ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

Branch
File: PP# 2F1230

Date: June 14, 1972

Reply to Attn of:

Subject: Daconil*; Chlorothalonil: tetrachloroisophthalonitrile and its 4-OH meatabolite on various crops and in meat and milk.

To:

Mr. Drew M. Baker, Jr., Chief
Petitions Control Branch
Pesticides Tolerances Division

Pesticide Petition No. 2F1230

Diamond Shamrock Chemical Co.
300 Union Commerce Building
Cleveland, Ohio 44115

Toxicology Branch has been asked to comment on Chemistry Branch review of 5/23/72, W.S. Cox (IAR of D.M. Baker, 5/24/72).

CB considers that several of the proposed residue levels of Daconil and its 4-OH metabolite (DAC-3701)** are inadequate for the RACs specified. These include:

RAC	Proposed tolerance	CB suggested tolerance
Bean Vines	50 ppm	100 ppm (or PHI increased from 7 to 14 days)
Beans, Snap	5 ppm	15 ppm
Meat and Milk	0.2 ppm	1 ppm
Sugar beets	0.2 ppm	0.3 ppm
Peanuts	0.3 ppm	0.3 ppm (change to include peanut hulls)

In our recent toxicological review, (memo of D.L. Ritter, 5/10/72), we defered to CB the following:

1) the question of transfer of residues of daconil and its 4-OH metabolite into refined sugar from sugar beets.

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* Tolerances established in 40 CFR 180.275
** 4-hydroxy-2,5,6-trichloroisophthalonitrile

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2) the possible transfer of combined residues into the flesh and milk of livestock being fed residue-bearing feedstuffs.

CB now finds that:

1) residues of daconil and its metabolite in sugar beets will not concentrate into sugar; hence a food additive tolerance is not needed;

2) a tolerance of 15 ppm for snap beans is more appropriate;

3) sugar beets should have a tolerance of 0.3 ppm (roots);

4) eggs and poultry can be placed in category 180.6(a)(3);

5) a tolerance of 1.0 ppm is necessary for residues in milk and in the flesh of cattle, horses, goats, sheep and hogs. Residues in meat and milk consist principally of the 4-OH metabolite.

TB finds the added tolerances in 2 and 3 will not contribute appreciably more residues of daconil to the dietary load. We cannot find favorably for the suggested tolerance of 1.0 ppm combined residues in meat and milk.

The ADI of residues of daconil has been calculated to be 1.8 mg/day, with amounts contributed from existing and proposed tolerances being about 1.0 mg/day (memos of H. Blumenthal, 3/1/71 and E.C. Hagan, 3/1/71, PP#1F1024). A level of 1.0 ppm in milk would add 1.5 mg/day.

We understand that the residue of interest in meat and milk is the 4-OH metabolite, and that it can be present at up to 0.7 ppm in whole milk. TB has no toxicity data on this compound. We note from previous CB reviews that this 4-OH metabolite (DAC-3701) is found to only a slight extent in the liver, kidney and urine of rats and dogs following long-term exposure to levels of daconil as high as 1500 - 30,000 ppm for two years (DFCT memo of A. Rathman, 10/9/68, PP#9F0743). In addition, 85 - 90% of administered daconil appears unchanged in the feces in rats and dogs (memo of B. Malone, 8/28/67, PP#7F0599).

As a result of these findings, we conclude the metabolite DAC - 3701 is not elaborated metabolically to a significant degree in the daconil-fed rat and dog; hence, exposure to it is minimal and we therefore cannot conclude that the toxicity data generated from animal ingestion of the parent compound, daconil per se,

adequately reflect the toxicity of the metabolite.

Recommendations:

TB cannot find favorably for the suggested tolerance of 1 ppm combined daconil residues in meat and milk, such residues consisting principally of the 4-OH metabolite.

Tolerances for daconil residues in meat and milk are considered separately:

Meat

To establish the tolerance, the following toxicity studies using the 4-OH metabolite must be submitted:

1) Acute oral LD_{50}'s in two species;

2) A three generation rat reproduction study, first litters only. The original parent-breeders should remain on test diet for the duration of the study in order that we might have some idea of the long-term toxicity of the metabolite.

Milk

The ingestion of 1.5 mg/day of any pesticide residue from milk sources, regardless of its lack of toxicity, is of concern to TB. We do not, as matter of policy, permit tolerances as high as 1 ppm in milk. TB therefore finds that CB's suggested tolerance of 1 ppm combined daconil residues in milk is unacceptable. It may be feasible to change the applicable PHI's, or to continue the feeding restriction as it applies to dairy cattle.

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Division Reading File
Branch Reading File
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