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OFFICE OF
PESTICIDES AND TOXIC SUBSTANCES

MEMORANDUM

SUBJECT: PP# 9F3703/9H5570. Abamectin (Avermectin B_1) on Tomatoes. Evaluation of Analytical Methodology and Residue Data. MRID Nos. 408709-00 thru -20. DEB Nos. 4627, 4628, 4629.

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)

Merck Sharp and Dohme is requesting the establishment of tolerances for abamectin (avermectin B_1) and its delta 8,9-isomer in tomatoes, wet tomato pomace, and dry tomato pomace at 0.005, 0.01 and 0.07 ppm, respectively.

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. A tolerance on celery is pending (PP# 8F3649). Several emergency exemption requests have been granted.

No Registration Standard has been prepared for abamectin.

Conclusions

1. The manufacturing process of technical grade avermectin has been adequately described. There is no concern for any of the probable impurities. All inerts in the formulation intended for use on tomatoes have been cleared.

2. The proposed label is adequate. The residue data adequately reflect the proposed use.

3. The nature of the residue in plants and animals is adequately understood for the purposes of the proposed use on tomatoes. Avermectin B_1 and its delta-8,9 isomer are the residues to be regulated in plant and animal commodities. Additional metabolism studies may be needed to support additional tolerances.

4. Methodology for avermectin B_1 and its delta-8,9 isomer has been validated by the agency and is adequate for enforcement purposes. Avermectin has been subjected to testing under FDA multiresidue protocol methodology.

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.

6. The established tolerances in animal commodities are adequate to cover the probable levels of avermectin that are likely to result from the proposed use on tomatoes.

7. An International Residue Limit status sheet is attached to this review. There are no Codex, Canadian or Mexican tolerances established for avermectin.

Recommendations

DEB recommends against the establishment of tolerances of abamectin on tomatoes because the proposed tolerance of 0.005 ppm is inappropriate. The proposed tolerance on tomatoes (RAC) should be increased to 0.01 ppm. Also, there is no need to propose a separate tolerance for wet tomato pomace. DEB could recommend for the establishment of tolerances on/in tomatoes and tomato pomace if Section F of the petition were revised.

Detailed Considerations

Manufacture and Formulation

The manufacturing process of abamectin, produced by a fermentation process using a strain of Streptomyces avermitilis, has been previously described (see memo of L. Cheng dated 5/1/86). The technical product is a mixture of AVM B_1a and AVM B_1b where the

ratio is >80:20. The technical material is about 95% AVM B_1 and contains about 0.5% of other AVMs of elucidated structures. The technical also contains about 1% of unidentified impurities related to the AVMs. There are not toxicological concerns for any of the AVM-related impurities (see PP# 5G3287, memorandum of W. Dykstra, 3/3/86).

The formulation proposed for use on tomatoes is AGRI-MEK 0.15 EC. One gallon of the EC contains 0.15 lb active ingredient. All inerts have been cleared for use under 40 CFR 180.1001 (see PP# 6G3320, memorandum of A. Smith dated June 23, 1986).

Proposed Use

For control of dipterous leafminers, mites and tomato pinworm, the label specifies application as a foliar spray when infestation first appears at a rate of 8 to 16 oz formulation/acre (0.01 to 0.02 lb ai/acre/application), with a maximum yearly application 0.2 lb ai/acre. An application interval of 7 days is specified for control of leafminers. For control of mites and pinworms, no application interval is specified. The PHI specified is 3 days for all varieties except cherry tomatoes, where the PHI is 7 days.

The proposed label is adequate. The residue data adequately reflect the proposed use.

Nature of the Residue

Plants

No new plant metabolism data were submitted with this tolerance request. Metabolism data have been previously submitted on celery, cottonseed and citrus in support of other tolerance requests (PP#'s 5G3220, 5G3287, and 8F3649). The petitioner has submitted a discussion of results of studies to determine the metabolic fate of avermectin. The report is entitled "Comparative Degradation of Avermectin B_1a in Cotton Leaf, Citrus Fruit, Celery and In Vitro" (MRID No 408709-19). The degradation of ^{14}C- or ^{3}H-avermectin B_1a on citrus fruit, cotton leaves, and celery from plants exposed to sunlight was compared to ^{14}C-avermectin B_1a degradation on glass under simulated sunlight by HPLC analysis of the residues.

Approximately 100 ug of ^{14}C-B_1a was applied to cotton leaves with a micropipette. Plants were protected during periods of inclement weather and the leaves harvested at 2, 4, and 8 days post treatment. Plant leaves were subjected to a surface rinse with methanol, followed by extraction with 10% aqueous acetone. The methanol rinses and aqueous acetone extracts of cotton leaves were stored in a freezer prior to assay (see also memo of C. Deyrup dated 7/29/87).

A group of mature celery plants were treated with 10 weekly applications of 3H-B_1a, equivalent to 0.1 lb ai/A. A second group of mature plants were treated with 14C-B_1a at a rate equivalent to 0.015 lb ai/A. The pesticide was applied with a syringe. Plants were protected during periods of freezing temperatures and were harvested at 0 or 7 days after the last application. The leaves and stalks from three 3H-B_1a-treated celery plants were extracted with acetone and stored frozen prior to assay (see also memo of V.F. Boyd dated 11/16/88).

Nearly mature Hamlin oranges were treated with 14C-B_1a by applying with a brush 0.5 ml of an aqueous suspension in EC formulation containing 0.006 mg/ml (1X maximum use rate on citrus, which is 0.075 lb ai/A), or 0.18 mg/ml (30X maximum use rate, or 2.25 lb ai/A). Oranges were harvested at 1 and 2 weeks post application. Surface residues were removed from the fruit by rinsing with methanol. The individual rinses from each orange were stored separately in a refrigerator prior to HPLC assay. A composite sample from rinses of 5 to 10 oranges was used for the HPLC assay. This experiment was conducted in order to generate degredates to be used for toxicity testing (see memo of V.F. Boyd dated 2/13/89).

To produce <u>in vitro</u> degradates, 8 ml aliquots of a methanol solution of ^{14}C-B_1a, containing approximately 115 mg abamectin was placed in two glass petri dishes and allowed to dry at room temperature. The dishes were then placed under artificial light located 66 cm from the dish bottoms and contained in a fume hood. After 2 hours of continuous illumination the amount of light was decreased for the remainder of the experiment. After 19 hours, 1 dish was removed from the light, the abamectin film was solubilized in 5 ml methanol, an aliquot removed, and the remaining methanol solution contained in the dish was allowed to dry again at room temperature. The dish was replaced beneath the light as before. This process was repeated at 30, 60, and 137 hours. The temperature under the lights was about 50°C. A control dish not exposed to light and containing about one half of the material of the light-exposed dishes was run in parallel. An experiment similar to the one above was performed except that 5 mg ^{14}C-B_1a was used per petri dish and the material was removed from the light after 2 hours.

The avermectin B_1a residues in methanol rinses of ^{14}C-treated citrus fruit, cotton leaves, or petri dishes or acetone extracts of ^{14}C- or ^{3}H-B_1a-treated celery were cochromatographed with standards by reverse phase HPLC (two different columns) using a methanol/water gradient. This HPLC analysis was used to broadly classify and quantitate B_1a residues as polar, moderately polar, B_1a, and D-8,9. Avermectin residues were also fractionated by RPHPLC for further HPLC characterization. The polar residues of plant surface, petri dish rinses, or plant homogenates were rechromatographed on 2 different HPLC systems: C18HPLC using a methanol/water solvent gradient; and DIOLHPLC and a cyclohexane/1-butanol gradient. The

moderately polar B_1a residues were rechromatographed by SIHPLC with 8-OH and ^{3}H-OH standards eluted with a isooctane/ethanol solvent gradient. Typical radiochromatograms from all analyses were submitted.

Rechromatography of moderately polar B_1a residues from in vitro photolysis, cotton leaf rinse, citrus fruit rinse, and celery leaf by SIHPLC indicated the presence of at least 2-6 components. At least 1 moderately polar residue from each plant cochromatographed with added 8-OH standard. This degradate has been identified as a rat metabolite. The contribution of moderately polar B_1a residues to the total residue at 7 to 8 days post-application was 4-7% in citrus fruit or cotton, and therefore no single moderately polar residue contributes significantly to the total residue. The proportion of moderately polar residues in celery stalk and leaves was higher at 0 and 7 days post application than in cotton or citrus. It has been shown that no single moderately polar residue contributes significantly to the total residue in celery (see PP# 8F3649, memo of V.F. Boyd dated 11/16/88).

The polar residues obtained by isocratic C18HPLC of the total residues remaining after 19, 30, 60 and 137 hr photolysis of B_1a in vitro were rechromatographed by C18HPLC using a step gradient. Four broad peaks of radioactivity eluted which corresponded to changes in solvent composition. The early eluting peaks contain degradates which have been characterized by NMR and MS as being unlike avermectin. The greatest change in polar residues in vitro occurred between 19 and 30 hours, with relatively little change in polar residues after 30 hours. Avermectin represents about 7% of the total residue after 30 hr photolysis.

Reverse phase HPLC of polar B_1a residues from cotton leaf rinse indicated that with increasing post-B_1a application there was a reduction in the late-eluting peak and an increase in the early eluting peak with only slight changes in the polar residues profile from 4 to 8 days. Chromatography of the polar residues from cotton leaf homogenate (obtained after approximately 50% of extractable residues were removed by rinsing the leaf surface) 8 days post-B_1a application indicated similarity with the surface rinse at the same time except for an increase in the early-eluting peak for the leaf homogenate. The petitioner contends that the polar cotton residues at 8 days are very similar to those obtained after 30 hr photolysis in vitro.

The polar residues from citrus fruit did not appear to change greatly from 7 to 14 days post application as determined by step gradient C18HPLC. In general there were slightly more early eluting peaks and slightly less late-eluting residues in the 1X treatment group as compared with the 30X treatment group, especially at 7 days post-application.

The C18HPLC radioprofile of polar residues in the acetone extract of ^{3}H-B_1a-treated celery stalk harvested on the same day as the last of 10 applications did not closely resemble polar residues at the earliest time points for in vitro photolysis (19 hr) or cotton leaf (2 days), but were comparable to those obtained at later point for in vitro photolysis, cotton and citrus. There was considerably more degradation of B_1a in Day 0 stalk from ^{14}C-treated (0.015 lb ai/A) plants vs ^{3}H-B_1a treated (0.1 lb ai/A; 5X) plants. Little change in acetone-extractable polar residues in celery stalk was observed from 0 to 7 days after the last ^{14}C-B_1a application. As with stalks from ^{14}C-B_1a-treated plants there appeared to be little change in polar residues from celery leaf 0-7 days after the last pesticide application. The polar residues from the ^{3}H-B_1a-treated celery leaf were also similar to those of leaf from the ^{14}C-B_1a treated plants. HPLC radioassay of polar residues from celery stalk and leaves indicated similarity to those from cotton leaf, citrus fruit, and in vitro at later time points. Cochromatography of polar residues from ^{3}H-B_1a-treated celery leaf with those from ^{14}C-B_1a treated citrus fruit or ^{14}C-B_1a-treated cotton leaf by C18HPLC resulted in co-elution of 4 major peaks of radioactivity.

Rechromatography by step gradient DIOLHPLC of polar residues obtained after 30 hr photolysis of B_1a in vitro resulted in 3 broad peaks of radioactivity corresponding to changes in solvent composition. The late eluting peak was split and tailed to nearly the end of the chromatogram indicating the complexity of the degradation products. DIOLHPLC of polar residues from cotton leaf surface rinse also resulted in 3 broad peaks. Increased residues were apparent in the early eluting peak for day 4 and day 8 cotton leaf rinse samples, compared to the 30 hr in vitro sample. The two early-eluting major peaks were of relatively constant proportion to each other during the time course of B_1a degradation on cotton while the late-eluting major peak appeared to broaden with time. The late eluting peak of the 2 day cotton leaf sample did not tail as severely in contrast to the polar residues obtained in vitro. DIOLHPLC of polar residues from citrus harvested 7 days post treatment also resulted in three broad peaks. There were somewhat less early-eluting polar residues in the 1X citrus fruit and the late eluting peak was somewhat broader when compared with the 30X sample at 1 week post-application. There were apparently increased residues in the early-eluting peak for day 14 citrus fruit rinse, 30X. The DIOLHPLC radioprofile of polar residues from day 14 1X and 30X citrus fruit was comparable to that of the in vitro system, according to the petitioner. The DIOLHPLC radioprofile of polar degradates from 30X citrus 2 weeks post application was similar to that of cotton leaf rinse 4 days post application. The late eluting peak for 1X orange fruit at 2 weeks post-application was split and tailed to the end of the chromatogram as with cotton and in vitro samples. DIOLHPLC radioprofiles from both 0 and 7 day celery leaf were close to those obtained in vitro and on citrus fruit. There was an apparent increase in ^{14}C-polar residues from Day 0 celery leaf in the early-eluting peak as for Day 4 cotton

leaf rinse and Day 14 citrus fruit, compared with other time points in the 3 plants. The DIOLHPLC radioprofile of celery leaf polar residues from ^{3}H-B_1a-treated plants 7 days post application resembled that from the in vitro system as well as Day 4 cotton leaf.

From these experiments the petitioner concludes that:

1) The degradation of avermectin B_1a on plants or in vitro appears to be similar and results in a complex residue.

2) At least 2 avermectin B_1a degradates were formed in all systems examined; the conformational isomer of the parent compound, delta-8,9 avermectin B_1a, and an oxygenated product of the parent compound, 8-alpha hydroxy avermectin B_1a.

3) When the proportion of avermectin B_1a is less than about 10-15% of the total remaining residue, which usually occurred in a week or less post-application in plants, most of the remaining residue is present as unidentified multiple polar compounds which appear to degrade slowly with extended exposure to sunlight.

According to the petitioner, the studies further indicate that photodegradation on exterior surfaces rather than metabolism is the major pathway for B_1a disposition in plants. The progression from B_1a to polar degradates in the presence of light (and oxygen) may involve intermediate species which are present in a steady-state as long as B_1a remains available for degradation and these intermediates are further degraded to a complexity of forms which are considerably more polar than the parent compound. This complexity of extensively degraded components and the very low level of total residues remaining in abamectin-treated plants at typical post harvest intervals argues **prima facie** against any significant concentration of toxic degradates.

DEB previously concluded, as did the petitioner, that the metabolism of abamectin in plants is very complex. The majority of the terminal residue is composed of several unidentified polar degradates. The parent compound, its delta-8,9 isomer, the alpha 8-OH degradate have been identified in plants, with only the parent and its delta isomer each accounting for 10% or more of the total residue. The petitioner has submitted experimental data to show that the residues present in citrus surface rinses, celery extracts, and cotton leaf rinses and extracts at typical PHI's are similar to in vitro photodegradation products. To support the uses on cotton and citrus, the polar degradates generated on citrus (30X, 7 day PHI) and in vitro (30 hr sample) have be tested for toxicity and were found to be of no toxicological significance at the levels tested (see TOX memos 007080 and 007801 of W. Dykstra dated 3/13/89, and DEB memo of F. Boyd dated 6/21/89).

The proposed use on tomatoes specifies multiple applications, up to 10, and a maximum application rate of 0.2 lb ai/year. DEB can surmise from the metabolism study where celery received 10 applications of radiolabeled abamectin, in 7 day intervals for a total equivalent to 1.0 lb ai/A, and the exaggerated application to citrus (30X, 2.25 lb ai/A) that the proposed use on tomatoes probably will not produce, to any large extent, components that have not already been produced and subjected to toxicity testing. The growing season for tomatoes is 100 to 120 days, comparable to celery (115 to 135 days), and the post harvest interval is short, 3 or 7 days. DEB concludes that metabolism data are sufficient to support the use on tomatoes. The residues to be regulated are the parent and the delta 8,9 isomer.

DEB does not agree with the petitioner's conclusion that the experiments discussed here cumulatively indicate that abamectin is degraded on all plants in a similar manner. The metabolism of abamectin is admittedly complex and will probably need to be studied further. Photodegradation on the exterior of plant surfaces is not the only transformation taking place on plants, and may not necessarily be the major degradative pathway at some time point, and under certain conditions. This is indicated by the fact that a significant amount of the activity was not removed by surface rinse of cotton leaves (compare 8 day cotton leaf surface rinse to 8 day cotton leaf extract after surface rinse). Also, radiolabeled abamectin has also been extracted from citrus pulp and peel in experiments reported earlier, and as the amount of surface residues removed by the surface rinse decreased, the amount retained by the pulp increased (see memo of L. Cheng dated 12/19/85). Radioactive residues have also been detected in plants grown in soil treated with radiolabeled abamectin, although none were identified (see EFGWB report dated 9/10/87). Questions remain 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. Could the moderately polar residues ever be present in significant amounts? What is the rate limiting factor of photodegradation of abamectin on plants? Since we have no idea as to what the future uses of abamectin might be, DEB cannot make any final conclusions regarding the metabolism of abamectin in **plants**. The petitioner should be prepared to conduct additional plant metabolism studies on other crops to support future uses, particularly if the use patterns differ significantly from those of cotton, celery, citrus and tomatoes. In future studies, treatment should more closely simulate actual uses (e.g. incidental application to soil, and moderate rainfall). The account of the total radioactivity should be improved. A ^{14}C-labeled compound should be used.

Animals

No additional animal metabolism study data were submitted with this petition.

Rat metabolism data were submitted in conjunction with PP#'s 4F3065, 5F3287, and 7G3468. The major metabolite identified in rats was 3" desmethyl AVM, with a minor metabolite (<10%) of the TRR identified as 24-hydroxymethyl. Since the delta 8,9-isomer is a degradation product of AVM found in plants and not in animals, its metabolism in rats has been investigated. Metabolites analogous to those detected in the AVM study were found, namely the corresponding 24-hydroxymethyl and 3" desmethyl isomers. The delta-8,9 isomer and its metabolites accounted for 92 to 98% of the extractable activity from rat tissues.

Data from a goat metabolism study have previously been reviewed (PP# 7G3468, memo of L. Cheng dated 2/11/87). Three groups of two goats were fed 0.005, 0.05 and 1 mg ^{3}H-avermectin B_1a per day for 10 consecutive days. A total of 99% of the radiolabeled dose was excreted in the feces with ca. 70% as B_1a, 20% as the 24-hydroxymethyl and 5% as 3"-desmethyl compound. The residue levels in tissues and organs at the higher dose rate of 1 mg/day are given below:

Tissue	ppb, B_1a equivalents
liver	98, 16.4
kidney	22.7, 4.8
peripheral fat	50, 7.6
omental fat	49.3, 6.8
leg muscle	7.6, 1.7
loin muscle	9.9, 1.2

Undegraded avermectin accounted for the majority of the residue (37-99%) with the 24-hydroxymethyl metabolite being the major metabolite (<1-43%). Residues in milk in the two goats dosed at 1 mg/day plateaued at day 7 at a maximum of 4.71 ppb. Residues were characterized and consisted of 79 to 92% unchanged avermectin and 2 to 11% of the 24-hydroxymethyl metabolite.
Although not preferred, the ^{3}H-B_1a study was accepted in support of the uses on cotton and citrus since sufficient specific activity could not be obtained using a ^{14}C-label. The maximum dose rate in the ^{3}H-label study was equivalent to 20 times the levels expected in feed items from the either of the proposed uses (see memo of V.F. Boyd dated 6/21/89). The levels expected in animal feed items from tomatoes are lower than those expected in citrus pulp. Since the dietary burden to livestock will most likely not be increased as a result of this proposed use, the goat metabolism study is acceptable in support of this tolerance proposal (see memo of V.F. Boyd dated 6/29/89, and discussion on probable secondary residues

in this memo). The compounds to be regulated in animal commodities are the parent and its delta-8,9 isomer. The petitioner is reminded that if registration is proposed on additional feed items such that the dietary burden to livestock is increased, a new goat metabolism study with elevated feeding levels and use of a ^{14}C-label may be required.

Analytical Methodology

The analytical methodology has been described in previous DEB memos (see memoranda of L. Cheng, 2/11/87, and V.F. Boyd dated 11/16/88). Residues of avermectin B_1 and its delta-8,9 isomer are extracted with organic solvent, derivatized, and quantified by reverse phase HPLC using a fluorescence detector. The detection limit ranges from 1 to 10 ppb, depending on the commodity.

Method validation of analytical methodology to determine residues of avermectin and its delta-8,9 isomer in plant and animal commodities have been conducted by the agency. Both Merck Method 1009R3 (citrus methodology) and Method 32A (animal commodities) were determined to be adequate for enforcement purposes (see method evaluation reports of V.F. Boyd dated 9/2/88, and S.H. Willett dated 9/11/89). The methodology was recently sent to the FDA for publication in PAM II (see memo of S.H. Willett, 9/21/89). In the interim, the methodology may be obtained from PIB/FOD.

Avermectin has been tested using methodology described in PAM I, multiresidue method protocol A, which is the only applicable protocol. The data from the MRM study has been forwarded to FDA for evaluation (see memo of V.F. Boyd, 6/21/89).

Residue Data

Data from twenty-one field studies were submitted in support of the tolerance proposal on tomatoes. Trials were conducted 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. Field trials were conducted during the 1986 and 1987 growing seasons. Application was made using ground equipment at rates ranging from 0.01 lb ai/A to 0.04 lb ai/A (0.5 to 2X), and post harvest intervals from 0 to 14 days. Tomatoes received 10 applications of avermectin at 2 to 14 day intervals, typically 7 days. Exceptions were one test conducted in Michigan, where tomatoes received only 8 applications, but the total amount of active ingredient was 1 or 2X, and one test in Florida where tomatoes received 12 applications for a total of slightly more than 0.5 and 1X. Samples were frozen immediately after harvest, and remained frozen until analyzed (< 0°C). Residue samples were stored for 1 to 9 months prior to analysis.

An interim report on a 2 year storage stability study was submitted (MRID No. 40870914). Control tomato samples were fortified at approximate levels of 10 ppb of B_1a and the delta 8,9 isomer, and 50 ppb. Samples were analyzed using Merck Method 9003 (essentially the same as enforcement method) after 0 days, 1, 3 and 6 months of storage. The recovery data are summarized in the table that follows.

Table I. Storage Stability Data for Abamectin

Approx. Amount Added (ppb)	Sampling Interval	% Recovery
10, B_1a	0 days	46-65
	1 month	72-79
	3 months	59-68
	6 months	57-64
10, delta 8,9 isomer	0 days	63-72
	1 month	49-52
	3 months	26-61
	6 months	43-53
50, B_1a	0 days	75, 77
	1 month	57, 69
	3 months	59, 63
	6 months	69, 63

A set of fresh spiked samples were analyzed with each analysis set of storage stability samples. The average recoveries of these samples analyzed with the 0 day, 1, 3, and 6 month samples were 71, 77, 69 and 62%. Reanalysis of incurred residue samples from study 301R from 0 day samples at both application rates and from day 7 from the 2X rate occurred 19 months after the initial analyses. The reassayed values agreed well with values initially obtained.

All residue samples were analyzed using Merck Method No. 9003 which quantifies B_1a and the delta 8,9 isomer as a single component. Validation data have been submitted which indicate that method 9003 adequately quantifies residues of B_1a and its delta 8,9 isomer in the range of 5 to 75 ppb, as indicated by the acceptable recoveries of $\geq$ 70% (MRID No. 408709-16, -17, -20). The method is also capable of quantifying levels of avermectin B_1b and its delta 8,9 isomer. Additionally, fortified samples were analyzed with each analytical set, and recoveries were acceptable. A summary of the residue data follows.

Table II. Field Trial Residue Data for Avermectin B_1a and its Delta-8,9 isomer on Tomatoes

Study No./ Location	Sample Interval Days	0.5X Rate Residues[1]	1X Rate Residues	2X Rate Residues
030R, Florida	0	ND-NQ[2]	NQ-NQ	NA[3]
	1	ND-ND	ND-ND	
	3	ND-ND	ND-NQ	
	5	ND-ND	ND-ND	
	7	ND-ND	ND-ND	
031R, Florida	0	ND-NQ	ND-5.4	NA
	1	ND-ND	ND-6.0	
	3	ND-ND	ND-ND	
	5	ND-ND	ND-ND	
032R, Florida	0	NA	ND-7.8	9.5-24.1
	1		ND-NQ	NQ-11.6
	3		ND-NQ	NQ-9.6
	5		ND-ND	ND-NQ
	7		ND-NQ	ND-NQ
	14		ND-ND	ND-NQ
033, Florida	0	NA	6.5-11.8	8.7-24.5
	1		ND-NQ	5.6-6.1
	3		ND-NQ	NQ-NQ
	5		ND-ND	ND-NQ
	7		ND-ND	ND-NQ
	14		ND-ND	ND-ND
148R, CA	0	NA	05.4-9.6	15.1-33.5
	1		NQ-NQ	6.6-9.1
	3		ND-NQ	NQ-9.7
	5		ND-NQ	NQ-9.9
	7		ND-ND	NQ-NQ
	14		ND-NQ	ND-NQ
149R, Michigan	0	NA	ND-NQ	NQ-6.7
	1		ND	NQ
	3		ND	ND
301R, PA	0	NA	8.0-13.7	ND-35.0
	1		NQ-5.6	8.9-12.1
	3		ND-ND	ND-NQ
	5		ND-ND	ND-ND
	7		ND-ND	ND-5.9
559R*, CA	0	NA	NQ-29.7	20.2-32.6
	1		NQ-6.3	8.6-14.8
	3		NQ-7.5	7.0-13.8
	5		NQ-6.2	7.3-11.3
	7		NQ-5.4	5.8-9.9
	14		ND-NQ	5.9-13.4
672R, Texas	0	NA	5.1-8.6	8.0-13.2
	1		ND-ND	ND-ND
	3		ND-ND	ND-ND
	5		ND-ND	ND-ND
595R, CA	3	NA	ND-NQ	NQ-9.1

Table II. Field Trial Residue Data for Avermectin B_1a and its Delta-8,9 isomer on Tomatoes

Study No./ Location	Sample Interval Days	0.5X Rate Residues[1]	1X Rate Residues	2X Rate Residues
0010R, SC	0	NA	6	18.8
	3		ND	NQ
0011R, NC	0	NA	NQ	12.3
	3		ND	ND
1000R, CA	0	NA	ND	6.5
	3		ND	ND
	5		ND	ND
	7		ND	ND
1011R, CA*	0	NA	25.2	84.7
	1		20.0	57.3
	3		12.6	36.4
	7		NQ	21.2
	10		NQ	8.5
3004R, *	0	NA	NQ	6.3
	3		ND	ND
	7		ND	ND
	10		ND	ND
3012R, TX	0	NA	NQ	9.2
	3		ND	ND
3036R, TX	0	NA	NQ	9.1
	3		ND	ND
5024R, MI	0	NA	NQ	22.1
	3		ND	ND
5025R, NY	0	NA	16.7	25.7
	3		NQ	6.7
5026R, PA	0	NA	NQ	8.0
	3		ND	ND
6001R, CA	0	NA	8.7	18.0
	3		ND	NQ

1 - ppb
2 - NQ = not quantitated, values between 2 and 5 ppb
ND = not detected, values less than 2 ppb
3 - not applicable
* - cherry tomato variety

Residue levels in tomatoes from 1986 field trials (denoted by 3 digit trial numbers) were determined by analyzing 4 replicate samples. Residue levels in tomatoes in 1987 field trials were determined by analyzing composite samples. No quantifiable levels of avermectin B_1b were found in any tomato samples harvested at the proposed PHIs.

The petitioner has submitted processing study data. Tomatoes from trial number 595R which were treated at 2X and harvested 3 days after the last treatment were processed and residues of abamectin in the various fractions were determined. The following data were submitted.

Table III. Summary of Results from Tomato Processing Study

Sample	ng/g or ng/ml B_1a/delta 8,9	ng/g or ng/ml B_1b/delta 8,9
RAC	NQ-9.1	ND-ND
fresh whole tomato*	NQ	ND
washed whole tomato	ND	ND
wash soak water	ND	ND
wash rinse water	1.3	ND
canned puree	ND, ND	ND, ND
wet pomace	16.2, 16.4	ND, ND
dry pomace	93.5, 116	9.5, 12.5

* composite of RAC samples
ND = Non detected (<2 ng/g or 0.1 ng/ml)
NQ = Not quantitated 2-5 ng/g

Fresh tomatoes were processed immediately. Samples of tomato processing fractions were stored frozen for up to one year before analyses.

DEB concludes that the residue data submitted are adequate. Although the storage stability study data on tomatoes is in insufficient since the duration of the study is shorter (6 months) than the length of time that some of the samples were stored (up to 1 year), DEB can translate from the storage stability data on citrus and conclude that avermectin B_1 and its delta 8,9 isomer are stable in frozen storage (see memo of V.F. Boyd dated 6/21/89). We note also that the storage stability data on tomatoes is only marginally acceptable since reported recoveries are low. It appears that problems are associated with those particular analyses (e.g. incomplete derivatization) rather than methodology, since recoveries of same day spiked samples are low.

No quantifiable residues were found in any tomato samples treated at the 1X rate and harvested at the proposed PHI of 3 or 7 days, except in one field trial on cherry tomatoes conducted in California (559R), where one of the 4 replicate samples analyzed contained 5.4 ppb B_1a/delta-8,9 isomer. No quantifiable residues were found in any of the tomatoes treated at the 1X rate and harvested after the proposed PHIs. However, residue levels in

cherry tomatoes treated at 2 times the maximum label rate and harvested at the proposed PHI of 7 days were as high as 21.2 ppb (1011R), and 13.4 ppb B_1a/delta 8,9 isomer were detected in cherry tomatoes harvested 14 days after the last treatment (559R). The data indicate that the proposed tolerance of 0.005 ppb on tomatoes may be inadequate, particularly for cherry tomatoes. A more appropriate tolerance level would be 10 ppb. This should be reflected in a revised Section F. Since abamectin does not appear to concentrate in tomato processed food items, no food additive tolerance is required.

Residue levels of B_1a/delta 8,9 in tomatoes used for processing ranged from NQ to 9.1, and B_1b residues were ND (see table III above). The highest level of B_1a residues in wet pomace from tomatoes treated at 2 times the maximum label rate was 0.0164 ppm, with no detectable B_1b residues. The highest level of B_1a residues in dry pomace of tomatoes treated at 2 times the maximum label rate was 0.116 ppm, with 0.0125 ppm B_1b detected in the same sample. The petitioner has proposed tolerances of 0.010 ppm in wet tomato pomace and 0.070 ppm for dry tomato pomace.

DEB concludes that a feed additive tolerance of 0.070 ppm for tomato pomace is appropriate based on the concentration observed in the processing study. We note that cherry tomatoes are not typically processed (see memo of Y. Hopkins dated 3/10/88). No distinction between wet and dry tomato pomace is necessary. This should be reflected in a revised Section F.

Secondary Residues in Meat, Milk, Poultry and Eggs

Tomato pomace is an animal feed item. Wet pomace may comprise up to 3% of the poultry diet, and 10% of the swine diet. Dry tomato pomace may comprise up to 25% of the cattle diet. The maximum contribution of abamectin in the animal diet expected from this proposed use is 0.018 ppm.

DEB recently recommended for the establishment of tolerances of 0.02 ppm in cattle meat and meat byproducts, and 0.005 ppm in milk. These levels were based on data from a study where cattle were fed up to 100 ppb of avermectin (see memo of V.F. Boyd dated 6/21/89). These tolerances are adequate to cover the secondary residues expected in cattle commodities as a result of the proposed use on tomatoes. There is no reasonable expectation of finite residues in poultry and swine commodities, therefore no tolerances are necessary at this time.

Other Considerations

An International Residue Limit status sheet is attached to this review. There are no Codex, Canadian or Mexican limits established for abamectin. Therefore no compatibility problems exist.

Attachment: IRL Status Sheet

cc: PP#9F3703/9H5570, Willett, RF, PMSD/ISB (Eldredge)

CM2:H7509C:RM810C:X1439:SHWillett:shw-11/20/89
RDI: D.E. Edwards, 12/14/89; R. Loranger, 12/14/89

Attachment 1

F. Kiss 11/27/89

INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL abamectin

CODEX NO. _____

CODEX STATUS:

☑ No Codex Proposal Step 6 or above

Residue(if Step 8): _____

Crop(s)	Limit (mg/kg)

PROPOSED U.S. TOLERANCES:

Petition No. 9F3703/9H5570

RCB Reviewer S. H. Willett 11/20/89

Residue: abamectin * and its delta 8,9-isomer

Crop(s)	Limit (mg/kg)
tomatoes	0.005
tomato wet pomace	0.01
tomato dry pomace	0.07

CANADIAN LIMITS:

☑ No Canadian limit

Residue: _____

Crop(s)	Limit (mg/kg)

MEXICAN LIMITS:

☑ No Mexican limit

Residue: _____

Crop(s)	Limit (mg/kg)

NOTES: