PP# 7F4844
9-16-98

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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

DATE: 9/16/98

SUBJECT: PP# 7F4844 AVERMECTIN. Request for Tolerances on Grapes, Raisins, and Peppers. Evaluation of Analytical Method and Magnitude of the Residue Data.

DP Barcode: D238327 PRAT Case#: 288940
PC Code: 122804 Caswell#: 063AB
Trade Name: AGRI-MEK EPA Reg#: 618-98
Class: Insecticide 40 CFR: §180.449
MRID: 443000-00 to -03, 443460-01

FROM: William D. Cutchin, Chemist
Registration Action Branch 2
Health Effects Division (7509C)

THRU: Richard Loranger, Branch Senior Scientist
Registration Action Branch 2
Health Effects Division (7509C)

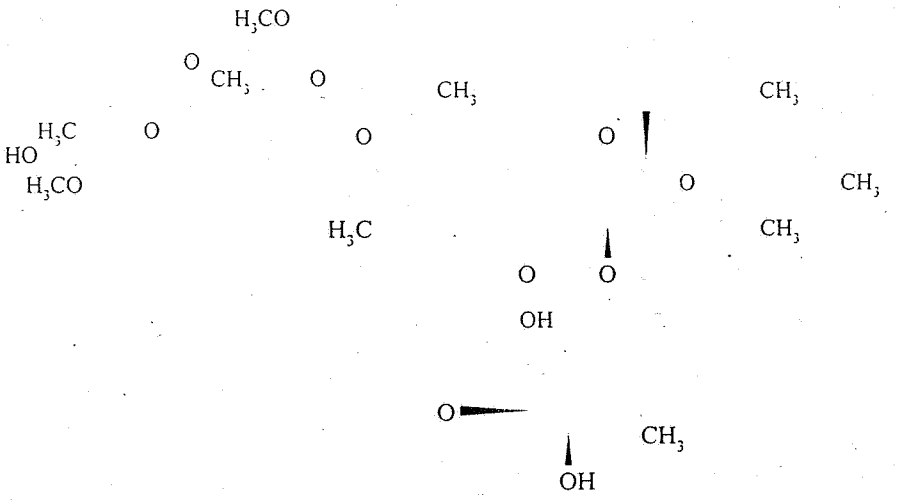
TO: Susan Lewis, Product Manager
Stephanie Willett, Team 3 Reviewer
Insecticide/Rodenticide Branch
Registration Division (7505C)

Summary of Residue Chemistry Deficiencies Remaining to be Resolved

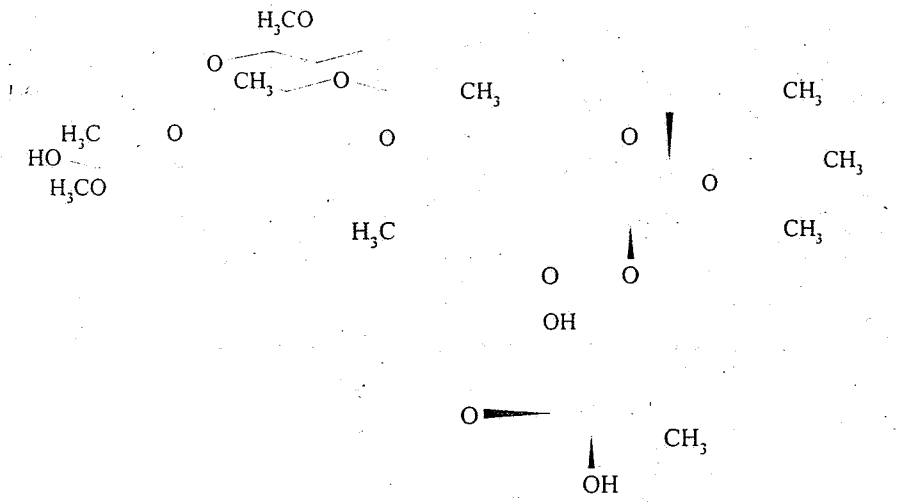
- Revise Section F: replace chili peppers with peppers and raise proposed tolerance to 0.02 ppm
- Revise Section F: delete grape juice and raisin tolerances

Background

Avermectin B1a



Avermectin B1b



Merck & Co., Inc., has submitted a request to establish tolerances for the combined residues of avermectin [≥80% avermectin B1a (5-O-demethyl avermectin A_{1a}) and ≤20% avermectin B1b (5-O-demethyl-25-de (1-methylpropyl)-25-(1-methylethyl) avermectin A_{1a})] and its delta-8,9-isomer in or on the commodities grapes, raisins, and grape juice at 0.02 ppm. The registrant has

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also submitted data on the residues of avermectin in or on chili peppers and, with the existing tolerance on bell peppers, requests a tolerance on chili peppers at 0.01 ppm. Tolerances are established for various plant and animal commodities ranging from 0.005 ppm on walnuts to a time-limited tolerance on hops at 0.2 ppm and including a tolerance for bell peppers at 0.01 pp (40 CFR §180.449).

Conclusions

1. The manufacturing process of technical avermectin has been adequately addressed. The end-use product, AGRI-MEK 0.15 EC, contains 0.15 lbs ai/ gallon as a mixture of avermectins containing ≥80% avermectin B1a and ≤20% avermectin B1b.

2. The directions for use of the product AGRI-MEK on grapes and chili peppers are adequate. The product is to be applied when pests or pest damage is observed. Apply the product at 0.019 lb ai /A twice on grapes and three times on chili peppers. Apply at 21 day intervals for grapes and 7 days for peppers. Do not apply the product through any type of irrigation system or by aircraft. The label specifies preharvest intervals (PHI) of 28 days for grapes and 7 days for peppers.

3a. No new metabolism data were submitted with this petition. The available plant metabolism data are adequate for the proposed uses on grapes and chili peppers. The residues of concern are the parent compounds (avermectin B1a and B1b) and their delta-8,9-isomers (also referred to as (Z)-8,9 isomers).

3b. Since there are no grape or chili pepper animal feed commodities, a discussion of avermectin animal metabolism is not germane to this petition.

4. The registrant has used the analytical procedure designated Method 91-1 for data gathering purposes in these grape and chili pepper field trials for avermectin and its delta-8,9-isomer. Acceptable independent method validations (ILV) were submitted for both commodities. The samples are extracted with acetonitrile/water/hexane, cleaned up with an aminopropyl column, and derivatized with trifluoroacetic anhydride. Quantitation of the residues of interest is accomplished by high performance liquid chromatography (HPLC) with fluorescence detector. The limit of quantitation (LOQ) varies from 1 ppb for grapes to 4 ppb for chili peppers. Method 91-1 is adequate for data collection purposes. The method is similar to the registrant's method for hops, Method M-036.2, which has been submitted for inclusion in FDA's PAM II. Method M-036.2 is adequate for tolerance enforcement.

5. Avermectin is not recovered or not likely to be recovered by FDA multiresidue methods.

6a. The submitted storage stability study information on the grape and grape processed commodities is not adequate. The sampling-to-analysis time for samples in the grape studies ranged up to 19 months. If the registrant intends for this grape commodity storage stability

study to became part of the avermectin database, additional information concerning fortification solutions, and the date, place, and sample chromatograms are required. However, avermectin has been shown to be stable under frozen conditions in similar high moisture raw agricultural commodities including up to 19 months in tomatoes. The available storage stability data are adequate to support the field study residue trials for high moisture or watery grape commodities.

6b. The storage stability study on raisins is not adequate. In addition to the lack of supporting documentation concerning fortification solutions, and the date, place, and sample chromatograms, the recoveries from field fortifications were reported as inadequate, 21 to 81%. No other similar commodity has been the subject of an avermectin storage stability study. At this time, RAB2 will assume that half of the residue on raisins degrades during storage (average recovery of 48% for the four raisin samples).

6c. No new storage avermectin stability on chili peppers has been submitted. Sampling-to-analysis times for the submitted pepper residue studies ranged up to 9 months. However, avermectin has been shown to be stable under frozen conditions in other raw agricultural commodities including up to 19 months in tomatoes. The available storage stability data are adequate to support the field study residue trials in chili peppers.

7a. The residue field trial data on grapes submitted with this petition are adequate to support the proposed use. The highest residue found on grapes at the 28-day PHI was 6.7 ppb (0.007 ppm). This supports the tolerance of 0.02 ppm proposed by the registrant. Pending the outcome of the avermectin human health risk assessment, RAB2 recommends for the proposed avermectin tolerance on grapes at 0.02 ppm.

7b. The residue field trial data on chili peppers submitted with this petition are adequate to support the proposed use. The highest residue found on chili peppers at the 7-day PHI was < 5 ppb (<0.005 ppm). This supports the tolerance of 0.01 ppm on peppers proposed by the registrant. However, the submitted Section F lists chili peppers, not peppers. A revised Section F with the correct listing is required. In addition, in order to harmonize with international residue limits discussed below, RAB2 recommends that the tolerance be established at 0.02 ppm on peppers. Provided a revised Section F is submitted with the corrected commodity listing and tolerance level, and pending the results of the human health risk assessment, RAB2 recommends for an avermectin tolerance on peppers at 0.02 ppm.

8a1. The grape processing study and existing storage stability database are adequate to support the proposed tolerance on juice. Starting with raw grapes bearing residues of 10 ppb, the highest residues found in fresh and processed juice were < 2 ppb (< 0.002 ppm) in juice. Since the processing study shows that avermectin does not concentrate in juice, a tolerance on grape juice is not required. RAB2 recommends that the registrant remove the tolerance on grape juice and submit a revised Section F.

8a2. Starting with raw grapes bearing residues of 10 ppb, the highest avermectin residues found

on raisins were10.2 ppb (0.01 ppm). Based on the results of the raisin storage stability study, the residues in raisins could have been as high as 20 ppb (2x concentration factor). Using this concentration factor and the highest field trial value of 0.007 ppm, residues in raisins would be 0.014 ppm versus the grape tolerance of 0.02 ppm. Therefore, a tolerance for raisins is not necessary; a revised Section F deleting the 0.02 ppm raisin tolerance should be submitted.

8b. There are no chili pepper processed food items; therefore a discussion of processed food items is not germane to this action.

9. Since grapes and chili peppers have no animal feed items of regulatory concern, a discussion of animal feed items is not germane to this action.

10. The requirements for rotational crop studies have previously been waived. No rotational crop data are required to support this action.

11. There are no Codex, Canadian, or Mexican maximum residue limits (MRL) for avermectin on grapes or grape processed commodities. There is a Codex MRL for avermectin, using the same regulable residues as the domestic registration, on sweet peppers at 0.02 ppm. In order to harmonize with this MRL, RAB2 recommends that the proposed tolerance on peppers be raised. The registrant should submit a revised Section F for an avermectin tolerance of 0.02 ppm on peppers.

Summary

Provided the registrant submits a revised Section F for peppers at 0.02 ppm, and deletes the requested tolerances for juice and raisins, RAB2 can recommend for the establishment of avermectin tolerances on peppers and grapes at 0.02 ppm.

In addition, if the registrant intends to use the grape commodity storage stability study (excluding raisins) as part of the storage stability database for avermectin, additional information is required (see Conc. 6a). Also, the registrant should note our assumption that residues on raisins may have degraded up to 50% during storage (see Conc. 6b).

Note: The above recommendations are contingent on the support of the forthcoming separate FQPA risk assessment for avermectin to be conducted using the tolerance levels recommended by RAB2 in this review. If the FQPA risk assessment for avermectin is found to be below the Agency's level of concern, when the updated Section F is received an updated risk assessment will not be necessary.

Note to P.M.: Upon establishment of the pepper tolerance at 0.02 ppm, the existing tolerance of 0.01 ppm on bell peppers should be deleted from the CFR.

Detailed Considerations

Product Chemistry

The manufacturing process of technical grade avermectin has been adequately described (see our memo of 5/1/86, L. Cheng, CBRS # 388). AGRI-MEK 0.15 EC, (EPA Reg. No. 618-98) contains 0.15 lbs ai/ gallon (2.0 wt%) as a mixture of avermectins containing ≥80% avermectin B1a and ≤20% avermectin B1b.

Directions for Use

Do not apply the product, AGRI-MEK 0.15 EC, through any type of irrigation system or by aircraft.

Grapes:

The product may be applied to grapes up to 2 times at 0.019 lb ai (16 fl oz product) /A/application in a minimum of 50 gallons of water per acre (gpa) at an interval of 21 days. Always apply in combination with a non-ionic surfactant. Apply when western grapeleaf skeletonizer larvae are observed. For spider mite control, apply before motiles exceed 20 per leaf. Total seasonal applications are not to exceed 0.038 lb ai (32 fl oz product) /A. The minimum pre-harvest interval (PHI) is 28 days. Do not allow grazing in treated vineyards.

Chili peppers:

The product may be applied to chili peppers up to 3 times at 0.019 lb ai (16 fl oz product) /A/application in a minimum of 20 gpa of water at intervals of 7 days. Apply for broadmites and spider mites when mite damage appears. For leafminers, apply when adult flies are observed Total seasonal applications are not to exceed 0.057 lb ai (48 fl oz product)/A. The minimum PHI is 7 days.

Nature of the Residue - Plants and Animals

No new plant or animal metabolism data were submitted with these tolerance requests. Metabolism data have been previously submitted on cottonseed, citrus, and celery (PP#'s 5G3500, 5G3287, and 8F3649, respectively). In addition, a report titled "Comparative Degradation of Avermectin B_1a in Cotton Leaf, Citrus Fruit, Celery, and In Vitro" was submitted in support of PP#9F3703 (reviewed by S. Willett, 12/15/89).

The proposed use in this petition on grapes and chili peppers specifies multiple applications up to a maximum application rate of 32 fl oz/A/season (0.038 lb ai/A/season). Previously, the metabolism components have been examined from radio-labeled avermectin on celery (10 applications at 7 day intervals for a total equivalent of 1.0 lb ai/A/season), radio-labeled

avermectin on cotton (3 applications at 50 to 89 day intervals for a total equivalent of 0.60 lb/A/season), and exaggerated application rates to citrus (30X, 2.25 lb ai/A). The available metabolism data on cotton, celery, and citrus represent a wide enough range of crop matrices, growth modes, and use rates. It is unlikely that application of avermectin to grapes and chili peppers will result in new degradation compounds that have not previously been produced and subjected to toxicity testing. While the registrant should be prepared to conduct additional plant metabolism studies on other crops to support future uses (especially if the use patterns differ significantly from those of cotton, celery, and citrus), RAB2 concludes that the metabolism data are sufficient to support the proposed use on grapes and chili peppers. The residues of concern in/on grapes and chili pepper commodities are the parent compounds (avermectin B1a and B1b) and their delta-8,9-isomers (also known as (Z)-8,9 isomers).

Since there are no grape or chili pepper animal feed items of regulatory concern, a discussion of animal metabolism is not germane to this petition.

Residue Analytical Methods (MRIDs 443000-01& -03)

The registrant has submitted two independent method validations (ILV) for Method 91-1, one each for grapes (MRID 443000-01) and chili peppers (MRID 443000-03). Both studies were conducted by Analytical Development Corp., Colorado Springs, CO.

The 10 g of fortified grape samples are extracted with acetonitrile/water/hexane (1:1:5). The analytes are partitioned into hexane and the hexane extract were concentrated and loaded onto an aminopropyl solid phase extraction column. The column was washed with a series of solvents and the analytes eluted with acetone/dichloromethane (1:1). The residues were then evaporated to dryness, reconstituted in acetonitrile, and derivatized with trifluoroacetic anhydride in the presence of N-methylimidazole and analyzed by reversed phase HPLC using fluorescence detection with excitation and emission wavelengths of 365 and 470 nm, respectively. The instrument was calibrated only with avermectin B1a. Although not strictly correct analytical procedure, Merck has previously provided sufficient data showing the accuracy of using the avermectin B1a calibration curve to quantitate avermectin B1b and the delta-8,9 isomer (PP#3F4258, 6/21/94). The method was validated for both forms of avermectin B1 and the delta-8,9 isomer. The limits of quantitation (LOQ) and detection (LOD) for individual residues of avermectin B_1 and its delta-8,9-isomer were 0.002 ppm and 0.001 ppm, respectively. The performing laboratory provided adequate calibration curves and chromatograms.

Table 1. Independent Laboratory Validation of Method 91-1 for Avermectin Residues on Grapes.

compound	spike level (ppb)	avg % recovery (n = number)
B1a	2.0	82 (8)
	2.5	89 (2)
	50	83 (9)
B1b	4.6	80 (9)
Δ-8,9-isomer	2.0	78 (8)
	2.5	80 (2)
	25	77 (8)

RAB2 concludes that Method 91-1 has been adequately validated for collection of residue data on grapes.

The procedure for chili peppers was identical to that of grapes above except that the LOQ and LOD were reported as 0.004 ppm and 0.002 ppm, respectively. The performing laboratory provided adequate calibration curves and chromatograms.

Table 2. Independent Laboratory Validation of Method 91-1 for Avermectin Residues on Chili Peppers.

compound	spike level (ppb)	avg % recovery (n)
B1a	5.0	76 (5)
	75	79 (5)
B1b	3.7	77 (5)
Δ-8,9-isomer	5.0	73 (5)
	25	79 (5)

RAB2 concludes that Method 91-1 has been adequately validated for collection of residue data on chili peppers.

Method 91-1 is similar to the registrant's method for hops, Method M-036.2, which has been submitted for inclusion in FDA's PAM II (PP#5E4566. DP Barcodes: D225120, D225898, W. Wassell, 6/11/96). Since the methods are very similar and considering the results of the ILV's, Method 91-1 is adequate for enforcement purposes.

Multiresidue Methods

The 1990 Pestrak data base indicates that avermectin and its metabolites are not recovered or not likely to be recovered by FDA multiresidue methods.

Storage Stability Data

Grapes (MRID: 443460-01 Vol. 7)

In order to assist in demonstrating the storage stability of incurred avermectin residues in grape processed fractions, processing samples from 001-94-5006R were fortified at 20 ppb with B1a, or B1b, or 8,9-Z in the field, stored frozen for over one year, and analyzed. Recoveries ranged from 21 to 89% (avg=71%, n=38). Recoveries were acceptable for all the processed commodities except for raisins, 21, 41, 50, and 81% (average 48%). The registrant's explanation for the poor recoveries suggests that the raisins were dry (10% moisture) and dusty (not washed), and were difficult to homogenize indicating that the extraction solvent may not have achieved sufficient contact with the residues. Since the concurrent recoveries were acceptable, 70 to 103% for all processed commodities including fortified ground raisins (see Processed Food/Feed below), the registrant performed an additional fortification study to verify the field stability results. The fortification, extraction, and analysis was conducted using whole untreated raisins, with, according to the registrant, acceptable results.

The information submitted with the grape and grape processed commodities is not adequate to support a storage stability study. If the registrant intends for this grape commodity storage stability study to became part of the avermectin database, additional information concerning fortification solutions, the date, place, chromatograms, and calibration curves.

The sampling-to-analysis time for samples in the grape field residue studies ranged from 2 to 19 months (first samples obtained in 5/94 to last analysis in 12/95). The sampling-to-analysis time for processed grape samples in the ranged from 6 to 9 months (first samples obtained in 5/94 to last analysis in 2/95). Frozen storage stability data are available in/on pears for one year (PP#9F3787, J.Stokes,7/9/91), celery for two years (PP#8F3649, S. Willett, 5/4/90), oranges, lemons and grapefruits for one year (PP#8F3592, V.F. Boyd, 6/21/89), tomatoes for 19 months (PP#3F4258, 6/21/94), and cottonseed (parent compound only) for 14 months (PP#7F3500, C. Deyrup, 7/29/87). The available storage stability data are adequate to support the field study residue trials for grapes and the grape processing study (except raisins). With respect to raisins, RAB2 will conclude that residues could have degraded by 50% during storage based on the average recovery of 48% for the four samples cited above.

Peppers

No new frozen storage stability studies on peppers were submitted with this action. Sampling-to-analysis times for the submitted pepper residue studies ranged up to 9 months (first sampling in

5/94 to last analysis in 2/95). Frozen storage stability data are available in/on pears for one year (PP#9F3787, J.Stokes,7/9/91), celery for two years (PP#8F3649, S. Willett, 5/4/90), oranges, lemons and grapefruits for one year (PP#8F3592, V.F. Boyd, 6/21/89), tomatoes for 19 months (PP#3F4258, 6/21/94), and cottonseed (parent compound only) for 14 months (PP#7F3500, C. Deyrup, 7/29/87). The available storage stability data are adequate to support the field study residue trials for chili peppers.

Magnitude of the Residues

Grapes (MRID: 443460-01):

Thirteen residue field trials on various grape varieties were conducted in 1994 and 1995 with two applications of 0.15 EC at 0.019 lb ai/A/application. The trials were conducted with spray adjuvants; 1994 trials with paraffinic crop oil and the 1995 trials with non-ionic surfactant. The trials were conducted in California (8), Washington (2), Michigan, New York, and Pennsylvania. Two composite samples of grapes from each field trial were collected at 0 and 28 days preharvest interval (PHI). In addition, samples were also collected at 7, 14, and 42 days PHI in the 1994 trials. The collected samples were frozen and shipped to the performing laboratory. The samples were coarsely ground in the presence of dry ice using a Hobart food chopper, placed in Nalgene bottles, and returned to frozen storage until analyzed.

The method used for gathering data was Merck Research Laboratories' Agricultural and Veterinary Analytical R&D (AVARD) Method 936-94-4 which is a modification and update of Method 91-1. The grape samples were extracted by homogenization with acetonitrile:water:hexane (1:1:5). The homogenate was centrifuged, the hexane supernatant collected, and the extraction repeated. Each combined hexane extract was loaded onto a prepared aminopropyl solid phase extraction (SPE) column. The column was washed with a series of solvents and the analytes eluted with acetone:dichloromethane (1:1). The samples were evaporated to dryness and derivatized with trifluoroacetic anhydride in the presence of N-methylimidazole. Analysis was by reversed phase HPLC using fluorescence detection. Quantitation was based on comparison to an external standard of avermectin B1. The 8,9-Z isomer forms the same derivative as the parent avermectin, consequently the chromatographic peak at the retention time of the parent B1a or B1b represents the sum of parent plus 8,9-Z isomer. LOD and LOQ were 1 ppb and 2 ppb, respectively. Samples fortified with avermectin B1a at 2 to 50 ppb were analyzed concurrently with each set of field samples. The recoveries ranged from 70 to 92% (avg.= 79% , n = 25). Untreated controls, analyzed with each set of samples, showed no detectable residues.

The performing laboratory, Analytical Development Corp., provided sufficient calibration curves and chromatograms. The method and documentation are adequate to support the residue field trial data presented below.

Table 3. Residues of Avermectin in/on Grapes.

Study # Location Variety	PHI (days)	Avermectin residues (ppb)		
		B1a+Z	B1b+Z	Highest Total
001-94-1009R CA Thompson Seedless	0	43.3 29.6	4.7 3.2	48.0
	7	10.1 7.1	NQ ND	10.1
	14	9.6 3.3	NQ ND	9.6
	28	4.3 5.3	ND ND	5.3
	42	4.4 3.1	ND ND	4.4
001-94-1010R WA White Riesling	0	39.1 21.9	4.2 2.3	43.3
	7	3.9 3.0	ND ND	3.9
	14	3.3 2.4	ND ND	3.3
	28	2.4 ND	ND ND	2.4
	42	ND 2.3	ND ND	2.3
001-94-2002R NY Catawba	0	40.7 47.0	4.7 5.4	52.4
	7	3.0 2.8	ND ND	3.0
	14	NQ ND	ND ND	NQ
	28	ND ND	ND ND	ND
	42	ND ND	ND ND	ND
001-94-2003R MI Concord	0	38.3 35.5	4.2 3.9	42.5

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Study # Location Variety	PHI (days)	Avermectin residues (ppb)		
		B1a+Z	B1b+Z	Highest Total
	7	ND NQ	ND ND	NQ
	14	ND ND	ND ND	ND
	28	ND ND	ND ND	ND
	42	ND NQ	ND ND	NQ
001-94-5004R CA French Columbard	0	24.3 18.5	3.0 2.2	27.3
	7	4.2 4.5	ND ND	4.5
	14	4.1 6.5	ND ND	6.5
	28	5.0 6.7	ND ND	6.7
	42	5.8 5.1	ND ND	5.8
001-94-5006R CA Thompson Seedless	0	23.4 20.3	2.4 2.0	25.8
	7	7.0 5.2	ND ND	7.0
	14	4.0 3.6	ND ND	4.0
	28	NQ 2.7	ND ND	2.7
	42	NQ NQ	ND ND	NQ
001-95-1005R WA Riesling	0	21.1 20.8	2.3 2.2	23.4
	28	ND ND	ND ND	ND
001-95-2008R PA Niagra	0	16.7 29.2	2.0 3.3	32.5

Study # Location Variety	PHI (days)	Avermectin residues (ppb)		
		B1a+Z	B1b+Z	Highest Total
	28	ND ND	ND ND	ND
001-95-5003R CA Flame Tokay	0	28.7 15.2	3.1 NQ	31.8
	28	ND ND	ND ND	ND
001-95-5009R CA Cabernet Sauvignon	0	16.1 13.5	NQ NQ	16.1
	28	NQ NQ	ND ND	NQ
001-95-5010R CA Chardonay	0	42.8 57.2	4.4 6.0	63.2
	28	3.0 NQ	ND ND	3.0
001-95-5011R CA Thompson Seedless	0	34.1 25.3	4.0 2.9	38.1
	28	ND ND	ND ND	ND
001-95-5025R CA Carignane	0	9.2 7.6	ND ND	9.2
	28	ND ND	ND ND	ND

ND= <1 ppb
NQ= <2 ppb, but > 1 ppb

The number and location of the trials are in accordance with EPA's published guidelines (EPA 712-C-96-169, 8/96). The highest residue found on grapes at the 28-day PHI was 6.7 ppb. This supports the 0.02 ppm tolerance proposed by the registrant. **Pending the forthcoming human health risk assessment, RAB2 recommends for the proposed avermectin tolerance on grapes at 0.02 ppm.**

Chili Peppers (MRID: 443000-02):

Four field residue trials were conducted during 1994 in California, New Mexico, Texas, and Arizona. Six applications were made in each trial with 7 ± 1 day intervals. Avermectin 0.15 EC was applied at 0.02 lb ai (17.0 fl oz)/A in water without spray adjuvants. Spray volume varied

from 10 to 30 gpa. Samples were collected from all four trials at 0, 3, and 7 days PHI. Samples were frozen and shipped to the performing laboratory.

The method used for gathering data was Method 91-1. Samples were extracted with organic solvent, purified using an aminopropyl solid phase extraction column, derivatized with trifluoroacetic acid and analyzed by HPLC using fluorescence detector. Quantitation was based on comparison to an external standard of avermectin B1. Limit of detection (LOD) and limit of quantitation (LOQ) were 2 ppb and 5 ppb, respectively. Samples fortified with avermectin B1a at 5 to 25 ppb were analyzed concurrently with each set of field samples. The recoveries ranged from 72 to 78% (avg.= 75% , n = 5). Untreated controls, analyzed with each set of samples, showed no detectable residues.

The performing laboratory, Analytical Development Corp., provided sufficient calibration curves and chromatograms. The method and documentation are adequate to support the residue field trial data presented below.

Table 4. Residues of Avermectin in/on Chili Peppers.

Study # Location Variety	PHI (days)	Avermectin residues (ppb)		
		B1a+Z	B1b+Z	Highest Total
001-94-8000R TX Mild Jalapeno	0	6.6 5.4	ND ND	6.6
	3	NQ NQ	ND ND	NQ
	7	NQ NQ	ND ND	NQ
001-94-8001R NM Serrano Hot Chili	0	11.7 10.5	ND ND	11.7
	3	NQ NQ	ND ND	NQ
	7	NQ NQ	ND ND	NQ
001-94-8002R AZ Serrano	0	13.2 12.3	ND ND	13.2
	3	ND NQ	ND ND	NQ
	7	ND ND	ND ND	ND

Study # Location Variety	PHI (days)	Avermectin residues (ppb)		
		B1a+Z	B1b+Z	Highest Total
001-94-8003R CA Jalapeno	0	13.8 15.2	ND ND	15.2
	3	NQ ND	ND ND	NQ
	7	ND ND	ND ND	ND

ND= <2 ppb
NQ= <5 ppb, but > 2 ppb

The number and location of the trials are in accordance with EPA's published guidelines (EPA 712-C-96-169, 8/96). The highest residue found on chili peppers at the 7-day PHI was < 5 ppb. This supports the tolerance on peppers proposed by the registrant. However, the submitted Section F lists chili peppers, not peppers. A revised Section F with the correct listing is required. In order to harmonize with international maximum residue levels, RAB2 recommends raising the proposed tolerance to 0.02 ppm (see International Harmonization below). **Provided a revised Section F is submitted, and pending the forth coming human health risk assessment, RAB2 recommends for an avermectin tolerance on peppers at 0.02 ppm.**

Processed Food/Feed

Grapes (MRID: 443460–01):

On the day of the second of two applications of 0.15 EC at 0.019 lb ai/A in trial 001-94-5006R, grapes were collected for processing. Untreated and two treated grape samples were put down for drying. The grapes were allowed to dry in the field where harvested for 25 days before processing into raisins and raisin waste, frozen, and sent for analysis.

Additional grape samples were sent to a processing facility. The fresh treated and untreated grape samples were sent at ambient temperature to Wm J. Englar & Associates, Inc., Moses Lake WA for processing. Washed and unwashed grapes, fresh and processed juice, wet and dry pomace, stems, and wash water were frozen immediately after processing and submitted for analysis.

The method used for gathering data was Merck Research Laboratories' Agricultural and Veterinary Analytical R&D (AVARD) Method 936-94-4 which is a modification and update of Method 91-1. The processing samples were extracted by homogenization with acetonitrile:water:hexane (1:1:5). The homogenate was centrifuged, the hexane supernatant collected, and the extraction repeated. The combined hexane extracts were loaded onto a

prepared aminopropyl solid phase extraction (SPE) column. The column was washed with a series of solvents and the analytes eluted with acetone:dichloromethane (1:1). The sample was evaporated to dryness and derivatized with trifluoroacetic anhydride in the presence of N-methylimidazole. Analysis was by reversed phase HPLC using fluorescence detection. Quantitation was based on comparison to an external standard of avermectin B1. The 8,9-Z isomer forms the same derivative as the parent avermectin, consequently the chromatographic peak at the retention time of the parent B1a or B1b represents the sum of parent plus 8,9-Z isomer. LOD and LOQ were 0.25 ppb and 5 ppb, respectively depending on the processed commodity (See Table 5).

Table 5. Avermectin LOD and LOQ for Grape Processed Commodities

Commodity	Avermectin	
	LOD ppb	LOQ ppb
Grapes	1	2
Water	0.25	0.5
Juice	1	2
Raisins	2	5
Pomace, wet	1	2
Pomace, dry	2	5
Stems	0.6	1
Raisin waste	0.6	1

Control washed and unwashed grapes, fresh and processed juice, wet and dry pomace, stems, wash water, raisins, and raisin waste, fortified with B1a, or B1b, or 8,9-Z at 2 to 200 ppb, were analyzed concurrently with each set of field samples. The concurrent recoveries ranged from 70 to 103% (avg.= 84%, n = 40). Untreated controls, analyzed with each set of samples, showed no detectable residues.

The performing laboratory, Analytical Development Corp., provided sufficient calibration curves and chromatograms. The method and documentation are adequate to support the processing data presented below.

Table 6. Residues of Avermectin in/on Grape Processed Commodities.

Commodity	Avermectin residues (ppb)		
	B1a+Z	B1b+Z	Highest Total
Grapes, unwashed	10.0	NQ	10.0
Grapes, washed	12.9	NQ	12.9
Raisins	10.2 9.7	ND ND	10.2
Raisin waste	12.1 21.6	1.2 2.5	24.2
Stems	20.1	2.2	22.3
Pomace, wet	51.6	5.5	57.1
Pomace, dry	164	17.8	181.8
Juice, fresh	NQ	ND	NQ
Juice, processed	NQ	ND	NQ
Wash water	1.3	ND	1.3

ND = No Detect
NQ = No Quantitation

The treated grapes used for this study show residues approximately half of those reported for 001-94-5006R in the Magnitude of the Residues section above. This discrepancy is most likely due to the shipment of the grapes to the processing facility at ambient temperature; 80°F upon arrival.

The grape processing study is adequate. The highest residues found on commodities of regulatory concern were < 2 ppb in juice. This supports the requested tolerance. However, since the processing study shows that avermectin does not concentrate in juice, a tolerance on grape juice is not required. **RAB2 recommends that the registrant remove the tolerance on grape juice and submit a revised Section F.**

Starting with raw grapes bearing residues of 10 ppb, the highest avermectin residues found on raisins were10.2 ppb (0.01 ppm). Based on the results of the raisin storage stability study, the residues in raisins could have been as high as 20 ppb (2x concentration factor). Using this concentration factor and the highest field trial value of 0.007 ppm, residues in raisins would be 0.014 ppm versus the grape tolerance of 0.02 ppm. Therefore, **a tolerance for raisins is not**

necessary; a revised Section F deleting the 0.02 ppm raisin tolerance should be submitted.

Chili Peppers:

Chili peppers do not have processed food/ feed items, therefore a discussion of associated food/feed items is not germane to this petition.

Meat, Milk, Poultry, Eggs

Since there are no grape or chili pepper (or pepper) animal feed items of regulatory concern, a discussion of animal residues as a result of the proposed tolerances is not germane to this petition.

Rotational Crops

No rotational crop studies were received with this submission. Review of the results of the confined rotational crop study indicated that avermectin residues accumulated in some rotational crops at levels up to 10 - 12 ppb. However, the radioactivity was due to polar degradates that were of little toxicological concern as compared to the parent compound avermectin B1 and/or the delta-8,9-isomer (see memo of P. Mastradone dated 4/24/88). Therefore, the requirements for field rotational crop studies have been waived (PP#7F3500, #8F3592, and #5E4566, DP Barcodes: D230333, D230352, D230880, G. Herndon, 1/10/97).

International Residue Harmonization

There are no Codex, Canadian, or Mexican maximum residue limits (MRL) for avermectin on grapes or grape processed commodities. Therefore, international harmonization is not an issue for the action on grapes.

There are no Canadian or Mexican MRLs for peppers. There is a Codex MRL for avermectin B1a, B1b, (Z)-8,9-avermectin B1a, and (Z)-8,9-avermectin B1b on sweet peppers at 0.02 ppm. The regulable residues for the U.S. and Codex are identical. In order to harmonize with this MRL, RAB2 recommends that the proposed tolerance be raised. **The registrant should submit a revised Section F for an avermectin tolerance of 0.02 ppm on peppers.**

Attachment: International Residue Status Sheet

cc: Cutchin, RAB2 Reading File, PP# 7F4844

RDI: RAB2:8/18/98, Branch Senior Scientist: R. Loranger:9/15/98

Attachment:

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INTERNATIONAL RESIDUE LIMIT STATUS

CHEMICAL Avermectin

CODEX NO. 177

CODEX STATUS:

[ ] No Codex Proposal
Step 6 or Above

PROPOSED U.S. TOLERANCES:

Petition No. 7F 4844

DEB Reviewer Cutchin

Residue (if Step 8): ~~Avermectin~~ B1a aver. B1b, (Z)-8,9-aver. B1, (Z)-8,9-aver. B1a

Residue: Avermectin B1a, B1b, + 8,9-Z isoma

Crop(s)	Limit (mg/kg)
Peppers, sweet	0.02 (Step 6)

Crop(s)	Limit (mg/kg)
Grapes	0.02
Raisins	0.02
Grapejuice	0.01
Peppers	

CANADIAN LIMITS:

[X] No Canadian Limit

Residue:_____

MEXICAN LIMITS:

[X] No Mexican Limit

Residue:_____

Crop(s)	Limit (mg/kg)

Crop(s)	Limit (mg/kg)

NOTES

Form Revised 1989

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