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1. PP#7G0516

Petitions Control Branch and
Division of Toxicological Evaluation

August 26, 1966

AF 25-202

Pesticides Branch, Division of Food
Standards and Additives

PP #7G0516: Temporary tolerance for Daconil 2787 on potatoes.

The Diamond Alkali Company proposes a temporary tolerance for residues of tetrachloroisophthalonitrile (Daconil 2787), at 1 ppm on potatoes from its use as a preharvest fungicide.

The use on potatoes was previously submitted for registration on a no-residue basis (see PCB Ref. No. 65-9). At that time, it was finally decided that there was a reasonable expectancy of small residues on potatoes within the limits of detectability of the method and that these should be covered by a tolerance.

Conclusions:

We do not feel that the question of metabolites in or on potato tubers and in animals has been adequately resolved. Although metabolites of this compound have been looked for, they have not been found to date in the tubers. While this in our opinion, does not negate the request for this temporary tolerance, the metabolism will have to be explored for a future permanent tolerance.

The microcoulometric or electron capture gas chromatographic method is adequate for determining residues of the parent compound tetrachloroisophthalonitrile. Supplemented by the described thin layer identification technique, it is adequate for enforcement of the proposed temporary tolerance. For a permanent tolerance a method tryout should be conducted.

Residues of the parent compound would not exceed the proposed tolerance if Daconil 2787 is used as directed and isused with a 12-day PHI. However, in view of the small residuss actually present which do not exceed 0.1 ppm, the tolerance sought on potatoes is unnecessarily high.

Because the studies made to show safety also showed lack of absorption in the gut, we would not expect the feeding of unwashed treated cull potatoes to result in residues in meat and milk. For added assurance we feel that the label should bear a restriction against feeding such potatoes to livestock.

Recommendations:

We recommend that the proposed temporary tolerance of 1 ppm not be established. If USDA considers this an experimental usage and pharmacological considerations permit, we recommend as an alternative a temporary tolerance of 0.1 ppm for the parent compound. This recommendation is contingent upon the petitioner's acceptance of a 12-day PHI and of a label restriction reading: Do not feed cull potatoes to livestock.

The petitioner should be notified that before considering a future permanent tolerance, we will need:

1. A study to more adequately delineate the metabolism on potato tubers and in animals.

2. Improvement in the analytical method to eliminate the interference occurring at the elution time of the parent compound.

3. A feeding study of Daconil 2787 with cattle to determine transfer of residues to meat and milk.

4. Additional studies for different types of soil to determine the fate of Daconil 2787 in the soil.

Detailed Considerations

General

No tolerances have been established for Daconil 2787.

Proposed Use

The petitioner has applied for a temporary tolerance for residues which would result from the use of 98,100 pounds of the fungicide on potatoes. Assuming three applications at the maximum dosage, this amount would treat about 22,000 acres or 1.6% of the acreage planted to potatoes in the United States.

A 75% wettable powder formulation is to be applied as a foliar spray at 0.75-1.12 lbs. active/A application beginning when the plants are 6 inches high or when disease threatens and continued at 7-10 day intervals throughout the season or as needed up to vine-killing time. Under severe conditions, the maximum rate is to be used and the spray interval shortened.

Nature of the Residue

Data on potato tubers indicate that the parent compound is not absorbed and translocated (A. E. Houk memo, PCB Ref. #65-9 on 2-11-66). It would be present however in the soil adhering to the unwashed tubers as a result of contamination of the soil by foliar applications. When dry brushed or washed free of adhering soil, no detectable residue of the parent compound could be found in or on the tubers.

Chronic feeding studies on dogs and rats indicate that Daconil 2787 is excreted in the feces as the parent compound or as a conjugate of trichlorodicyanoaniline with some other metabolites as yet unidentified. The percentage of the parent compound in the feces is dependent on the feeding level and a progressively lower percentage is excreted unchanged as the feeding level is decreased. Blood, urine, and tissue analyses showed no residues of the parent compound or metabolites, and indicate the absence of absorption in the gut.

Metabolites were looked for but were not found in or on the tubers. However, in view of the presumably biodegraded metabolites shown by the feeding studies, we must assume that unknown metabolites could be present in the soil, and thus in or on the tubers.

Residue Method

Residues are extracted with either dichloromethane or an isopropanol-dichloromethane mixture. The extract is filtered and then cleaned-up on an alumina column. The fraction containing the residue is collected and injected into a gas chromatograph. The parent compound is determined by GLC using either microcoulometric or electron capture detectors.

Some control samples give a peak on the chromatograms at the same elution time as tetrachlorisophthalonitrile presumably due to poor clean-up. The maximum blank encountered is 0.04 ppm although almost all values were of the order of 0.00-0.02 ppm. We consider the sensitivity of the method to be about 0.02 ppm. Recoveries at fortification levels of 0.05 and 0.4 ppm are variable and averaged 86% with most values in the 60-112% range, and only an occasional value ranging as low as 45% or as high as 132%. In a thin layer method used for the metabolism study, the sample is macerated and extracted with acetone. The macerate is filtered and the filtrate evaporated to dryness. Aliquots equivalent to 50 grams of sample were

spotted on a silica gel thin-layer plate and the plate developed with benzene. The developed plate is then photographed while under 2540 A° U. V. light. The sensitivity of this method is estimated to be about 0.02 ppm.

In our opinion, the parent compound could satisfactorily be determined by GLC (ME or EC). Supplemented by the thin layer technique described above, this method could be used for enforcement purposes for the parent compound. The FDA multi-detection screening procedure might be useful for these purposes, but would require study.

Until the metabolism is delineated, we can not determine whether the total toxic residue would be determined by these methods.

Residue Data:

Studies made in 9 states reflect multiple applications (3-13 times) of 0.75 to 1.50 lb. active/100 gallons (estimated 0.94-1.88 lbs. active/A), the last application being at 12-23 days before harvest. No data were submitted for applications up to vine-killing time which we would estimate to be 5-7 days before harvest. Therefore, because there are no residue data for any interval less than 12 days we believe a 12-day PHI should be included in the label.

The maximum residue value reported was 0.07 ppm of parent compound on unwashed tubers after 8 applications, the last application in this study being 14 days before harvest. This associated control value is zero. Had this control value been at the top of its range (normally 0.02 ppm, occasionally 0.04 ppm), the uncorrected value would be slightly more than 0.1 ppm. However, tubers for marketing and human consumption are normally washed or brushed and a tolerance level of 0.1 ppm is considered adequate for the described usage. The maximum residue on such cleaned tubers was reported as 0.03 ppm of the parent compound.

Therefore, we consider the proposed 1 ppm tolerance as unnecessarily high and would propose an alternative a more appropriate tolerance of 0.1 ppm for the parent compound.

Another study was submitted in which both peelings and edible portions of treated tubers were analyzed. These data show the residue of the parent compound to be on the peel, and support the premise that Daconil 2787 is not translocated.

Milk and Meat

Since unwashed cull potatoes may legally contain up to 0.1 ppm at least of the parent compound and can be fed to livestock, there is a theoretical possibility of the transfer of residues to meat and milk. However, the data

for the dog and the rat, indicate that the residue would not be absorbed in the gut. Presumably this would also apply to ruminants. On this basis, we would not expect the feeding of treated potatoes to result in residues in meat and milk. However, in view of the large acreages of potatoes involved on this temporary tolerance, we feel that for added assurance the label should bear a restriction against feeding cull potatoes to livestock.

A feeding study should be carried out for purposes of a future permanent tolerance.

Soil Persistence:

The fate of Daconil 2787 in soil has not yet been determined. Data submitted show that it is "lost" in the soil and attempts made to date to trace it have been unsuccessful. The rate of loss is seen to increase with both increased heat and organic content of the soil. Before a permanent tolerance can be established the fate of Daconil 2787 and its rate of dissipation should be determined in different types of soil.

R. Quick

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SCI-R
FSA/OD
FSA/PB
PP #7G0516
PCB Ref. #65-9
DFC(Jones)
ERC(Johnson)

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