

2-19-71

REney:RCook:ASchlosser:ow
February 19, 1971

Reevaluation No. 2 of Pesticide Petition No. OF0972
for Mono(N,N-dimethylalkylamine) salt of endothall
[7-oxabicyclo (2.2.1) heptane-2,3-dicarboxylic acid]
calculated as endothall
Submitted by Pennwalt
Filed April 24, 1970
Amended November 25, 1970, Section D

I. Introduction

1. Refer to PP No. 7F0570 and 6G0503.
2. Refer to Evaluation dated June 8, 1970, (a favorable opinion was given June 8, 1970, and sent on June 12, 1970, for a proposed tolerance of 0.1 ppm in or on cottonseed for the salt expressed as endothall).
3. The petitioner submitted on November 25, 1970, a study on residues of Endothall on lint and seed from cotton treated with Accelerate (trade name of product containing endothall).

The petitioner also submitted metabolism studies in goats and white leghorn chickens.

II. Discussion of Data - Cotton Studies

1. The level of residue found in field grown cottonseed sprayed with double the recommended rate was 0.02 ppm and 0.05 ppm, and in lint 0.2-0.3 and 0.4-0.6 ppm with the higher level resulting from air application and PHI of 11 days and the lower level from ground application and PHI of 16 days. (Ratio 10:1).

2. Laboratory treated cotton was analyzed. The lint contained an average of 27% of the sprayed amount, even 10 days after application. A composite sample of all the seed collected over 10 days contained 1% of the applied amount (Ratio 30:1).

Radioassay of laboratory treated cotton showed an average of 29% (range 22%-40%) endothall in lint and approximately 3% in seed (Ratio of residue in lint to seed 10:1).

TLC and autoradiography showed no breakdown products or metabolites. All residues found were present as endothall acid. Note that application was made directly to open bolls.

Conclusions

The conclusions of the study appear reasonable.

- a. Results of analyses from field treatment and laboratory treat-

ment by GLC, radioassay, thin layer chromatography, and autoradiography correlate closely.

- b. The ratio of residue in lint to seed which can be expected is about 10:1.
- c. No significant difference in residue level in lint or seed throughout sampling period (one questionable result) and are in accord with previously determined levels.
- d. Residues in lint and seed were endothall and no evidence of any residue other than endothall.

3. Chicken Study

Preconditioning of white-leghorn chickens with non-radiolabeled ^{14}C does not effect tissue (and egg) residues as determined by ^{14}C assay following treatment for several (10) days with ^{14}C labeled endothall. Replacement of stored non-tagged endothall or metabolites with ^{14}C material is effectively completed within the ten day radio-isotope treatment period.

This study supports the conclusions of previous studies that endothall does not buildup in tissue or eggs of white-leghorn chickens. It is of interest that eggs present in the ovary contained 0.0063 ppm and egg in the oviduct contained 0.01374 ppm. These residues would be reduced when layed.

4. Distribution and Characterization of ^{14}C - Endothall Residues in the Goat

The residue levels in meat, milk, and excreta were determined by radiochemical methods and the residues were characterized by aqueous-organic partition, TLC, and radioassay procedures.

^{14}C activity in milk samples was apparent five hours after initial dose. Afternoon samples, five hours after dose, contained considerably more radioactivity than did milk samples obtained in the morning, twenty-two hours after dosing. This cyclical pattern was observed in all animals and for urine and fecal samples also, the fecal residue level peaking 22 hours after dosing. The cyclical pattern was confirmed by the results of the hourly milking study, which showed the residue level to peak in four hours and decrease sharply after that the highest level of residue found in milk was 83.4 ppb.

No additive effect (i.e. increasing concentration of ^{14}C in milk) following repeated daily doses was indicated.

Goats fed endothall at 1 ppm in the diet showed no detectable radioactivity in milk 76 hours after the last dose of ^{14}C .

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However, ^{14}C could be detected in milk about 24 hours after feeding and is eliminated.

Tissue storage of endothall was minimal. For animals fed at the 5 ppm rate liver contained 17 ppb, kidney 15 ppb, brain tissue 14 ppb, muscle contained from 10 to 35 ppb.

80 to 93% of total dosage is estimated to be eliminated in feces with most of the remainder eliminated in feces with some in the urine.

Pre-treatment with non-radioactive endothall did not alter the residue detected in milk. The cyclic plateau of residues in milk was reached by the second day of feeding. Petitioner claims that studies were of sufficient duration to demonstrate that endothall would transfer to milk in only insignificant amounts.

III. Conclusions

We have already given a favorable opinion on this petition on June 12, 1970.

FDA in letter of September 18, 1970, raised questions as to possible degradation products of endothall in cotton and in animals. Studies to determine the propensity for endothall per se to transfer to meat, milk, poultry, and eggs were also requested.

Petitioner responded to FDA by submitting a revised Section D on November 30, 1970. These data were reviewed for our information. No further action is required.

IV. Recommendation

A revised opinion is not needed at this time.

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