US EPA ARCHIVE DOCUMENT

(5-17-94)

MEMORANDUM

Subject: PP#3F04258, Abamectin (AGRI-MEK 0.15 EC, EPA Reg No. 618-98) in or on the fruiting vegetables crop grouping. Evaluation of analytical method and residue data. CBTS# 12519, 13174; DP Barcode D194897, D198987; MRID 429000-00, -01.

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Merck & Co., Inc. requests the establishment of a permanent tolerance for the combined residues of the insecticide avermectin B_1 (also referred to as abamectin) and its delta-8,9 isomer on the raw agricultural commodity group fruiting vegetables (tomatoes, peppers, eggplants) at 0.01 ppm.

Permanent tolerances for the combined residues of the insecticide avermectin B_1 and its delta-8,9-isomer have been established for tomatoes at 0.01 ppm (40 CFR §180.449) and tomato pomace at 0.07 ppm (40 CFR §186.300). Tolerances for residues in citrus, whole fruit at 0.02 ppm, cottonseed at 0.005 ppm, milk at 0.005 ppm, and cattle, meat and meat byproducts at 0.02 ppm (40 CFR §180.449); citrus oil at 0.10 ppm (40 CFR §185.300); and dried citrus pulp at 0.10 ppm (40 CFR §186.300) expired on 3/31/93. It is our understanding that RD is presently working on reinstating these tolerances. Avermectin B_1 and its delta-8,9-isomer are comprised of ≥80% avermectin B_{1a} and ≤20% avermectin B_{1b}. Avermectin B_{1a} is 5-O-demethyl avermectin A_{1a}; Avermectin B_{1b} is 5-O-demethyl-25-di(1-methyl-propyl)-25-(1-methylethyl) avermectin A_{1a}.

Tolerances are pending for avermectin use in or on various agricultural commodities including pears, strawberries, celery,

lettuce, almonds, almond hulls, walnuts.

A Reregistration Standard has not been prepared for avermectin.

CONCLUSIONS

1. The manufacturing process of technical grade avermectin has been adequately described.

2. The maximum application rate must be clearly stated on the proposed draft label and Section G. Currently, each section states a different maximum application rate. Revised Sections B and G should be submitted to resolve this discrepancy.

3. CBTS concludes that the available metabolism data is sufficient and the nature of the residue on fruiting vegetables is understood. The residues of concern are avermectin B_1 and the delta-8,9-isomer.

4. The ^{3}H-avermectin goat metabolism study is considered adequate to support this use on fruiting vegetables. The residues of concern in animals remain avermectin B_1 and the delta-8,9-isomer.

5. CBTS concludes that adequate enforcement methods are available in PAM II for detecting avermectin residues in or on peppers, tomatoes, and other fruiting vegetables.

6a. The analytical method used for residue data collection quantitates residues of avermectin B_{1b} against the avermectin B_{1a} standard curve. Although not analytically correct, Merck has previously provided sufficient data to show that the quantitation of avermectin B_{1b} residues with the B_{1a} curve would accurately measure the contribution of B_{1b} in the total avermectin residue up to approximately 100 ppb total. Since the proposed tolerance for fruiting vegetables (tomatoes, peppers, eggplant) is less than 100 ppb (ie: 0.01 ppm), CBTS considers this procedure for quantitation is adequate for peppers.

6b. CBTS concludes that Merck method #8004 has been adequately validated for data collection of avermectin residues in or on peppers. However, as per the instructions of the Analytical Chemistry Laboratory/EPA, the method write-up should be revised so that the term "delta-8,9 isomer" is defined as either 8,9-Z-avermectin B_{1a} or 8,9-Z-avermectin B_{1b}. Although CBTS does not consider this a deficiency, future submissions for avermectin analytical methods should include this terminology.

6c. CBTS concludes that Merck method #9003 has been adequately validated for data collection of avermectin residues in or on tomatoes.

7. Because of the demonstrated stability in tomato field samples up to 19 months and in celery up to 24 months, CBTS concludes that storage stability data are adequate to support the field trial residue data for tomatoes and peppers.

8a. The proposed crop group tolerance will adequately cover residues in or on tomatoes.

8b. Because of the questions raised by the petitioner as to the quantity of active ingredient present in the formulation at the time of the pepper field trials (Nos. 001-90-1014R (NM), 001-90-1013R (CA), and 001-90-6011 (CA)), the petitioner may need to repeat the three field trials in question.

8c. CBTS cannot determine whether the proposed tolerance of 0.01 in or on the fruiting vegetable crop grouping is adequate. The petitioner needs to submit additional residue data for a variety of peppers which is smaller than the bell pepper. At least three additional field trials would be necessary. These three field trials could replace the three trials of which Merck has raised concerns. Two of the three would need to be conducted in CA if they were intended to replace the three trials in question. At least one non-bell pepper trial is required in New Mexico.

8d. CBTS could consider a petition for a tolerance for bell peppers based on the data submitted in conjunction with this petition for the crop group tolerance. The petitioner would need to submit a revised Section F which proposes a tolerance for peppers, bell at 0.01 ppm and address all remaining deficiencies cited in this review. The petitioner would be requesting the tolerance for bell peppers in lieu of the crop group tolerance.

9. Adequate processing studies are available for processed fractions of tomatoes. No further processing studies are required for the fruiting vegetable crop group.

10. The meat, meat byproduct, and milk tolerances which expired in March, 1993 would be adequate to cover transfer of secondary residues to meat and milk. Either RD needs to reinstate these tolerances or the petitioner should repropose their establishment. In addition, the petitioner should submit a revised section F proposing the 0.015 ppm tolerance on fat, cattle. There is no reasonable expectation of finite residues in poultry and swine commodities. Therefore, poultry and/or swine feeding studies are not necessary.

11. For EPA to harmonize residues with Codex, the established (tomatoes) and proposed (fruiting vegetables) tolerances would need to be increased to 0.02 ppm. The tolerance expression would not need to be changed. The increase for the purposes of harmonization would need to be based on toxicological considerations.

RECOMMENDATIONS

CBTS cannot recommend for the establishment of a tolerance for residues of avermectin in or on members of the fruiting crop group at 0.01 ppm because of conclusions 2, 8b, 8c, 8d, and 10. The petitioner must submit further information, including technical data, to explain their statement that the amount of active ingredient in the formulation used at the time of the three field trials in question could not be confirmed. In addition, the petitioner must submit revised Sections B, F, and G. If and when a permanent tolerance is established, assuming the petitioner has satisfied all data requirements, CBTS would recommend for the establishment of a crop group tolerance for Fruiting Vegetables without the qualification "tomatoes, peppers, eggplants".

DETAILED CONSIDERATIONS

Manufacturing Process and Formulation:

The manufacturing process of technical grade avermectin has been adequately described (memo, L. Cheng, 5/1/86). All inerts have been cleared under 40 CFR §180.1001 for AGRI-MEK 0.15 EC, (EPA Reg. No. 618-98), 0.15 lbs. ai/gallon (memo, A. Smith, 6/23/86, PP#5G3287).

Proposed use:

AGRI-MEK 0.15 EC is an emulsifiable concentrate of avermectin B_1 (0.15 lbs. ai/gal.). Mix 8-16 oz. (0.01-0.02 lbs. ai)/Acre of formulated product with water for control of insects and mites on tomatoes, peppers (Bell and non-bell types), and eggplants. Apply thoroughly as a foliar spray to assure good upper and lower leaf coverage. Apply when pests are first observed and repeat applications at no less than 7-day intervals to maintain control. The following restrictions apply:

- *Do not exceed 48 fl. oz. of AGRI-MEK per acre in a growing season.
- *Do not apply within 7 days of harvest.
- *Do not apply in less than 20 gallons of water per acre.
- *Do not make more than two sequential applications in order to manage the onset of resistance.
- *Do not use in aerial application equipment.

According to the proposed draft labeling and Section G of the petition, the maximum use rate will be 48 oz. (0.06 lbs. ai) per acre per growing season (ie: 3 applications of 16 oz. or 6 applications of 8 oz.). However, Section G also states that five weekly applications of 16 oz. can be made which would thus increase the maximum use rate per season to 0.10 lbs. ai/A. This discrepancy between the proposed draft label and Section G must

be resolved. Revised Sections B and G should be submitted to resolve this discrepancy.

Nature of the Residue-Plants:

Plant metabolism studies were not submitted with this petition. However, metabolism studies on citrus, celery, and cotton have been reviewed in conjunction with PP#s 5G3220, 5G3287, and 8F3649; and summarized in conjunction with PP#9F3703 (memo, S. Willett, 12/15/89).

CBTS has concluded that the metabolism of avermectin was adequately understood for the above commodities but could not make any conclusions regarding the metabolism of abamectin on plants in general. CBTS further concluded that the metabolism of abamectin in tomatoes was understood based on the use pattern and rate but noted that additional metabolism studies may be needed. Questions remained as to the composition of terminal residues in plants treated with multiple applications of abamectin, with higher application rates then those applied to cotton, celery, citrus, and tomatoes, and/or with long PHIs. The metabolism studies on cotton, citrus, and celery were conducted at rates of 0.6 lbs. ai/A to 2.25 lbs. ai/A. Since the proposed use rate for abamectin on fruiting vegetables is 0.06 lbs. ai/A/growing season, CBTS concludes that the available metabolism data is sufficient and the nature of the residue on fruiting vegetables is understood. The residues of concern are avermectin B_1 and the delta-8,9-isomer.

Nature of the Residue-Animals:

Animal metabolism studies were not submitted with this data package. However, avermectin metabolism in goat and rat has been reviewed. The residues of concern in animals were determined to be avermectin B_1 and the delta-8,9-isomer based on a feeding level of 1.0 mg/goat/day of ^{3}H-avermectin. An additional metabolite (24-hydroxymethyl avermectin B_{1a}) was identified and is potentially of toxicological significance but was not included in the tolerance expression because of its presence at low levels. However, CBTS has noted that if the tolerances for residues in meat and milk need to be raised at some future time due to registration of avermectin on additional feed items, the 24-hydroxymethyl metabolite may need to be included in the tolerance expression and appropriate enforcement methods developed. In addition, new animal metabolism studies using ^{14}C-avermectin would be needed if the expected dietary burden exceeded the dose level in the goat metabolism study. (memos, F. Boyd, 6/21/89, PP#8F3592/8H5550 and G. Herndon, 11/26/91, 1F3973/1H5611).

Based on the theoretical dietary burden of 0.021 ppm, the residue levels are still within the range used in setting the dose

concentrations in the goat metabolism study. Therefore, the ^{3}H-avermectin goat metabolism study is considered adequate to support this use on fruiting vegetables. Finite residues of avermectin are not expected to transfer to poultry and/or swine commodities (see Meat, Milk, Poultry, and Eggs section, this review). The residues of concern in animals remain avermectin B_1 and the delta-8,9-isomer.

Analytical Method-Enforcement:

Enforcement methods are available for avermectin in PAM II for citrus and processed fractions (Method I), ginned cottonseed (Method IA), and bovine tissues and milk (Method II). A method tryout for avermectin in or on pears (Merck method #8000) was completed at the Analytical Chemistry Lab in Beltsville, MD (memo, J. Stokes, 4/16/92). After Merck revised the method, CBTS concluded that Merck method #8000, rev. 4 was adequate for enforcement purposes. The method has been forwarded to FDA to be published in PAM II (memo, G.J. Herndon, 12/16/93, PP#1F3787). Merck Method No. 8004 for determining avermectin residues on peppers (submitted with this petition) is essentially the same as Merck Method No. 8000, Rev. 4. Analytical reference standards for avermectin are available from the Pesticide and Industrial Chemicals Repository, Research Triangle Park, NC.

Merck and Analytical Development Corporation, Colorado Springs, CO have validated Merck Method No. 8004 (HPLC-Fluorescence Determination for Avermectin B_1 and its delta-8,9-isomer in Peppers). Merck obtained samples of bell peppers and jalapeno peppers from a grocery store. The samples were fortified with 5-80 ppb of avermectin B_1 or the delta-8,9 isomer, and residues of avermectin B_{1a} and the delta-8,9 isomer or avermectin B_{1b} were quantitated with Method #8004. The B_{1b} fortification levels were quantitated versus the B_{1a} component from avermectin B_1 standards. Results are summarized in Tables 1a and 1b.

Table 1a. Recoveries of avermectin B_1 fortifications of bell peppers analyzed with Merck Method No. 8004.

ppb added	B_{1a} range (%)	B_{1a} ave (%)	delta-8,9 isomer range (%)	delta-8,9 isomer ave (%)	ppb added	B_{1b} range (%)	B_{1b} ave (%)
5	96-112 (n=6)	103	84-96 (n=5)	91	6	72-121 (n=8)	106
25	96-98 (n=3)	97	72-95 (n=10)	86	--		
70-80	83-105 (n=6)	94	--	--	--		

Table 1b. Recoveries of avermectin B_1 fortifications of jalapeno peppers analyzed with Merck Method No. 8004.

ppb added	B_{1a} range (%)	B_{1a} ave (%)	delta-8,9 isomer range (%)	delta-8,9 isomer ave (%)	ppb added	B_{1b} range (%)	B_{1b} ave (%)
5	94-104 (n=2)	99	82-92 (n=3)	87	6	86-95 (n=3)	90
25	--	--	70-80 (n=2)	75	--		
79	75-84 (n=3)	80	--	--	--		

Recoveries of avermectin B_1 in bell peppers ranged from 72-121%, and for jalapeno peppers from 70-104%. CBTS concludes that adequate methods are available for enforcement of tolerances on peppers. In addition, adequate enforcement methods are available in PAM II for enforcement of tolerances on tomatoes.

Analytical Method-Data Collection:

A description of the method for analysis of avermectin in or on peppers was included with this submission (HPLC-Fluorescence Determination for Avermectin B_1 and its delta-8,9-isomer in Peppers; Method No. 8004) and is essentially the same as Merck method #8000 for pears and apples. Method #8000 has undergone a successful PMV and has been submitted to PAM II for enforcement purposes (PP#1F3787, memos, J. Stokes, 4/16/92 and G.J. Herndon, 12/16/93).

Pepper samples are treated with pectinase and then residues of avermectin extracted with acetonitrile/water. The extract is filtered then passed through a C8 column; the eluant is discarded and the avermectins eluted with acetonitrile. The acetonitrile is concentrated, water added, and the aqueous acetonitrile is extracted with hexane. The hexane extracts are loaded onto an aminopropyl column, the hexane eluant discarded, the column washed with hexane, toluene, and methylene chloride, and the avermectin eluted with 50:50 acetone/methylene chloride. The eluant is then evaporated to dryness, and the residue dissolved and diluted to 10 mL in methylene chloride. The sample is split and evaporated to dryness, then derivatized with N,N-dimethylformamide, trifluoroacetic anhydride, and 1-methylimidazole followed by reaction with methanolic ammonium hydroxide. Derivatized residue is then separated from the reagents on a silica gel column, the eluant is dried and dissolved in methanol. The derivatization allows for reversed-phase HPLC with fluorescence detection. The limit of quantitation for avermectin B_{1a}/delta-8,9 isomer and for avermectin B_{1b} is 5 ppb.

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A description of the method for analysis of avermectin in or on tomatoes was included with PP#9F3703 (HPLC-Fluorescence Determination for Avermectin B_1 and its delta-8,9-isomer in Tomatoes; Method No. 9003, Rev. 1; MRID 408709-15). In conjunction with the permanent tolerance petition, CBTS has concluded that this method is adequate for data collection purposes (memo, S. Willett, 12/15/89). Method validation data indicated method recoveries of ≥70% in the fortification range of 5 ppb to 75 ppb for avermectins B_{1a}, B_{1b}, and the delta-8,9-isomer.

Residues of avermectin B1 and its delta-8,9-isomer are extracted from tomato fruit homogenate with methanol. The filtrate is extracted twice with isooactane and the isooctane discarded. A 10% NaCl solution is added to the methanol extract and this mixture is extracted twice with 0.01% t-butanol in methylene chloride. The combined organic extracts are concentrated, then cleaned-up on an acidic alumina column. The eluant is evaporated to dryness and a fluorescent derivative is formed according to the procedure described for pepper samples. Residues of avermectin B1 and its delta-8,9-isomer are detected with reversed-phase HPLC with fluorescence detection. The limit of quantitation for avermectin B_{1a}/delta-8,9 isomer and for avermectin B_{1b} is 5 ppb.

The derivatization of avermectin B_{1a} and the delta-8,9 isomer for both methods results in the same reaction products. Therefore, the single chromatographic peak of avermectin B_{1a} and its isomer are quantitated by comparing to an avermectin B_{1a} standard curve. The retention time for derivatized avermectin B_{1b} is less than that for avermectin B_{1a}. Nonetheless, residues of avermectin B_{1b} are quantitated against the avermectin B_{1a} standard curve. CBTS has concluded (memo, G.J. Herndon, 12/16/93) that, although not analytically correct, Merck has provided sufficient data to show that the quantitation of avermectin B_{1b} residues with the B_{1a} curve would accurately measure the contribution of B_{1b} in the total avermectin residue up to approximately 100 ppb total. Since the proposed tolerance for fruiting vegetables (tomatoes, peppers, eggplant) is less than 100 ppb (ie: 0.01 ppm), CBTS considers this procedure for quantitation adequate for peppers.

Method #8004 validation for peppers has been done by Merck and the independent laboratory ADC (discussed above). Recoveries were also determined concurrently with the residue analyses of the field trial data. Samples were fortified with avermectin B_{1a} at 5 ppb or 25 ppb. Recoveries ranged from 71-108% at 5 ppb, and 78-102% at 25 ppb (Table 2).

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Table 2. Recoveries of avermectin B_{1a} from fortified field trial samples.

Field Trial	B_{1a} added (ppb)	% recovery	average
001-89-3001R	25	91	
	25	88	
	5	71	83
001-89-3002R	25	81	
	25	78	
	5	88	82
001-90-0009R	25	90	
	25	102	96
001-90-1013R	5	101	
001-90-6011R	25	96	
	25	93	
	5	108	99

Recoveries for this set of validation data were not reported for avermectin B_{1b}. However, adequate recoveries of avermectin B_{1b} were reported in conjunction with the independent laboratory validation (see previous section). Therefore, CBTS concludes that Merck method #8004 has been adequately validated for data collection of avermectin residues in or on peppers. However, as per the instructions of the Analytical Chemistry Laboratory/EPA, the method write-up should be revised so that the term "delta-8,9 isomer" is defined as either 8,9-Z-avermectin B_{1a} or 8,9-Z-avermectin B_{1b}. Although CBTS does not consider this a deficiency, future submissions for avermectin analytical methods should include this terminology.

Storage Stability:

Storage stability studies were not submitted in conjunction with this petition. Pepper samples were frozen the same day as harvest and remained frozen until analysis. Samples were stored from 4 to 20 months prior to analysis. Storage stability data are available for tomatoes, citrus, and celery.

The tomato storage stability data is available for samples stored up to 6 months. Because of low method recoveries for the tomato storage stability studies, CBTS considered reanalysis of tomato residue data as well as citrus storage stability data in the recommendation for a tolerance (PP#9F3703, memo, S. Willett, 12/15/89). Several tomato field samples were reanalyzed after 19 months in storage and residues were found to agree well with the original residue data. In addition, citrus storage stability data indicated that residues of avermectin B_{1a}, the delta-8,9-isomer, and avermectin B_{1b} showed no detectable loss over 12 months of storage (PP#8F3592, memo, V.F. Boyd, 6/21/89). Therefore, CBTS concluded that adequate storage stability data was available to support the residue data of the field trial tomatoes samples which were stored up to 9 months.

Additional storage stability data is available for celery stored up to 24 months (PP#8F3649, memo, S. Willett, 5/4/90). Samples were fortified with avermectin B_{1a}, B_{1b}, and the delta-8,9 isomer. Recoveries were determined at day 0, and 1, 3, 6, 12, and 24 months. Residues were stable (>70% recovery) for the duration of the study.

Because of the demonstrated stability in tomato field samples up to 19 months and in celery up to 24 months, CBTS concludes that adequate storage stability are available and that residues of avermectin are stable in or on peppers up to 20 months. The petitioner should be notified that additional storage stability studies will be needed for the recommendation of tolerances on other, diverse commodities.

Magnitude of Residue-Crop Field Trials:

Field trials were conducted in CA (2), FL, NM, PA, SC, and TX (2) during the 1989 and 1990 growing seasons to determine residue levels of avermectin in or on bell peppers. These field trials adequately represent the geographical distribution of the pepper-growing regions in the U.S. The two field trials in TX were conducted at application rates of 1x (0.02 lb. ai/A) and 2x (0.04 lb. ai/A). All other trials were conducted at the 1x rate. Avermectin was applied at approximately 7 day intervals with 5-11 applications per trial. Samples were collected on the day of the last application (day 0), and at 3 and 7 days after the last application. Residue data was generated for the 0, 3, and 7 day PHIs for one CA trial; for all other trials, residue data was generated for the 0 and 3 day PHIs. Rainfall, irrigation, temperature, and relative humidity data were provided.

Merck has indicated in their report that the data from three field trials (Test Numbers 001-90-1013R (CA), 001-90-1014R (NM), and 001-90-6011R (CA)) from the 1990 growing season were compromised since the percentage of active ingredient at the time of applications could not be confirmed. No further information was given as to why the percentage of active ingredient could not be confirmed. CBTS has contacted Merck (Dr. Lou Grosso, 908-369-3022); Dr. Grosso will address this issue under separate cover in a letter to the Agency. CBTS will consider the results from these field trials for the current review. However, upon receipt of the technical information from Dr. Grosso, the trials may be considered invalid.

Table 3. Avermectin B_1 residues in or on bell peppers.

Field Trial	Application rate[1]	PHI (days)	Maximum residues (ppb)[2] B_{1a}	Maximum residues (ppb)[2] B_{1b}	Ave. B_{1a} Recovery	Total residue (ppb)[3]
001-89-3001R (TX)	0.02 x 10	0	6.9	ND		8.1
		3	NQ	ND		NQ
	0.04 x 10	0	13.4	ND		15.7
		3	NQ	ND	83%	NQ
001-89-3002R (TX)	0.02 x 11	0	10.4	ND		12.3
		3	ND	ND		ND
	0.04 x 11	0	12.8	NQ		15.1
		3	NQ	ND	82%	NQ
001-90-0009R (FL)	0.02 x 5	0	11.2	ND		11.6
		3	NQ	ND	96%	NQ
001-90-1014R (NM)[4]	0.02 x 5	0	NQ	ND		NQ
		3	ND	ND	96%	ND
001-90-0027R (SC)	0.02 x 5	0	NQ	ND		NQ
		3	NQ	ND	96%	NQ
001-90-1013R (CA)[4]	0.02 x 5	0	NQ	ND		NQ
		3	ND	ND	101%	ND
001-90-3042R (PA)	0.02 x 5	0	8.8	ND		8.8
		3	ND	ND	101%	ND
001-90-6011R (CA)[4]	0.02 x 5	0	48.6	NQ		49.1
		3	11.8	ND		11.9
		7	NQ	ND	99%	NQ

[1]Pounds ai/A x number of applications.
[2]NQ = residues of 2-5 ppb; ND = residues below 2 ppb. The LOQ is 5 ppb. Residues were reported as uncorrected for method recovery.
[3]Corrected for average B_{1a} method recoveries less than 100%.
[4]Merck has indicated that the results of these trials are compromised since it cannot be confirmed that the test material contained the correct percent active ingredient at the time applications were made.

Total avermectin residues at a 3-day PHI ranged from ND to 11.9 ppb. The maximum residue was detected in one of the field trials which may or may not be valid (001-90-6011R). The one sample analyzed at a 7-day PHI (#001-90-6011) was at NQ. Avermectin residues were not detected in any of the control samples. CBTS has corrected residue levels for method recoveries reported for the fortified controls run concurrently with the sample analysis. Avermectin B_{1b} recoveries were not reported; however, avermectin B_{1b} residues ranged from ND to NQ. Since Merck and ADC have validated the method for both forms of avermectin, CBTS considers the method adequately validated and has corrected only the avermectin B_{1a} residues for method recovery.

Tomato residue data was submitted in conjunction with PP#3703 (memo, S. Willett, 12/15/89). Residue field trials were

conducted during the 1986 and 1987 growing seasons in Florida (4), California (6), Texas (3), Michigan (2), Pennsylvania (2), South Carolina (1), North Carolina (1), Arkansas (1), and New York (1). Small, medium, and large varieties were represented in the trials. Ground applications were made at rates ranging from 0.01 lbs. ai/A to 0.04 lbs. ai/A (0.5x to 2x), and PHIs of 0 to 14 days. Tomatoes received from 8 to 12 applications at 2 to 14 day intervals. Tomato samples were analyzed for avermectin B1 residues with Merck method No. 9003; residue samples were stored frozen from 1 to 9 months prior to analysis. Residue data at a 1x application rate and 7-day PHI ranged from ND to NQ for non-cherry tomato varieties and from ND to 5.4 ppb for cherry tomatoes. A tolerance of 0.01 ppm for tomatoes has been established.

The petitioner has proposed a tolerance of 0.01 ppm for the crop group of fruiting vegetables. The representative commodities of the fruiting vegetables crop group are tomatoes and peppers. The proposed crop group tolerance will adequately cover residues in or on tomatoes. However, the term "peppers" includes the commodities: bell peppers, chili peppers, cooking peppers, pimentos, and sweet peppers. Residue data is necessary for various sizes of peppers listed under "pepper" as defined by 40 CFR §180.34. Therefore, the petitioner will need to generate residue data for a small variety of pepper before CBTS could recommend for a crop group tolerance. At least three additional field trials would be necessary. These three field trials could replace the three trials of which Merck has raised concerns. Two of the three would need to be conducted in CA if they were intended to replace the three trials in question. At least one non-bell pepper trial is required in New Mexico. CBTS could consider a petition for a tolerance for bell peppers based on the data submitted in conjunction with this petition for the crop group tolerance. The petitioner would need to submit a revised Section F which proposes a tolerance for peppers, bell at 0.01 ppm and address all remaining deficiencies cited in this review.

Processing studies:

Processed commodities of the fruiting vegetables crop group include tomato puree or catsup, tomato juice, wet and dry tomato pomace; there are no processed commodities for the other commodities of this crop group. Processing studies were submitted in conjunction with PP#9F3703 (memo, S. Willett, 12/15/89). CBTS concluded that residues of avermectin did not concentrate in processed foods and that a food additive tolerance was not required. Residues of avermectin were detected in wet and dry tomato pomace, however. A tolerance for these feed items has been established at 0.07 ppm under 40 CFR §186.300. No further processing studies are required for the fruiting vegetable crop group.

Meat, Milk, Poultry, and Eggs:

Tomato pomace is an animal feed item. Dry pomace can comprise up to 25% of beef cattle and 10% dairy cattle, poultry, and swine diets; wet pomace up to 30% of beef and 20% of dairy cattle, but is not used in poultry or swine diets. There are no established tolerances for poultry or swine. However, in conjunction with the petition for a tolerance on tomatoes (PP#9F3703, memo, S. Willett, 12/15/89), CBTS concluded that there was no reasonable expectation of finite residues in poultry and swine commodities. Therefore, poultry and/or swine feeding and metabolism studies were not necessary.

CBTS has calculated a maximum dietary burden on a dry matter (DM) basis (memo, D. Edwards and E. Zager, 7/12/93) for cattle fed a hypothetical diet of tomato pomace, cottonseed, and cottonseed meal. Avermectin residues would be present on 60% of the feed items of this hypothetical diet.

25% tomato pomace/92% DM at 0.07 ppm = 0.019 ppm
25% cottonseed/88% DM at 0.005 ppm= 0.001 ppm
10% cottonseed meal/89% DM at 0.005 ppm= 0.001 ppm

The theoretical dietary burden is 0.021 ppm.

Tolerances were established for cattle meat and meat byproducts at 0.02 ppm and for milk at 0.005 ppm, but expired on March 31, 1993. In conjunction with PP#7G3468 (memo, L. Cheng, 5/6/87), CBTS (then RCB) recommended that a tolerance for avermectin on cattle fat be proposed at 0.01 ppm. This recommended tolerance level was then increased to 0.015 ppm in response to the petition for a tolerance in or on almonds, meat and hulls (PP#1F3973, memo, J. Herndon, 11/26/91). These levels were based on data from a study where cattle were fed 10, 30, or 100 ppb avermectin (memo, V.F. Boyd, 6/21/89).

The theoretical dietary burden of 21 ppb does not exceed the highest feeding level; a new ruminant feeding study will not be required. The previously established meat and milk tolerances would have covered residues found in meat, milk, and meat byproducts at the highest feeding level. Either RD needs to reinstate these tolerances or the petitioner should repropose their establishment. In addition, the petitioner should submit a revised section F proposing the 0.015 ppm tolerance on fat, cattle. Also, if avermectin tolerances are established on additional feed items, the theoretical maximum dietary burden could exceed 100 ppb. In this case, a new feeding study may be required. Merck is reminded that the feeding levels for a new feeding study must be calculated on a dry matter basis (see memo, D. Edwards and E. Zager, 7/12/93).

Other Considerations:

An International Residue Limit status sheet is attached. Codex limits for the sum of avermectin B_{1a}, it's delta-8,9 isomer and avermectin B_{1b} have been established for tomatoes and sweet peppers at 0.02 ppm. No Canadian or Mexican limits have been established. For EPA to harmonize residues with Codex, the established (tomatoes) and proposed (fruiting vegetables) tolerances would need to be increased to 0.02 ppm. The tolerance expression would not need to be changed. An increase in the tolerance for the purposes of harmonization would need to be based on toxicological considerations.

cc:RF, PP#3F4258, Circ., M.Peters.
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5709C:MHP:mhp:CM#2:Rm804C:703/305-6380:5/17/94.