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Shaugh. No. 079402

EAB Log Out Date Jan 4, 1985

Init. CKO for SMC

To: George LaRocca
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Attached please find the environmental fate review of:

Reg./File No.: 50658-EUP-R

Chemical: Avermectin B1

Type Product: Insecticide/acaricide

Product name:

Company name: Merck and Co.

Submission Purposes: Worker reentry data in support of EUP on citrus

ZBB Code: 3(c)(5)

Action Code

Data In: 8/28/84

EAB #: 4548

Date Completed: 1/4/85

TAIS (Level II) Days 6

Deferrals To:

___ Ecological Effects Branch

___ Residue Chemistry Branch

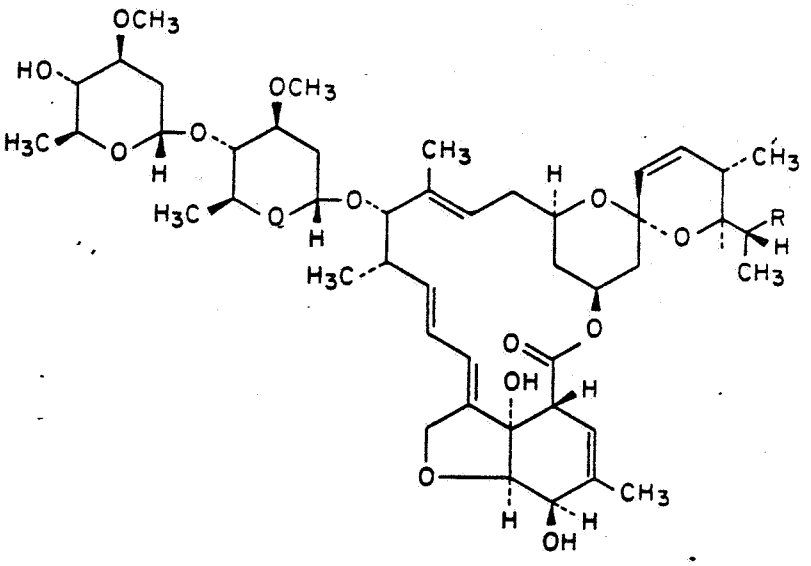
_X_ Toxicology Branch

1.0 INTRODUCTION

This submission is in response to a meeting held with Merck representatives on 7/28/84 to discuss their requested EUP for citrus. Tox branch expressed concern over the high fetotoxicity of Avermectin and requested further information before the EUP would be granted. Data was also requested at that meeting to allow EAB to estimate fieldworker exposure to Avermectin. Their response for estimation of fieldworker exposure consists of 3 studies in press or published by independent researchers. They contend that these studies support their proposed 24-hour reentry interval.

2.0 PESTICIDE STRUCTURE/NOMENCLATURE

Avermectin



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3.0 DISCUSSION

Avermectin is a natural product isolated from Streptomyces avermitilis. It is highly fetotoxic but would be used at very low application rates. The low usage rates would lead to initially lower than-normal pesticide residue levels in the worker environment. These lower residue levels would lead to lower worker exposure and tend to decrease worker hazard.

The applicant submits data (Accession #254459) in support of a request for an Experimental Use Permit (EUP) and proposes that a 24-hour reentry interval would provide adequate fieldworker protection during that study. They contend that the submitted studies show that Avermectin is unstable on experimental surfaces in laboratory studies. However, the crucial data for estimation of fieldworker exposure levels are the foliar dislodgeable residue levels, and this is the data required under 40 CFR § 158.140 and discussed in Subdivision K of the Pesticide Assessment Guidelines.

The studies submitted consist of: 1) D. C. Bull et al. 1984. J. Agric. Food Chem. 32:94; 2) Y. Iwata et. al. 1984. submitted to J. Agric. Food Chem.; and 3) a Merck, Sharpe and Dohme Research report, 'Metabolism of Avermectin $B_{1}a$ in Citrus Fruit. Of the data submitted, only the foliar residue levels reported in Attachment 2 (Iwata et al., 1984) have real utility for this purpose, and that data is severely flawed from the point of view of the Agency. First, Avermectin was applied to the test trees and fruit as a propylene glycol solution rather than as a typical end use product. Second, it is not possible with the submitted data to relate the usage rate in the submitted study to any proposed field usage rate. Since this is a submission in support of a request for an EUP, field data could not have been submitted. Third, the residue quantification was based on total radioactivity and not on the parent pesticide and any toxic alteration products. Much of the residue reported in Attachment 2 may be non-toxic residue. Fourth, foliar-residue recovery was not done by the accepted dislodgeable residue procedure.

Nevertheless, the submitted data can be used as a first estimation of dislodgeable residue levels at intervals after application if the registrant is willing to accept a worst-case calculation. This review proceeds on the assumption that that is their intent in submitting the data.

In Iwata et al., tritium-labeled avermectin was applied to lemon fruit and foliage and to orange fruit by dipping on-the-tree fruit and leaves into a 3 ppm avermectin solution. This is certainly not accepted agricultural practice for pesticide application, but with the given circumstances of low treatment level, radioactivity of the pesticide, and the limited amount of pesticide available for the test, this procedure is the best compromise. However, use of this procedure does raise question of the relationship of the applied pesticide usage-rate to the suggested commercial application rate for the pesticide.

Treated leaves and fruit were removed from the trees at 2 to 3 hours post application as '0' day samples and at 15, 30, 60, and 91 days after application. There was no sample at 24-hours. The foliar samples consisted of 6 lemon leaves per sample time. Each leaf had 2 disks [2.5 cm dia] removed for the sample. The surface residues were not removed from the disks, but rather the whole-leaf disks were lyophilized to be combusted for liquid scintillation counting.

The immediate post application foliar residue was reported to be 0.92 +/- 0.23 ppm. The ppm values were converted to ug/cm^2 and presented graphically. A discontinuous 2-slope regression line has been drawn in on that graph. I contend that this is not acceptable. [If two or more dissipation rate processes, e.g. volatilization, hydrolysis, photolysis, mass-transfer into the substrate, etc., occur simultaneously; the plot of the resulting residue data against time must be a continuous curve composed of the composite of the slopes of the rate processes. It can be shown mathematically that the graph can not be a discontinuous function as they have shown in their regression lines.] Although the residue level in numbers is not reported, the '0' day value from that graph appears to be 0.013 ug/cm^2. Using that value in conjunction with Popendorf's correlation [Am. Ind. Hyg. Assoc. J. 41:658], the citrus picker exposure rate would be 50 ug/hr or 400 ug/8-hr work-day.

There is no sample at 24-hours, but based on the company submitted graph and correcting their two slope line to be a continuous curve, the residue level after 24-hours is estimated to be 8 ng/cm^2. This would constitute about 40% reduction in the first 24 hours and is consistant with initial dissipation rates [of about 60% on the first day] seen with other pesticides on the same crop and in the same environment. Using the 8 ng/cm^2 value in conjunction with Popendorf's correlation, the expected fieldworker exposure rate would be 40 ug/hr or 320 ug/8-hr work-day.

4.0 CONCLUSIONS

Although the submitted data were not gathered according to the methodology suggested in Subdivision K of the Pesticide Assessment Guidelines, that data can be used for estimation of the exposure of citrus pickers to avermectrin. Those exposures are estimated to be 50 ug/hr or 400 ug/8-hr work-day on '0' day and 40 ug/hr or 320 ug/8-hr work-day 1 day after application.

5.0 RECOMMENDATIONS

If 320 ug/day is an acceptable level of human exposure, their proposed 24-hour reentry interval is acceptable. I defer to Toxicology Branch for that decision. If 320 ug/day is not acceptable and since this is a request for an EUP where the amount of work and therefore amount of exposure should be

lower than normal, granting of the EUP could be considered if the number of hours of foliar exposure were limited by the conditions of the EUP so that workers would not be exposed long enough to receive an unacceptable level of exposure.

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