UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

MAY 4 1990

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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP Nos. 8F3649 and 9F3703/9H5570. Abamectin (Avermectin B_1) on Celery and Tomatoes. Evaluation of Amendments dated 12/15/89 and 1/31/90. MRID No. 413284-01. DEB Nos. 6198, 6199, 6334, 6335, 6336. HED Project Numbers 0-0457, 0-0669A.

FROM: Stephanie H. Willett, Chemist
Tolerance Petition Section 2
Dietary Exposure Branch
Health Effects Division (H7509C)

THRU: Richard D. Schmitt, PhD, Branch Chief
Dietary Exposure Branch
Health Effects Division (H7509C)

TO: George LaRocca/Adam Heyward, PM 15
Registration Division (H7505C)
and
Toxicology Branch I-IR Support
Health Effects Division (H7509C)

Background

Merck Sharp and Dohme requested the establishment of tolerances for abamectin (avermectin B_1) and its delta 8,9-isomer in celery, tomatoes, wet tomato pomace, and dry tomato pomace at levels ranging from 0.035 to 0.07 ppm in the subject petitions. DEB recommended against the establishment of the requested tolerances because several data deficiencies were cited in the initial petition reviews (see memoranda of F. Boyd dated 11/16/88, and S. Willett dated 12/15/89).

Tolerances are established for avermectin B_1 on cottonseed, citrus, cattle meat, meat byproducts, and milk at levels ranging from 0.005 to 0.01 ppm (40 CFR 180.449). Food and feed additive tolerances for citrus pulp and oil are established at 0.1 ppm in 40 CFR 185.300 and 186.300.

No Registration Standard has been prepared for abamectin.

Conclusions

All deficiencies of PP Nos. 8F3649 and 9F3703/9H5570 previously cited by DEB have been resolved as a result of this submission, assuming that point b of the revised Section F of PP No. 9F3703/9H5570 indicating a 2 day PHI is a typographical error (see discussion under deficiency 5).

Recommendations

TOX and SACB considerations permitting, DEB recommends for the establishment of tolerances of abamectin and its delta 8,9 isomer on celery, tomatoes and tomato pomace at levels of 0.05, 0.01, and 0.07 ppm, respectively. **These tolerances should be adequate to cover residues expected when AGRI-MEK 0.15 EC is used according to label directions.**

Present Considerations

The petitioner has submitted amendments in response to the deficiencies cited by DEB (see memos of F. Boyd dated 11/16/88, and S. Willett dated 12/15/89). The deficiencies will be restated below, followed by the petitioner's response and DEB's comments and conclusions.

PP No. 8F3649

Deficiency 2

The proposed use for celery states that the maximum rate will be 0.02 lb ai/A with a maximum of 10 applications per growing season, and harvesting no sooner than 7 days after the last application. However, the labeling does not include mixing instructions or directions for spray volume and coverage per acre. A revised Section B including these labeling directions will be needed.

Petitioner's Response to Deficiency 2

In a letter dated January 31, 1990 from Louis Grosso of Merck Sharp and Dohme, the petitioner has indicated that the label will be revised to specify mixing 8 to 16 fl. oz. of AGRI-MEK 0.15 EC in a minimum of 10 gallons of water per acre. The volume of water may be increased to assure thorough coverage and optimal control.

The volume specifications will also apply to use on tomatoes.

DEB's Comments and Conclusions, re: Deficiency 2

Deficiency 2 is resolved.

Deficiencies 3a and 3b (paraphrased)

Polar degradates in celery are similar to those in citrus and cotton, and are of the same quantity (up to 70% of residues). Toxicological evaluation of these degradates may be of concern to the Toxicology Branch.

No new animal metabolism data were presented in this submission. However, data were presented to show that the alpha 8-OH metabolite identified in celery is also identifiable in the liver tissue of rats. DEB is still not convinced that a tritium label goat study is satisfactory for permanent tolerance setting. The nature of residue in animals is not adequately understood.

Petitioner's Response to Deficiencies 3a and 3b

None

DEB's Comments/Conclusions, re: Deficiencies 3a and 3b

In a comprehensive review of the plant metabolism studies conducted on oranges, cotton leaf and celery, DEB concluded that the degradates/metabolites resulting from use of avermectin as proposed were similar (see memo of S. Willett dated 12/15/89). Additional toxicity testing was performed using the fraction containing the unidentified polar degradates. The tests indicated that the components were of no toxicological significance at the levels tested (see TOX memos 007080 and 007801 of W. Dykstra dated 3/13/89). DEB has concluded that the residues to be regulated are avermectin B_1 and its delta-8,9 isomer. Although the alpha 8-OH metabolite was identified in celery, it accounted for less than 10% (<0.005 ppm) of the total residue and need not be regulated at this time (see also memo of S. Willett dated 12/15/89).

The animal metabolism of avermectin was considered to be adequately understood for supporting the tolerances on cottonseed, citrus and tomatoes (see memo of S. Willett dated 12/15/89). Since there are no animal feed items associated with celery, the metabolism of avermectin in animals is not an issue related to the establishment of a tolerance on celery.

Deficiencies 3a and 3b are resolved.

Deficiency 5

The residue data are adequate in number, geographic distribution, and are reflective of the proposed use to consider the setting of a tolerance level. However, the storage stability data (85% recovery at 3 months of freezer storage) are inadequate for validating the analytical data derived from samples stored up to 18 months. Further reporting of the ongoing storage stability

study will be necessary.

Petitioner's Response to Deficiency 5

The petitioner has submitted a report on the results of a study which assessed the stability of avermectin on celery over a period of 24 months (MRID No. 41328401). The study was conducted by Hazelton Laboratories.

Samples of untreated celery were fortified with avermectin B_1a, avermectin B_1b, and avermectin B_1a delta 8,9 isomer and stored in a freezer at approximately -20°C. Samples were analyzed at 0 days, and after 1, 3, 6, 12, 18 and 24 months of storage.

The analyses were conducted according to methodology described in Merck Method No. 1001, revision 1 dated March 11, 1987. The method involves solvent extraction, derivatization, and quantification by reverse phase HPLC using a fluorescence detector. The methodology has been previously validated by the petitioner and a similar version (Method No. 1001, revision 2) has been validated by OPP. The limit of quantification is 5 ng/g and the limit of detection is 2 ng/g for B_1a, B_1b and B_1a delta 8,9 isomer. In analyzing the storage stability samples, each analysis set consisted of five standards run before and after the samples and a fortified control sample (no fortified sample was analyzed when samples were reanalyzed because of the need for dilution). An analysis set was considered acceptable if the coefficient of determination, based on a minimum of 8 points, was greater than 0.97 and if the recovery of avermectin B1a from the fortified samples was in the range of 70 to 110%. The storage stability data submitted are summarized below.

Component	Fortification Level (ppm)	% Recovered[1] After Storage						
		0[2]	1[3]	3	6	12	18	24
B_1a	10.4	93	84	80	86	85	68	79
	206	89	85	86	92	91	78	71
B_1b	15.2	92	99	103	103	92	80	87
B_1a, delta 8,9	9.5	76	79	73	84	79	68	70

1 - average of 2 reported values
2 - days
3 - months

All control samples had no detectable residues. Sample chromatograms of standards, controls, recoveries and fortified storage stability samples were submitted.

DEB's Comments/Conclusions, re: Deficiency 5

The storage stability data indicate that avermectin B_1 and its delta 8,9 isomer are stable in frozen storage for up to 24 months since recoveries were generally greater than 70% through that period. These data adequately support the field trial residue data previously reviewed. This deficiency has been resolved.

Deficiency 7

A request for a tolerance of 0.035 ppm residues of AVM on celery is insufficient, according to the data presented. If the residue data are validated by storage stability data, then a revised Section F requesting a 0.05 ppm tolerance for AVM residues will be needed.

Petitioner's Response to Deficiency 7

A revised Section F requesting a 0.05 ppm tolerance for AVM B_1 and its delta 8,9 isomer has been submitted (see letter of L. Grosso dated 1/31/90).

DEB's Comments/Conclusions, re: Deficiency 7

This deficiency has been resolved.

PP No. 9F3703/9H5570

Deficiency 5

The residue data submitted are adequate. However, the residue data indicate that the proposed tolerance of 0.005 ppm on tomatoes, particularly cherry tomatoes, is inappropriate. DEB recommends that a tolerance of 0.01 ppm on tomatoes be proposed. The proposed tolerance of 0.07 ppm for tomato pomace is adequate. A distinction between wet and dry pomace is not necessary. These changes should be reflected in a revised Section F.

Petitioner's Response to Deficiency 5

A revised Section F requesting tolerances of 0.01 ppm for tomatoes and 0.07 ppm for tomato pomace has been submitted, as specified by DEB (see letter of L. Grosso dated 1/31/90).

DEB's Comments/Conclusions, re: Deficiency 5

This deficiency is resolved, assuming that point B of the section F indicating a 2 day PHI for cherry tomatoes is a typographical error. The tolerances are adequate to cover residues expected on tomatoes and in tomato pomace when the PHI is 3 and 7 days for large and cherry tomatoes, respectively, as specified in Section B of the petition.

cc: PP#'s 8F3649, 9F3703/9H5570, Willett, RF, PIB/FOD (C. Furlow), Circ., J. Kariya (SACB)

CM2:H7509C:RM810C:X1439:SHWillett:shw-11/20/89
RDI: M. Flood, 5/2/90; R. Loranger, 5/2/90