (by S. Malone 8/28/67) it was concluded that residues of the parent compound in potatoes would not exceed the proposed 0.1 ppm tolerance from the proposed use.

Additional residue data submitted in this petition include two studies on potatoes treated with Daconil and analyzed for residues of the 4-hydroxy metabolite, DAC-3701, only. Results reported by the petitioner show no DAC-3701 (<0.05 ppm) residues detected. However, because of the question regarding the sensitivity of the method for this compound (see Analytical Method), further clarification is needed before we can conclude this compound is in fact absent in possible residues.

Although the data are not as complete as we would have liked, they are nevertheless adequate to indicate that there would be little likelihood that residues of either the parent compound or the metabolite (DAC-3701) in treated potatoes would exceed 0.1 ppm.

#### Residues in Meat and Milk

Radiotracer studies with small laboratory animals (rats) fed exaggerated rates of  $\text{C}^{14}$  labeled Daconil show that 90-96% of the radioactivity is excreted in the urine or feces with the majority (ca. 88%) being excreted in the feces. Only a very small percent of the administered activity was detected in any of the organs. Total activity detected in the organs, tract and carcass amounted to about 0.3% of the administered dose.

The paper by Guttemann and Link, J. Dairy Science 49, 1272-1276, showing effects of feeding 5 ppm Daconil to a lactating cow, has more significance here than the previous evaluation (PP #7F0599 involved tolerances on feed items where 5 ppm would not have been an adequate exaggeration). This study shows no residues (<0.01 ppm) of Daconil, or any acid metabolites ✓ or conjugates of these found in milk, urine or manure. This 5 ppm level is at least a 100 fold exaggeration when considering the feeding of potatoes with residues at the proposed tolerance level of 0.1 ppm (assuming 50% of the daily diet of cattle to be potatoes).

We would expect no transfer of residues of Daconil or its 4-hydroxy metabolite to meat and milk from the feeding of potatoes treated with Daconil and this use qualifies for category (3), Sec. 120.6 (e), namely that no tolerances are needed for meat and milk.

#### Soil Persistence

In the evaluation of PP #7F0599 (by S. Malone 8/28/67), it was concluded that the parent compound Daconil would probably degrade before a subsequent year's planting. It was noted that the 4-hydroxy compound (DAC-3701) would replace Daconil and no studies were presented for DAC-3701.

Studies now presented on DAC-3701 show it to be more persistent than the parent compound. Half-life values for Daconil range from 4-40 days whereas half-life values for DAC-3701 range from 36 days for sandy loam soil to 220 days for a clay type soil. Because the 4-hydroxy metabolite has a half-life which is > 7 months in some soils, it is recommended that the U.S.D.A. be consulted as to whether a label warning is indicated with respect to rotation of crops.

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cc:  
SC-970; SC-430; SC-403  
SC-12; SC-1; CS-40; PP #980743

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