

US EPA ARCHIVE DOCUMENT

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MEMORANDUM

SUBJECT: PP#4E04419. Abamectin (AGRI-MEK 0.15EC miticide/insecticide, EPA Reg. No. 618-98) in or on Hops. Evaluation of analytical methods, magnitude of residue and storage stability data.

MRID Nos. 433791-01, 434515-01.

CBTS Nos. 14063, 14449, 14761.

DP Barcodes: D205257, D207864, D209820.

FROM: William D. Wassell, Chemist
Tolerance Petition Section I
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THROUGH: Edward Zager, Acting Chief
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TO: Hoyt Jamerson, PM-43
Emergency Response and Minor Use Section
Registration Division (7505C)

George M. Markle, Associate Director, Interregional Research Project No. 4 (IR-4), State Agricultural Experiment Station, Rutgers University, New Brunswick, NJ on behalf of the IR-4 Project, the Agricultural Experiment Stations of Idaho, Oregon and Washington, the Idaho, Oregon and Washington Hops Commissions and the Hops Growers of America requests the establishment of a tolerance with a expiration date of December 31, 1996 for residues resulting from the use of the miticide/insecticide abamectin [a mixture of avermectins containing $\geq 80\%$ avermectin B_{1a} (5-O-demethyl avermectin A_{1a}) and $\leq 20\%$ avermectin B_{1b} (5-O-demethyl-25-de (1-methylpropyl)-25-(1-methylethyl) avermectin A_{1a})] on hops. The time-limited tolerances are requested in terms of the combined residues of the insecticide avermectin B₁ and its delta-8,9-isomer in or on the raw agricultural commodity hops (dried) at 0.3 ppm. The time-limited tolerance is requested while IR-4 generates additional residue data to support the use of the product on hops.

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Permanent tolerances for the combined residues of the insecticide avermectin B₁ and its delta-8,9-isomer have been established (40 CFR §180.449) for tomatoes at 0.01 ppm (tolerance for imported tomatoes), celery at 0.05 ppm, and strawberry at 0.02 ppm. Time-limited tolerances with an expiration date of 4/30/96 for the combined residues of the insecticide avermectin B₁ and its delta-8,9-isomer have been established for the following raw agricultural commodities (40 CFR §180.449) and foods or feeds (40 CFR §185.300 and §186.300) for 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, citrus oil at 0.10 ppm, and tomato pomace at 0.07 ppm and dried citrus pulp at 0.10 ppm. A temporary tolerance with an expiration date of 12/31/95 has been established for residues of the insecticide avermectin B₁ and its delta-8,9-isomer in or on apple at 0.02 ppm. This tolerance was granted in conjunction with an experimental use permit. Avermectin B₁ 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 use of avermectin on various agricultural commodities including pears, lettuce, almonds, almond hulls, walnuts, and cucurbits.

Abamectin is not a FIFRA '88 reregistration pesticide active ingredient.

Previously, CBTS performed a comprehensive screen of residue data generated by IR-4 to support the use of abamectin on hops (see our memo of 11/1/93, M.H. Peters, DP Barcode: D194173). CBTS also participated in a meeting with representatives of Merck Research Laboratories (Three Bridges, NJ) and TAS, Inc. (Washington, DC) on March 22, 1994 to discuss data requirements for the registration of abamectin on hops (see our memo of 3/28/94, M.H. Peters).

Conclusions:

- 1a. Product chemistry data were not submitted with the subject petition. The manufacturing process of technical grade avermectin has been adequately described (see our memo of 5/1/86, L. Cheng).
- 1b. The determination as to whether the inerts contained in the formulated product are cleared under 40 CFR §180.1001 is under the purview of Registration Division.
2. CBTS concludes the directions for use of the product on hops are adequate.
3. Plant metabolism data were not submitted in conjunction with the subject petition. Previously metabolism data for abamectin on cotton, citrus, and celery were submitted in conjunction with PP#5G3500, PP#5G3287, and PP#8F3649,

respectively. CBTS concludes that the available metabolism data is sufficient to support the use of abamectin on hops. The residue of concern in plants is avermectin B₁ and the its delta-8,9-isomer.

4a. Animal metabolism data were not submitted in conjunction with the subject petition. However, the metabolism of abamectin in goat and rat has been reviewed (see our memos of 6/21/89 and 11/26/91, F. Boyd, PP#8F3592/8H5550, and G. Herndon, 1F3973/1H5611, respectively). For the purposes of the proposed time-limited tolerances only, CBTS concludes the available ruminant metabolism study is adequate to support the proposed use of abamectin on hops.

5a. Analytical methodologies for enforcement of residues from the use of abamectin are available in PAM II for citrus and processed fractions (Method I), ginned cottonseed (Method IA), and bovine tissues and milk (Method II). An additional enforcement method (Method 10001, Rev.2) has been successfully validated by the Agency's Analytical Chemistry Laboratory and has been recommended for inclusion in PAM II for enforcement of tolerances for abamectin in or on lettuce (see our correspondence of 11/29/94, G.J. Herndon, EPA to A. Marcotte, FDA). This method has not yet appeared in PAM II. These methods have not been validated for use with hops.

5b. Residues of abamectin are not recovered by the FDA Multiresidue protocols contained in PAM I.

5c. Analytical reference standards of avermectin B_{1a} and its delta-8,9-isomer are available from the Agency's Pesticide and Industrial Chemicals Repository, Research Triangle Park, NC.

5d. CBTS concludes the proposed enforcement method is not adequate for enforcement of the proposed tolerances and must be independently validated as per PR Notice 88-5 and validated by the Agency's Analytical Chemistry Laboratory prior to a favorable recommendation from CBTS for the proposed time-limited tolerances. CBTS further concludes adequate methodology is not available for the enforcement of the proposed tolerances for residues of abamectin in/on dried hops.

5e. CBTS concludes the method (with rehydration step) utilized for analysis of the magnitude of residue samples in the subject petition is adequate for data collection purposes. CBTS concludes the method (without rehydration step) is adequate for the purposes of data collection for residues of avermectin B_{1a} and the delta-8,9 isomer of avermectin B_{1a} in or on dried hops. The method has not been validated for determination of residues of avermectin B_{1b} in or on dried hops.

6a. As the petitioner is proposing a time-limited tolerance while additional residue data are collected, CBTS concludes the submitted storage stability data in conjunction with the previously submitted data are adequate to support the proposed time-limited tolerance for residues of abamectin in or on hops.

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6b. For the purposes of the granting of Section 3 registration and permanent tolerances, the submitted storage stability data are not adequate and the petitioner is instructed to submit data pertaining to the storage stability of residues of avermectin B_{1a}, B_{1b} and the delta-8,9 isomer of avermectin B_{1a} in or on dried and spent hops reflecting the conditions and interval of storage for the magnitude of residue samples.

7a. CBTS concludes the requested tolerance level of 0.3 ppm for the combined residues of avermectins B_{1a}, B_{1b} and the delta-8,9 isomer of avermectin B_{1a} in or on dried hop cones is not adequate for the purposes of the time limited tolerance. CBTS further concludes a tolerance limit of 0.5 ppm for the combined residues of avermectins B_{1a}, B_{1b} and the delta-8,9 isomer of avermectin B_{1a} in or on dried hop cones is appropriate to cover the residues resulting from the proposed use of the product on hops. The petitioner should submit a revised Section F in which the time-limited tolerance is requested at a residue level of 0.5 ppm.

7b. For the purposes of the granting of Section 3 registration and permanent tolerances, the petitioner must submit residue field trial data reflecting the proposed use in the Pacific Northwest of the United States (Region 11 from the EPA Guidance on Number and Location of Domestic Crop Field Trials For Establishment of Pesticide Residue Tolerances, June 1994). A minimum of 3 field trials each with two independently composited, treated samples per site will be required.

8. CBTS concludes the laboratory scale processing study does indicate that an approximate 29% decrease in residues is observed in the spent hops. This information will be accounted for when determining the adequacy of existing animal commodity tolerances.

9a. For the purposes of the proposed time-limited tolerances only, CBTS concludes the dietary burden for beef and dairy cattle is below the highest feeding level in the previously submitted feeding study. CBTS concludes that the existing tolerances for residues of abamectin in cattle meat, meat byproduct and milk are adequate for the purposes of the proposed time-limited tolerances for abamectin in/on dried hops.

Note to PM: Time-limited tolerances (expiration date: 4/30/96) are established (40 CFR §180.449) for residues of abamectin in cattle meat and meat byproducts at a level of 0.02 ppm. A time-limited tolerance for residues of abamectin in cattle fat had been established, but has expired as of 5/1/89. Based upon the established tolerances for abamectin in/on various raw agricultural commodities and the previously submitted ruminant feeding study, a tolerance for residues of abamectin in fat is needed and this tolerance must be reestablished prior to a favorable recommendation for the proposed time-limited tolerances for residues of abamectin in/on dried hops.

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9b. For the purposes of a future Section 3 registration and the establishment of permanent tolerances for residues of abamectin in/on dried hops, CBTS will utilize the maximum dietary burden figures presented in Table II (June 1994) for beef and dairy cattle. Using this approach, the dietary burden for both beef and dairy cattle may exceed the highest feeding level in both the ruminant metabolism and feeding studies. If the highest feeding level is exceeded in these studies, then CBTS will require an additional ruminant metabolism and feeding study. We Note: The previously submitted ruminant metabolism study utilized abamectin labeled with ³H.

10. The International Tolerance Status Sheet is attached and there are no established tolerances for abamectin acid in or on dried hops in Canada, Mexico or Codex. Therefore, there are no compatibility problems.

Recommendations:

CBTS recommends against the establishment of the proposed time-limited tolerance for abamectin in/on dried hops due to conclusions 5d, 7a and 9a above.

Detailed Considerations:

Manufacture and Formulation:

Product chemistry data were not submitted with the subject petition. The manufacturing process of technical grade avermectin has been adequately described (see our memo of 5/1/86, L. Cheng). AGRI-MEK 0.15 EC, (EPA Reg. No. 618-98), has been proposed for use on hops. This product contains 0.15 lbs ai/gallon as a mixture of avermectins containing $\geq 80\%$ avermectin B_{1a} (5-O-demethyl avermectin A_{1a}) and $\leq 20\%$ avermectin B_{1b} (5-O-demethyl-25-de (1-methylpropyl)-25-(1-methylethyl) avermectin A_{1a}). The determination as to whether the inerts contained in the formulated product are cleared under 40 CFR §180.1001 is under the purview of Registration Division.



Proposed use:

AGRI-MEK 0.15 EC miticide/insecticide is to be applied to hops for the control of twospotted spider mites at the rate of 16 fl oz of product per acre per application by ground equipment (0.02 lbs ai/A). A second application may be made approximately 21 days later if necessary to maintain control. The following restrictions are included on the label:

- *Do not exceed 32 fl oz of product per acre per growing season.
- *Do not apply within 28 days of harvest.
- *Do not apply in less than 40 gallons of water per acre.
- *If a second application is necessary to maintain control, do not retreat within 21 days of the first application.
- *Do not permit livestock to graze treated hop yards.

CBTS concludes the directions for use of the product on hops are adequate.

Nature of the Residue - Plants:

Plant metabolism data were not submitted in conjunction with the subject petition. Previously, metabolism data for abamectin on cotton, citrus, and celery were submitted in conjunction with PP#5G3500, PP#5G3287, and PP#8F3649, respectively.

In conjunction with PP#1F3973 (see our memo of 11/26/91, G.J. Herndon), CBTS concluded that the available metabolism studies for abamectin on cotton, citrus, and celery were sufficient to support the use of the product on almonds, walnuts, and lettuce. However, it was noted that the petitioner 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. The application rates in the metabolism studies on the above commodities were at 0.6 lbs ai/A to 2.25 lbs ai/A. As the proposed maximum application rate for abamectin on hops is 0.04 lb. ai/A/season, CBTS concludes that the available metabolism data is sufficient to support the use of the product on hops. The residue of concern in plants is avermectin B₁ and the its delta-8,9-isomer.

Nature of the Residue - Animals:

Animal metabolism data were not submitted in conjunction with the subject petition. However, the metabolism of abamectin in goat and rat has been reviewed. From these studies, it was determined that the residues of concern in ruminants are avermectin B₁ and its delta-8,9-isomer. This conclusion was based upon a feeding level of 1.0 mg/goat/day of ³H-avermectin. An additional metabolite

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(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 livestock dietary burden is increased and the tolerances for residues in meat and milk need to be raised, then the 24-hydroxymethyl metabolite may need to be included in the tolerance expression and appropriate enforcement methods would need to be developed. Furthermore, an additional animal metabolism study using ¹⁴C-avermectin would be needed if the expected ruminant dietary burden exceeded the dose level in the previously submitted goat metabolism study (see our memos of 6/21/89 and 11/26/91, F. Boyd, PP#8F3592/8H5550 and G. Herndon, 1F3973/1H5611, respectively).

For the purposes of the proposed time-limited tolerances only, CBTS concludes the available ruminant metabolism study is adequate to support the proposed use of abamectin on hops. With the addition of spent hops to the diet, the dietary burden for dairy cattle becomes 64.2 ppb and for beef cattle becomes 89.1 ppb (see the Meat, Milk, Poultry and Eggs - Feeding Studies section of this review for a discussion of the ruminant dietary burden).

For the purposes of a future Section 3 registration and the establishment of permanent tolerances for residues of abamectin in/on dried hops, the dietary burden for both beef and dairy cattle may exceed the highest feeding level in both the ruminant metabolism and feeding studies. If the highest feeding level in these studies is exceeded, then CBTS will require an additional ruminant metabolism and feeding study.

Analytical Methods - Enforcement and Data Collection:

Analytical methodologies for enforcing abamectin tolerances are available in PAM II for citrus and processed fractions (Method I), ginned cottonseed (Method IA), and bovine tissues and milk (Method II). An additional enforcement method (Method 10001, Rev.2) has been successfully validated by the Agency's Analytical Chemistry Laboratory and has been recommended for inclusion in PAM II for enforcement of tolerances for abamectin in or on lettuce (see our correspondence of 11/29/94, G.J. Herndon, EPA to A. Marcotte, FDA). This method has not yet appeared in PAM II. Residues of abamectin are not recovered by the FDA Multiresidue protocols contained in PAM I. Analytical reference standards of avermectin B_{1a} and its delta-8,9-isomer are available from the Agency's Pesticide and Industrial Chemicals Repository, Research Triangle Park, NC.

Some of the samples from the magnitude of the residue studies and the processing study were analyzed at Merck Research Laboratories (MRL) in Three Bridges, NJ. The analytical method utilized by MRL for the determination of the residue levels in the submitted residue studies is entitled: Liquid Chromatographic Method for the

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Quantitation of Total Avermectin B1 and 8,9-Z-Avermectin B1 in Dried Hops Using Fluorescence Detection" (dated: 6/15/94). This method is proposed for enforcement of the proposed tolerances and was utilized for the determination of residue levels of avermectin B_{1a}, its delta-8,9 isomer and avermectin B_{1b} in dried and spent hops. Briefly, the samples are rehydrated and extracted with a methanol-water mixture. The residues are partitioned into hexane and the hexane extract is purified utilizing an aminopropyl solid phase extraction column. The purified extract is derivatized with trifluoroacetic anhydride and the residue levels are quantified by HPLC utilizing fluorescence detection and the external standards method. The limit of quantification for the method is reported as 5 ppb for all analytes. The method was validated prior to and concurrent with the analysis of treated samples. The results of the method validation are reported in Table 1.

Table 1. Recovery of Avermectin and Its Metabolite from Hops.

Matrix	Analyte	Fortification Range (ppb)	Recovery Range (%)	Statistics ¹
Dried Hop Cones	avermectin B _{1a}	5 to 1000	101 to 108	Ave.: 105% S.D.: 2.7% n: 6
	avermectin B _{1b}	5 to 50	92 to 94	Ave.: 92.5% S.D.: 1.5% n: 4
	8,9-Z avermectin B _{1a}	5 to 1000	73 to 96	Ave.: 84.8% S.D.: 8.6% n: 6
Spent Hop Cones	avermectin B _{1a}	5 to 320	58 to 100	Ave.: 80.4% S.D.: 10.9% n: 11
	avermectin B _{1b}	5	66 to 71	Ave.: 68.5% S.D.: 3.5% n: 2
	8,9-Z avermectin B _{1a}	5 to 37	56 to 93	Ave.: 78.8% S.D.: 13.2% n: 6

¹ Ave. = average recovery; S.D. = standard deviation; n = number of recovery samples.

Some samples from the magnitude of residue studies and the storage stability study were analyzed at the Oregon State University Environmental Chemistry and Toxicology Laboratory (OSU EC&T). The analytical method utilized at OSU for the determination of the residue levels in the submitted residue studies is entitled: "Determination of Avermectin B1 Residues in Green and Dry Hops by HPLC with Fluorescence Detection" (dated: 9/24/93). As residue data on green hops is no

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longer required, we will limit our discuss of the method to the procedures utilized for analysis of the dried hop samples. Briefly, the samples are extracted by blending with dichloromethane and the concentrated extract is subjected to a column cleanup utilizing deactivated silica gel. The extract solvent is exchanged to hexane saturated with acetonitrile and the residues are partitioned into acetonitrile. The residues are derivatized with trifluoroacetic anhydride and the extract is passed through a silica gel mini column to remove excess derivatization reagents. The residue levels are quantified by HPLC utilizing fluorescence detection and the external standards method. The limit of quantification for this method was reported as 10 ppb for residues of avermectins B_{1a} and B_{1b} and the delta-8,9 isomer of avermectin B_{1a}. The results of fortification recovery for the method are reported in Table 2. We note that recoveries of avermectin B_{1b} were not reported.

Table 2. Recovery of Avermectin B_{1a} and the Delta-8,9 Isomer of Avermectin B_{1a} from Dried Hops.

Analyte	Fortification Range (ppb)	Recovery Range (%)	Statistics ¹
avermectin B _{1a}	10 to 300	72 to 106	Ave.: 91.2% n: 21
delta-8,9 isomer of avermectin B _{1a}	10 to 100	82 to 91	Ave.: 85.2% n: 5

¹ Ave. = average recovery; n = number of recovery samples.

CBTS concludes the method (with rehydration step) utilized for analysis of the magnitude of residue samples in the subject petition is adequate for data collection purposes. CBTS further concludes this method may be suitable for enforcement of the proposed tolerances, but the method must first be validated by the Agency's Analytical Chemistry Laboratory in Beltsville, MD prior to approval as an enforcement method. Prior to the Agency's validation of the method, an independent laboratory must validate the method as per PR Notice 88-5 (dated 7/15/88). Merck Research Laboratories and/or IR-4 has contended that the Agency has agreed to not require a PR 88-5 validation of the proposed enforcement method for the requested time-limited tolerance. It is further stated that the PR Notice 88-5 validation will be conducted upon completion of the additional hop residue trials to be conducted in the fall of 1994. CBTS can find no record that states we have waived the requirement of the PR Notice 88-5 validation of the proposed enforcement method in conjunction with the requested time-limited tolerances. CBTS concludes the proposed enforcement method is not adequate for enforcement of the proposed tolerances and must be independently validated as per PR Notice 88-5 and validated by the Agency's Analytical Chemistry Laboratory prior to a favorable recommendation from CBTS for the proposed time limited tolerances.

CBTS concludes the method (without rehydration step) is adequate for the purposes of data collection for residues of avermectin B_{1a} and the delta-8,9 isomer of avermectin B_{1a} in or on dried hops. The method has not been validated for determination of residues of avermectin B_{1b} in or on dried hops.

Storage Stability: (MRID No. 434515-01)

Data pertaining to the stability of residues of abamectin in or on fresh and dried hops were submitted. As we no longer require data on fresh hops our discussion of this data will be limited to the data on dried hops. Dried hop field trial samples were stored at -15°C for 1000 to 1650 days (approximately 33 to 54 months, respectively). These storage intervals represent the interval from harvest to final analysis. The submitted data pertain to the stability of residues of avermectin B_{1a} only in dried hops for a storage interval of approximately 627 days at -15°C. Data concerning the stability of residues of avermectin B_{1b} and delta-8,9-avermectin B_{1a} were not provided. The submitted storage stability data are summarized in Table 3.

Table 3. Storage Stability of Residues of Avermectin B_{1a} in Dried Hops.

Fortification Level (ppb)	Storage Recovery (%)	Fresh Recovery (%)	Corrected Storage Recovery (%)	Storage Interval (days)
20	59	76	78	561
20	71	76	93	561
20	60	76	79	561
50	65	80	81	600
50	67	80	84	600
50	72	80	90	600

Data reflecting the stability of avermectin B_{1a}, B_{1b} and/or the delta-8,9 isomer of avermectin B_{1a} in or on various crops during frozen storage have been submitted previously. The available data include the following: pears for one year (see our memo of 7/9/91, J.Stokes, PP#9F3787); celery for two years (see our memo of 5/4/90, S. Willett, PP#8F3649); oranges, lemons and grapefruits for one year (see our memo of 6/21/89, V.F. Boyd, PP#8F3592); tomatoes for six months (see our memo of 12/15/89, S. Willett, PP#9F3703); and cottonseed (parent compound only) for 14 months (see our memo of 7/29/87, C. Deyrup, PP#7F3500).

CBTS concludes residues of avermectin B_{1a} in dried hop samples stored at approximately -15°C may degrade slightly over a storage interval of approximately 600 days. As the petitioner is proposing a time limited tolerance while additional residue data are collected, CBTS concludes the submitted storage stability data in conjunction with the previously submitted data are adequate to support the

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proposed time limited tolerance for residues of abamectin in or on hops. For the purposes of the granting of Section 3 registration and permanent tolerances, the submitted data are not adequate and the petitioner is instructed to submit data pertaining to the storage stability of residues of avermectins B_{1a}, B_{1b} and the delta 8,9 isomer of avermectin B_{1a} in or on dried and spent hops reflecting the storage interval of the magnitude of residue samples.

Magnitude of Residue - Crop Field Trials: (MRID Nos. 434515-01 and 433791-01)

Field residue studies were conducted during the years 1989 through 1991 in order to determine the residue levels of avermectins B_{1a}, B_{1b} and the delta-8,9 isomer of avermectin B_{1a} resulting from the proposed use of the product on hops. Hop plants were treated with multiple applications (2 to 4) of abamectin at a rate of 0.02 lbs ai/A per application. The total seasonal application rate varied from 0.04 to 0.08 lbs ai/A. The proposed maximum seasonal application rate is 0.04 lbs ai/A with a 28 day preharvest interval. Samples of hop cones were harvested at intervals ranging from 0 to 21 days after the final application. The samples were analyzed according to the analytical methods described above. The results of the field trials and additional details are summarized in Table 4.

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Table 4. Details and Results of Abamectin Residue Trails in/on Dried Hops.

State/Year	Seasonal Application Rate (lbs ai/A)	PHI ¹ (days)	Residue Levels ² (ppm)	
			Avermectin B _{1a}	Avermectin B _{1b}
WA/90	0.08 (2x)	0	0.39	0.050
		14	0.058	<0.010
		21	0.075	<0.010
ID/89	0.06 (1.5x)	0	0.30	0.026
		14	0.053/0.071	<0.010/<0.010
		21	0.059	<0.010
OR/89	0.06 (1.5x)	0	1.37	0.11
		14	0.29/0.25	0.028/0.023
		21	0.29	0.041
OR/91	0.04 (1x)	13	0.14/0.13	0.010/0.012

¹ PHI = Preharvest Interval.

² Residue levels are not corrected for recovery and are the average of two values. In all cases, residue levels of the delta-8,9 isomer of avermectin B_{1a} were below the limit of quantification (0.010 ppm) for the analytical method. All samples were analyzed by the method which did not utilize a rehydration step prior to extraction. If two residue levels are indicated (separated by a slash (/)), the second value is from the reanalysis of the sample with a method that utilized a rehydration step prior to extraction.

CBTS concludes the requested tolerance level of 0.3 ppm for the combined residues of avermectins B_{1a}, B_{1b} and the delta-8,9 isomer of avermectin B_{1a} in or on dried hop cones is not adequate for the purposes of the time limited tolerance. CBTS further concludes a tolerance limit of 0.5 ppm for the combined residues of avermectins B_{1a}, B_{1b} and the delta-8,9 isomer of avermectin B_{1a} in or on dried hop cones is appropriate to cover the residues resulting from the proposed use of the product on hops. The petitioner should submit a revised Section F in which the time-limited tolerance is requested at a residue level of 0.5 ppm.

For the purposes of the granting of Section 3 registration and permanent tolerances, the petitioner must submit residue field trial data reflecting the proposed use in the Pacific Northwest of the United States (Region 11 from the EPA Guidance on Number and Location of Domestic Crop Field Trials For Establishment of Pesticide Residue Tolerances, June 1994). A minimum of 3 field trials each with two independently composited, treated samples per site will be required.

Magnitude of Residue - Processed Products: (MRID No. and 433791-01)

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Dried hop cone samples from the field trials identified above as OR/91, OR/89 and ID/89 (13 and 14 day PHI samples only) were extracted with hexane via a laboratory scale procedure for the generation of spent hops. The laboratory scale procedure was meant to approximate normal commercial practices for the extraction of dried hops. We note: i. A protocol for the bench scale extraction procedure was previously reviewed by CBTS (see our memo of 5/12/94, M.H. Peters, DP Barcode No. D202709); ii. The petitioner contends that the physical property differences between the spent hops of the laboratory scale extraction procedure and a scaled down commercial process indicate that the scaled down extraction procedure may be more rigorous and the residue levels in the spent hops may not be indicative of actual residue levels following commercial extraction of the hops; and iii. The petitioner has indicated that a full-scale hop processing study is to be conducted in conjunction with the additional hop residue data to be generated. The dried hop samples were analyzed by the method with the rehydration step prior to and after extraction with hexane. The results of the study are outlined in Table 5.

Table 5. Magnitude of Residues of Avermectin B_{1a} and Avermectin B_{1b} in Dried and Spent Hops.

State/Year	Residue Levels (ppm)				Residue Reduction Factor
	Dried Hops		Spent Hops		
	B _{1a}	B _{1b}	B _{1a}	B _{1b}	
ID/89	0.071	<0.010	0.051	<0.010	26%
OR/89	0.25	0.023	0.16	0.018	35%
OR/91	0.13	0.012	0.086	0.010	27%

CBTS concludes the laboratory scale processing study does indicate that an approximate 29% decrease in residues is observed in the spent hops. This information will be accounted for when determining the adequacy of existing animal commodity tolerances.

Meat, Milk, Poultry and Eggs - Feeding Studies:

Spent hops are an animal feed item. Table II (June 1994) indicates that spent hops can comprise up to 20% of the diet of beef cattle and up to 10% of the diet of dairy cattle, while Table II (October 1982) indicates that spent hops may comprise up to 5% of the diet of both dairy and beef cattle. At this time, we will consider the dietary burden increase based upon a maximum of 5% of spent hops in the diet of beef and dairy cattle and we will take into account an approximate 29% decrease in residues due to the extraction of dried hops to produce spent hops. The residue value in spent hops will be assumed to be 71% of the adjusted

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tolerance level of 0.50 ppm or 0.355 ppm abamectin residues in spent hops. The addition of spent hops to the diets increases the dietary burden for beef and dairy cattle by 21 ppb. CBTS has previously calculated a maximum dietary burden for both dairy and beef cattle utilizing our in-house Spartan Ration Evaluator program and anticipated residue levels (see our memo of 12/21/94, G.J. Herndon, PP#9F3787). From this analysis, we calculated a maximum dietary burden of 43.2 ppb for dairy cattle (acute exposure analysis) and 68.1 ppb for beef cattle (acute exposure analysis). With the addition of spent hops to the diet, the dietary burden for dairy and beef cattle will not exceed the highest dosing level in the feeding study.

An abamectin ruminant feeding study has been submitted in conjunction with PP#7G3468 (see our memo of L.Cheng, 2/11/87). The 28 day feeding study utilized dosing levels of 10, 30 and 100 ppb (0.010, 0.030 and 0.10 ppm, respectively). The results of the feeding study are summarized in Table 6.

Table 6. Avermectin Levels in Dairy Cattle Tissues.

Dose level (ppb)	Residue Levels (ppb)			
	Liver	Muscle	Fat	Kidney
10	3 to 4	1 to 2	2	1 to 2
30	5 to 8	2	4 to 6	2
100	18 to 20	2	10 to 14	4 to 5

For the purposes of the proposed time-limited tolerances only, CBTS concludes the dietary burden for beef and dairy cattle is below the highest feeding level in the previously submitted feeding study. As the existing livestock commodity tolerances are based upon the 100 ppb feeding level, CBTS concludes that the existing tolerances for residues of abamectin in cattle meat, meat byproduct and milk are adequate for the purposes of the proposed time-limited tolerances for abamectin in/on dried hops.

Note to PM: Time-limited tolerances (expiration date: 4/30/96) are established (40 CFR §180.449) for residues of abamectin in cattle meat and meat byproducts at a level of 0.02 ppm. A time-limited tolerance for residues of abamectin in cattle fat had been established, but has expired as of 5/1/89. Based upon the established tolerances for abamectin in/on various raw agricultural commodities and the previously submitted ruminant feeding study, a tolerance for residues of abamectin in fat is needed and this tolerance must be reestablished prior to a favorable recommendation for the proposed time-limited tolerances for residues of abamectin in/on dried hops.

For the purposes of a future Section 3 registration and the establishment of permanent tolerances for residues of abamectin in/on dried hops, CBTS will utilize

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the maximum dietary burden figures presented in Table II (June 1994) for beef and dairy cattle. Using this approach, the dietary burden for both beef and dairy cattle may exceed the highest feeding level in both the ruminant metabolism and feeding studies. If the highest feeding level is exceeded in these studies then CBTS will require an additional ruminant metabolism and feeding study. We Note: The previously submitted ruminant metabolism study utilized abamectin labeled with ³H.

Other Considerations - Harmonization of Tolerances:

The International Tolerance Status Sheet is attached and there are no established tolerances for abamectin in or on dried hops in Canada, Mexico or Codex. Therefore, there are no compatibility problems.

Attachment (1): 1. IRL Status Sheet

cc: WDWassell, RF, Circ., Avermectin SF, PP#4E4419.

RDl: RSQuick: 02/02/95; RALoranger: 02/03/95; EZager: 02/06/95.

7509C:CBTS:WDWassell:wdw:CM#2:Rm 804U:305-6135:1/27/95

Disk: WDW-4, File: FY95WDW.113

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Residue Chemistry Review

Subject: PP#4E04419. Abamectin (AGRI-MEK 0.15EC miticide/insecticide, EPA Reg. No. 618-98) in or on Hops. Evaluation of analytical methods, magnitude of residue and storage stability data. CBTS Nos.14063, 14449, 14761.

Document

Class:

Product

Chem:

Residue 860.1340 Residue analytical method

Chem: 860.1380 Storage stability data

860.1500 Crop field trials

860.1520 Processed food/feed

860.1550 Proposed tolerances

Biochemicals:

DP Barcode: D205257, D207864, D209820

MRIDs: 43379101, 43451501

PC Codes: Actives 122804 Abamectin (ANSI)

Inerts

Commodities: Hops

Administrative #: 000618-00098; 4E04419

Reviewers: William D. Wassell

Review Edward Zager

Approved on: February 6, 1995

Approver:



WP Document: Abamecti.028

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