PP#4508

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

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OFFICE OF
PREVENTION, PESTICIDES, AND
TOXIC SUBSTANCES

MEMORANDUM

Subject: PP#5F04508. Abamectin (Avermectin B_1) for Use in/on Potatoes. Evaluation of Analytical Methodology and Residue Data.
MRIDs# 436233-01 (7 volumes) and 436233-02.
DP Barcode# D214834.
CBTS# 15482.

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Merck and Co., Inc. is requesting the establishment of a permanent tolerance for abamectin (avermectin B_1) insecticide/miticide and its delta-8,9-isomer in/on the raw agricultural commodity potatoes at 0.002 ppm.

Tolerances have been established for avermectin B_1 on various RACs, processed commodities, and animal feeds (40 CFR 180.449, 185.300, and 186.300).

No registration standard has been prepared for abamectin.

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Conclusions

1. Data in this petition were generated by Merck Research Laboratories.

2. The manufacturing process of technical grade avermectin has been adequately described. No concern exists for any of the probable impurities. The formulation proposed for use on potatoes is AGRI-MEK 0.15 EC (EPA Reg.# 618-98). All inerts in this formulation have been cleared under 40 CFR 180.1001.

3. CBTS concludes that the available plant metabolism data are sufficient to support the proposed use on potatoes. The residues of concern are the parent compound (avermectin B_1a and B_1b) and its delta-8,9-isomer.

4. CBTS concludes that the available animal metabolism data are sufficient to support the proposed use on potatoes. The residues of concern are the parent compound (avermectin B_1a and B_1b) and its delta-8,9-isomer.

5a. Merck Method 8920 for analysis of avermectin B_1 and its delta-8,9-isomer in/on potatoes appears to be adequate and suitable for enforcement purposes. CBTS believes that Method 936-92-4 is essentially similar to the other avermectin methods that have been previously validated at the EPA Beltsville lab, and further validation will not be required. The method will be sent to FDA as a letter method.

5b. Avermectin has been subjected to testing under FDA multi-residue protocol methodology and cannot be recovered using any of the methods.

6a. Based on the limits of the analytical methodology testing, Merck will need to provide a revised Section F proposing a 0.005 ppm (not 0.002 ppm) tolerance on potatoes (RAC).

6b. CBTS recommends that the following residue values be used in the acute and chronic dietary risk assessment for avermectin.

Acute and Chronic Residue Values to be Used in the Dietary Risk Assessment of Avermectin

DRES entry	Entry for **ACUTE** Risk Assessment (ppm)	Entry for **CHRONIC** Risk Assessment (ppm)
potatoes, dry	0.005	0.0012
potatoes, peel only	0.005	0.00025
potatoes, peeled	0.005	0.00025
potatoes, whole	0.005	0.00025

7. Potato culls and processed potato waste are fed to beef and dairy cattle. Based on these and other avermectin-registered crops which involve beef and dairy cattle feed items, CBTS has calculated the following residue values to be used in the acute and chronic dietary risk assessment for avermectin.

Acute and Chronic Residue Values to be Used in the Dietary Risk Assessment of Avermectin

DRES entry	Entry for ACUTE Risk Assessment (ppm)	Entry for CHRONIC Risk Assessment (ppm)
beef fat	0.014	0.006
beef lean	0.002	0.002
beef kidney	0.005	0.002
beef liver	0.020	0.008
beef dried	0.002	0.002
beef meat byproducts	0.020	0.008
milk sugar	0.001	0.00025
milk fat	0.004	0.001
milk, non-fat solids	0.004	0.001

8. Avermectin tolerances on various commodities are under consideration by Codex, but have not been officially adopted. No Canadian or Mexican tolerances are established for avermectin and therefore no compatibility problem exists between the proposed U.S. and Codex tolerances.

Recommendations

Until Merck has submitted a revised Section F (see Conclusion 6a), CBTS cannot recommend in favor of the proposed tolerance. However, a DRES run should be initiated using the residue values given in Conclusions 6b and 7.

Detailed Considerations

Manufacturing and Formulation

Abamectin (avermectin B_1 or AVM B_1) is produced by a fermentation process using a strain of Streptomyces avermitilis. (This manufacturing process was reviewed in detail in L. Cheng's memo dated 5/1/86 reviewing EPA 618-OL). The technical product abamectin is a mixture of two homologs containing not less than 80% AVM B_1a and not greater than 20% AVM B_1b. These components differ by only one methylene unit at the 25-carbon position, wherein AVM B_1a contains a sec-butyl group and AVM B_1b contains an isopropyl group.

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. TOX has no concern over these AVM-related impurities (see PP# 5G3287, memo of W. Dykstra, 3/3/86).

The formulation proposed for use on potatoes is AGRI-MEK 0.15 EC, which is an emulsifiable concentrate (EC) containing 0.15 lbs active ingredient (ai.) per gallon (2.0 wt%). All inerts have been cleared for use under 40 CFR 180.1001 (see PP# 6G3320, memo of A. Smith, 6/23/86).

Proposed Use

For control of the Colorado potato beetle and *Liriomyza* leafminers on potatoes, apply AGRI-MEK 0.15 EC (EPA Reg.# 618-98) using ground equipment only, at the rate of 8 to 16 fl.oz./A. (0.00938 to 0.0188 lb.ai./A.) depending on the extent of infestation. For Colorado potato beetles, do not make more than two applications at least 7 days apart, up to 32 fl.oz./A./season (0.038 lb.ai./A./season). For *Liriomyza* leafminers, multiple applications may be made, at least 7 days apart, not to exceed 48 fl.oz./A./season (0.056 lb.ai./A./season). The minimum PHI is 14 days. Do not apply through any type of irrigation system. Do not apply in volumes of less than 20 gallons per acre. Do not graze or feed treated foliage to livestock.

Nature of the Residue

Metabolism in Plants

No new plant metabolism data were submitted with this tolerance request. 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 in a memo from 12/15/89).

CBTS (formerly DEB) has previously concluded that the metabolism of abamectin in plants results in a complex mixture of residues. The majority of the terminal residue is composed of several unidentified polar degradates. The parent compound, its delta-8,9-isomer, and the alpha 8-OH degradate have been identified in plants, with only the parent and its delta-8,9-isomer each accounting for at least 10% of the total residue. To support the uses on cotton and citrus, the polar degradates generated on citrus (30X, 7 day PHI) and *in vitro* (30 hour sample) have been tested for toxicity and were found to be of no toxicological significance at the levels tested (see TOX memos 7080 and 7081 of W. Dykstra dated 3/15/89, and DEB memo of F. Boyd concerning 8F3592 dated 6/21/89).

The proposed use on potatoes specifies multiple applications up to a maximum application rate of 48 fl. oz./A./season (0.056

lb.ai./A./season). Previously, the metabolism components have been examined from radio-labeled abamectin on celery (10 applications at 7 day intervals for a total equivalent of 1.0 lb.ai./A./season), radio-labeled abamectin 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 to conclude that it is unlikely that application of abamectin to potatoes will form new compounds that have not previously been produced and subjected to toxicity testing. While 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), CBTS concludes that the metabolism data are sufficient to support the proposed use on potatoes. The residues of concern are the parent compound (avermectin B_1a and B_1b) and its delta-8,9-isomer.

Metabolism in Animals

No additional animal metabolism data were submitted with this petition. Data from a goat metabolism study were previously reviewed in PP#7G3468 (memo of L. Cheng, 2/11/87) and summarized by S. Willett in her memo of 12/15/89 regarding PP#9F3703. Based on this study, the residues of concern in ruminants was determined to be the parent compound (avermectin B_1a and B_1b) and its delta-8,9-isomer. If the tolerances for residues in meat and milk need to be raised at some future time due to registration of abamectin on additional feed items, the 24-hydroxymethyl metabolite may need to be included in the tolerance expression and appropriate enforcement methods developed (see F. Boyd memo of 6/21/89).

Analytical Method

The petitioner has submitted the following method for the analysis of avermectin B_1 and its delta-8,9-isomer in raw potatoes.

> "HPLC-Fluorescence Determination For Avermectin B_1 and its Delta-8,9-Isomer in Raw Whole Potatoes", T. Wehner, Ph.D., 7/25/92, Merck Research Laboratories, Method #936-92-4, (MRID# 436233-01, vol. 7).

Samples were ground in a blender, homogenized with methanol, and diluted with water. The aqueous/methanol layer is passed through a C-8 column. The C-8 column is coupled with an aminopropyl column and eluted with methanol. The eluent is brought up to a 10 mL volume with methanol, split, and evaporated to dryness. The sample is dissolved in acetonitrile and reacted with trifluoroacetic anhydride/1-methylimidazole reagent to form a fluorescent derivative. The samples are analyzed by HPLC using a C-18 column and fluorescence detection. Since derivatization of the

delta-8,9-isomer produces the same derivative as avermectin B_1, the derivatized residue quantitated represents the sum of avermectin and its delta-8,9-isomer. The recoveries are shown in Table 1 (whole potatoes) and Table 2 (potato peels).

Table 1

Lab Validation of Method 936-92-4 for Avermectin Residues on Whole Potatoes

compound	spike level (ppb)	% recovery
B_1a	5	89
		83
		86
		98
		95
		83
		95
		97
		102
	7.5	103
	10	103
		103
		88

Table 2

Lab Validation of Method 936-92-4 for Avermectin Residues on Potato Peels

compound	spike level (ppb)	% recovery
B_1a	2	116
		80
		90
	5	82
	100	84
		83
		86
Δ-8,9-isomer	2	75
		77
		78
	50	76
		73
		86
B_1b	4.9	83
		80
		84

Comments and Recommendations

The lowest fortification level attempted on whole potatoes was 5 ppb. Therefore, based on Method 936-92-4 on whole potatoes, residues of avermectin B_1a/delta-8,9-isomer below 2 ng/g are non-detectable (reported as ND). The peak representing avermectin B_1a/delta-8,9-residues between 2 and 5 ng/g is identified but not quantitated (reported as NQ) and the peak for residues above 5 ng/g is identified and quantitated. Since avermectin B_1b is at most 20% (usually less than 10%) of the active ingredient, its residue levels are generally less than the quantitation limit (5 ng/g) or the detection limit (2 ng/g). The peak representing avermectin B_1b is identified but not quantitated when the residue level is between 2 and 5 ng/g. Residues of avermectin B_1b above 5 ng/g are identified and quantitated in the same manner as the avermectin B_1a/delta-8,9-isomer, using the avermectin B_1a standard curve for quantitation.

In general, it is inappropriate to quantitate one compound using the standard for another. The petitioner states that because it has been found that a standard curve of B_1b will produce a slightly higher slope than that of B_1a, attempts to quantitate avermectin B_1b from B_1a will, at worst, result in an overestimation of actual B_1b residues. In addition, the contribution of B_1b to the total B_1 is very small (typically about 10%). Therefore, CBTS does not believe that this questionable practice adversely affects the

total residue values, in this case.

Method validations of analytical methodology to determine residues of avermectin B_1a, its delta-8,9-isomer, and B_1b in plant and animal commodities have been conducted by the Agency. Merck Method 1009R3 (citrus methodology) and Method 32A (animal commodities) were determined to be adequate for enforcement purposes (see method evaluation reports of F. Boyd dated 9/2/88, and S. Willett dated 9/11/89). The methods were recently sent to the FDA for publication in PAM II. A method for cottonseed has also been submitted as a letter method (see memo of S. Willett, 9/21/89). The methodology has not yet been published in PAM II but may be obtained from PIB/FOD. Pending some minor changes, Method 8000 for use on pears and apples and Method 8920 for use on cucurbits have undergone successful validation at Beltsville (see memos of G.J. Herndon dated 9/18/95 and 9/18/95, respectively).

Merck Method 936-92-4 for analysis of avermectin B_1 and its delta-8,9-isomer in/on potatoes appears to be adequate and suitable for enforcement purposes. CBTS believes that Method 936-92-4 is essentially similar to the other avermectin methods that have been previously validated at the EPA Beltsville lab, and further validation will not be required. The method will be sent to FDA as a letter method.

Avermectin has been tested using methodology described in PAM I, multi-residue method protocol A, which is the only applicable protocol. Avermectin is not recovered using the multi-residue methodology.

Residue Data

Storage Stability

No storage stability data were provided with this petition. In conjunction with PP#1F3973/1H5611 (see memo 5/19/94), Merck referenced previously submitted storage stability data on various crops. The composite crops/recoveries are shown in Table 3.

Table 3

Storage Stability Recoveries for Abamectin Residues in Various Crop Matrices (stored at ≤ -10°C)

Matrix	Length of Frozen Storage (months)	Fortification Level (ppm) and Compound	Method Recovery at Longest Time Interval#	Storage Stability Recovery at Longest Time Interval*
celery	24	0.010 - B1a	70%	79%
		0.206 - B1a		70%
		0.015 - B1b		87%
		0.010 - Δ8,9 isomer		70%
pears	35	0.010 - B1a	95%	84%
		0.071 - B1a		86%
		0.005 - B1b		72%
		0.010 - Δ8,9 isomer		94%
strawberries	24	0.010 - B1a	105%	98%
		0.071 - B1a		102%
		0.005 - B1b		109%
		0.010 - Δ8,9 isomer		94%
tomatoes	24	0.010 - B1a	87%	88%
		0.051 - B1a		86%
		0.004 - B1b		90%
		0.009 - Δ8,9 isomer		74%
cottonseed	14	0.010 - B1a	73%	58%
whole oranges	29	0.010 - B1a	86%	89%
		0.052 - B1a		89%
		0.004 - B1b		95%
		0.010 - Δ8,9 isomer		84%
whole grapefruit	29	0.010 -B1a	96%	92%
		0.052 - B1a		82%
		0.004 - B1b		104%
		0.010 - Δ8,9 isomer		85%
whole lemons	29	0.010 - B1a	84%	86%
		0.052 - B1a		86%
		0.004 - B1b		98%
		0.010 - Δ8,9 isomer		83%
orange peel	52	0.025 - B1a	87%	67%
grapefruit peel	47	0.005 - B1a	unk.	85%
		0.025 - B1a		70%
lemon peel	47	0.005 - B1a	88%	93%
		0.025 - B1a		79%

- fresh fortification
* - uncorrected for method recovery

Samples from the submitted field trials were stored frozen up to 7 months between harvest and analysis. The previously submitted storage stability data on tomatoes should be representative and sufficient in duration to insure the stability of avermectin residues in the potato field residue samples.

Magnitude of the Residue

The following field trial data from 12 sites were submitted with the current petition:

"Determination of the Magnitude of the Residues of Avermectin B_1 and 8,9-Z Avermectin B_1 in/on the Raw Agricultural Commodity, Potatoes, from Abamectin 0.15 EC Applied with Paraffinic Crop Oil by Ground Equipment", J.A. Norton, 4/3/95, (MRID# 436233-01, vols. 1 - 7).

The following field trial data from 4 sites were submitted in conjunction with the EUP/temporary tolerance petition (PP#4G4295), which was reviewed in the memo of M. Flood dated 6/2/94:

"Determination of the Magnitude of the Residues of Avermectin B_1 and 8,9-Z Avermectin B_1 in/on the Raw Agricultural Commodity, Potatoes, from Abamectin 0.15 EC Applied with Paraffinic Crop Oil by Ground Equipment", J.A. Norton, 11/17/93, (MRID# 430352-01).

In total, twenty (20) field trials were conducted on potatoes in 1992, 1993, and 1994. Six (6) applications of AGRI-MEK® 0.15 EC were made using ground equipment and spray volumes of 20 to 50 gallons per acre. The rate per application varied from 0.019 lb.ai./A. (1X) to 0.10 lb.ai./A. (5.3X), with the resulting season rate of 2X to 10.7X the proposed rate. Half of the applications were made with the addition of paraffinic oil to the tank mix. Merck Method 936-92-4 was used to quantitate both the B_1a/delta-8,9-isomer and B_1b/delta-8,9-isomer.

None of the potato samples analyzed at any PHI exhibited detectable residues (<2 ug/g). The location and number of field trials satisfy the requirements outlined in the document "EPA Guidance on Number and Location of Domestic Crop Field Trials for Establishment of Pesticide Residue Tolerances", 6/2/94. The results are summarized in Table 4.

Table 4

Residue Summary of Avermectin Residues in/on Potatoes

trial state	study	average spray volume/application (gal./A.)	rate (lb.ai./A.) average (per application)	rate (lb.ai./A.) total	PHI (days)	# replicate samples analyzed	maximum total residues in ppb (uncorrected for method and storage recoveries) B_1a	maximum total residues in ppb (uncorrected for method and storage recoveries) B_1b
NY	001-92-5017R	30	0.10	0.60	0	6	ND	ND
					3	6	ND	ND
					7	6	ND	ND
PA	001-92-5018R	30	0.10	0.60	0	6	ND	ND
					3	6	ND	ND
					7	6	ND	ND
OR	001-92-5019R	30	0.10	0.60	0	6	ND	ND
					3	6	ND	ND
					7	6	ND	ND
FL	001-93-0002R	50	0.019	0.11	0	4	ND	ND
					14	4	ND	ND
FL	001-92-0038R	50	0.10	0.60	0	6	ND	ND
					3	6	ND	ND
					7	6	ND	ND
ID	001-93-1004R	50	0.019	0.11	0	4	ND	ND
					14	4	ND	ND
ID	001-93-1005R	20	0.019	0.11	0	4	ND	ND
					14	4	ND	ND
MI	001-93-1007R	20	0.019	0.11	0	4	ND	ND
					14	4	MD	ND
WA	001-93-5004R	50	0.019	0.11	0	4	ND	ND
					14	4	ND	ND
CA	001-93-5005R	40	0.019	0.11	0	4	ND	ND
					14	4	ND	ND
CA	001-93-5006R	40	0.019	0.11	0	4	ND	ND
					14	4	ND	ND
MD	001-93-7000R	30	0.019	0.11	0	4	ND	ND
					14	4	ND	ND
NY	001-93-7001R	20	0.019	0.11	0	4	ND	ND
					14	4	ND	ND
ME	001-93-7002R	20	0.019	0.11	0	4	ND	ND
					14	4	ND	ND
ND	001-94-1017R	20	0.019	0.11	0	4	ND	ND
					14	8	ND	ND
CO	001-94-1022R	40	0.10	0.60	0	4	ND	ND
					14	4	ND	ND

ND - not detected (< 2 ppb)

Processing Study

The following potato processing study was submitted with the current petition:

"Determination of the Magnitude of the Residues of Avermectin B_1 and 8,9-Z Avermectin B_1 in/on the Raw Agricultural Commodity, Potatoes, from Abamectin 0.15 EC Applied with Paraffinic Crop Oil by Ground Equipment", J.A. Norton, 4/3/95, (MRID# 436233-01, vol. 7).

Potatoes from one trial, 001-94-1022R, which were treated at the exaggerated rate of 0.10 lb.ai./A./application (5.3X) and season rate of 10.7X the proposed rate, were collected at a 14 day PHI, and processed by washing and steam peeling at an Englar and Associates processing facility in Moses Lake, Washington. Samples of unwashed and washed potatoes, wet and dried peel, wash water, and peeled potatoes were collected, frozen and shipped to ADC for analysis. The samples of unwashed potatoes, washed potatoes, and wet peel were assayed for abamectin and its 8,9-Z isomer. The methodology for wet peel was validated down to a limit of quantitation (LOQ) of 2 ppb. **None of the samples analyzed (wet peel) contained detectable residues of avermectin.** Because no residues were found in the wet potato peel samples, Merck did not assay the samples of wash water, peeled potatoes, and dried peel.

Comments

Handling of Non-Quantifiable (NQ) and Non-Detectable Residues in Setting the Tolerance (Acute Risk Assessment)

The matrix and methodology allow for a limit of quantitation (LOQ) of 5 ppb and a limit of detection (LOD) of 2 ppb on the whole potato matrix. In Table 4, the designation ND is used. ND refers to samples that were not detected (< 2 ppb). A value of 2 ppb will be assigned to these samples for the purposes of tolerances (and therefore, acute risk assessment).

In Table 4, having a ND for both B_1a and B_1b will result in a total avermectin residue concentration of 4 ppb (2 ppb + 2 ppb). However, CBTS does not believe that a tolerance value should be set below the limit of quantitation (LOQ) of the major component of the residue (in this case, B_1a). **Therefore, a tolerance value of 0.005 ppm (the LOQ) should be established for residues of avermectin on whole potatoes.**

Merck will need to provide a revised Section F proposing a 0.005 ppm (not 0.002 ppm) tolerance on potatoes (RAC).

Based on the non-detectable residues in the wet potato peel from exaggerated rates, **the same tolerance value of 0.005 ppm should be established for residues of avermectin on the processed**

commodities (granules/flakes, chips, and wet peel) and potato feedstuffs (culls and processed potato waste).

Handling of Non-Quantifiable (NQ) and Non-Detectable Residues in the Chronic Risk Assessment

The potato processing study that was submitted did not show any detectable residues of avermectin on wet potato peels from rates up to 10.7X of the proposed seasonal rate. The matrix and methodology allow for a limit of quantitation (LOQ) of 2 ppb on the wet peels. Based on the non-systemic nature of avermectin, residues in the whole potato are not expected to exceed those of the wet potato peel. Based on a 1X rate and for the purposes of chronic risk assessment, a value of 1 ppb (½ X 2 ppb) would be used for the non-quantifiable B_1a residues in the wet potato peel. However, since the processing study was conducted on samples that were treated at 10.7X the proposed seasonal rate, and resulted in non-quantifiable B_1a residues in the wet potato peel, a value of 0.2 ppb (1/10 X 2 ppb) will be used for the non-quantifiable B_1a residues in the wet potato peel.

If B_1a is non-quantifiable, the following discussion pertains to the level of B_1b present. Abamectin (avermectin B_1) is produced by a fermentation process using a strain of <u>Streptomyces avermitilis</u>. (This manufacturing process was reviewed in detail in L. Cheng's memo dated 5/1/86 reviewing EPA 618-OL). The technical product abamectin is a mixture of two homologs containing not less than 80% avermectin B_1a and not greater than 20% avermectin B_1b. These components differ by only one methylene unit at the 25-carbon position, wherein avermectin B_1a contains a sec-butyl group and avermectin B_1b contains an isopropyl group. Based on the residue data reviewed to date, the metabolism in plants does not seem to alter this ratio of B_1a to B_1b (at least 4 to 1). Therefore, for the purposes of chronic risk assessment, for the non-quantifiable residues in the wet potato peel samples which exhibit non-quantifiable B_1a residues, a value of ¼ of the B_1a residues will be used to estimate B_1b residue levels. Since a value of 0.2 ppb will be used for B_1a residues, a value of 0.05 ppb (¼ X 0.2 ppb) will be used to estimate the B_1b residue contribution of those samples. This results in a total B_1a + B_1b concentration of 0.25 ppb.

CBTS recommends that a value of 0.00025 ppm be used as the chronic anticipated residue for whole potatoes, wet potato peel, culls, and processed potato waste.

As noted in the "Maximum Theoretical Concentration Factors (1/93)", the concentration factor from potatoes to dried flakes/granules is 4.7. Based on this, CBTS calculates a total B_1a + B_1b concentration of 1.2 ppb (4.7 X the whole potato residue value of 0.25 ppb).

CBTS recommends that a value of 0.0012 ppm be used as the

chronic anticipated residue for potato granules/flakes and potato chips.

In summary, CBTS recommends that the residue values listed in Table 5 be used in the acute and chronic dietary risk assessment for avermectin.

Table 5

Acute and Chronic Residue Values to be Used in the Dietary Risk Assessment of Avermectin

DRES entry	Entry for ACUTE Risk Assessment (ppm)	Entry for CHRONIC Risk Assessment (ppm)
potatoes, dry	0.005	0.0012
potatoes, peel only	0.005	0.00025
potatoes, peeled	0.005	0.00025
potatoes, whole	0.005	0.00025

Meat, Milk, Poultry, and Eggs

Potato culls, processed potato waste, and other crops which have avermectin registrations are not routinely fed to poultry. Therefore, this section only addresses the meat, meat byproducts, and fat of beef cattle.

Meat

Acute

Based on a intake figure of 1.8 pounds of crude protein and 18 pounds of dry matter, a realistic diet for an 800 pound steer was established based on our in-house Spartan Dairy Ration Evaluator program. The residue levels used for the feed items in Table 6 are taken from those developed in the memo of G.J. Herndon dated 12/21/94 concerning PP#9F3787.

Table 6

Maximum Avermectin Residues in Beef Cattle from Various Crops

Ingredients	pounds of dry matter	pounds (as fed)	% in diet (based on dry matter)	% in diet (as fed)	Maximum Avermectin Residues (ppb) In Feed Items	Maximum Avermectin Residues (ppb) In the Diet (normalized to 100% total of all feed items)
almond hulls	2.0	2.2	11.0%	7.18%	100	7.18
cottonseed	0.3	0.33	1.6%	1.08%	5	0.054
fescue hay	4.0	4.4	21.8%	14.36%	N/A	N/A
tomato pomace (dried)	4.5	4.9	24.6%	16.00%	70	22.86
apple pomace (wet)	7.5	18.8	41%	61.38%	100	61.38
TOTAL	18.3	30.63	100%	100%	N/A	92

Using the feed factor (dose) for dairy cattle at 92 ppb, the potential maximum residues of avermectin in meat, fat, and meat byproducts can be estimated. The 28 day feeding study submitted with PP#7G3468 (see memo of L. Cheng dated 2/11/87) was performed on dairy cattle at levels of 10, 30, and 100 ppb of avermectin residues in the diet. The levels are summarized in Table 7.

Table 7

Avermectin Levels in Dairy Cattle Tissues from a 28 Day Feeding Study

	Avermectin Levels in Various Tissues and Organs (ppb)			
Dose (ppb)	Liver	Muscle	Fat	Kidney
10	3 - 4	1 - 2	2	1 - 2
30	5 - 8	2	4 - 6	2
100	18 - 20	2	10 - 14	4 - 5

The residue levels from the 100 ppb feeding were chosen to best represent the residue levels from a theoretical 92 ppb diet. Based on this, **the following residue values should be used for estimating the acute anticipated residues for the following DRES beef entries.**

beef

fat	0.014 ppm	
lean	0.002 ppm	
kidney	0.005 ppm	
liver	0.020 ppm	
dried	0.002 ppm	(same as lean)
byproducts	0.020 ppm	(taken from liver)

Due to the non-detectable levels of residues in potato feedstuffs, these worst-case diets have been constructed without the inclusion of potato residues. Therefore, these values are unchanged from the ones recommended in the memo of G.J. Herndon dated 12/21/94 concerning PP#9F3787.

The established tolerances for cattle meat (0.02 ppm), cattle meat by-products (0.02 ppm), and cattle fat (0.015) are adequate to cover the increased dietary burden from the addition of the feed items potato culls and processed potato waste.

Chronic

Based on a intake figure of 1.8 pounds of crude protein and 18 pounds of dry matter, a realistic diet for an 800 pound steer was established based on our in-house Spartan Dairy Ration Evaluator program. The residue levels used for the feed items in Table 8 are taken from those developed in the memo of G.J. Herndon dated 12/21/94 concerning PP#9F3787.

Table 8

Maximum Avermectin Residues in Beef Cattle from Various Crops

Ingredients	pounds of dry matter	pounds (as fed)	% in diet (based on dry matter)	% in diet (as fed)	Maximum Avermectin Residues (ppb)	
					In Feed Items	In the Diet (normalized to 100% total of all feed items)
almond hulls	2.0	2.2	11.0%	7.18%	39	2.80
cottonseed	0.3	0.33	1.6%	1.08%	0.5	0.0054
fescue hay	4.0	4.4	21.8%	14.36%	N/A	N/A
tomato pomace (dried)	4.5	4.9	24.6%	16.00%	11	1.76
citrus pulp (dried)	7.5	18.8	41.0%	61.38%	15	9.21
TOTAL	18.3	30.63	100%	100.5%	N/A	14

Using the feed factor (dose) for dairy cattle at 14 ppb, the potential maximum residues of avermectin B^1 in meat, fat, and meat byproducts can be estimated. Data from the same 28 day feeding study that was used for the acute dietary risk assessment (see Table 7 above) was used. The residue levels from the 30 ppb feeding were chosen to best represent the residue levels from a theoretical 14 ppb diet. Based on this, **the following residue values should be used for estimating the chronic anticipated residues for the following DRES beef entries.**

beef

fat	0.006 ppm	
lean	0.002 ppm	
kidney	0.002 ppm	
liver	0.008 ppm	
dried	0.002 ppm	(DRES uses beef lean value)
byproducts	0.008 ppm	(taken from liver)

Due to the non-detectable levels of residues in potato feedstuffs, these worst-case diets have been constructed without the inclusion of potato residues. Therefore, these values are unchanged from the ones recommended in the memo of G.J. Herndon dated 12/21/94 concerning PP#9F3787.

Milk

Acute

The established tolerance for residues of avermectin in milk is 0.005 ppm.

Based on a production figure of 50 pounds of milk per day, a realistic cow diet was established based on our in-house Spartan Dairy Ration Evaluator program. The residue levels used for the feed items in Table 9 are taken from those developed in the memo of G.J. Herndon dated 12/21/94 concerning PP#9F3787.

Table 9

Maximum Avermectin Residues in Dairy Cattle from Various Crops

Ingredients	pounds of dry matter	pounds (as fed)	% in diet (based on dry matter)	% in diet (as fed)	Maximum Avermectin Residues (ppb)	
					In Feed Items	In the Diet (normalized to 100% total of all feed items)
alfalfa hay	13	14.8	32.5%	33.26%	N/A	N/A
almond hulls	6	6.7	15%	15.06%	100	15.06
cotton hulls	6	6.6	15%	14.83%	5	0.742
cottonseed meal	3	3.2	7.5%	7.19%	5	0.360
tomato pomace (dried)	4	4.3	10%	10%	70	7.00
citrus pulp (dried)	8	8.9	20%	20%	100	20.0
TOTAL	40	44.5	100%	100%	N/A	43.2

Using the feed factor (dose) for dairy cattle at 43 ppb, the potential maximum residues of avermectin B^1 in milk can be estimated. The 28 day feeding study submitted with PP#7G3468 (see memo of L. Cheng dated 2/11/87) was performed on dairy cattle at levels of 10, 30, and 100 ppb of avermectin residues in the diet. The milk levels are summarized in Table 10.

Table 10

Avermectin Levels in Cows Milk from a 28 Day Feeding Study

	Avermectin Residues (ng/mL) in Various Milk Samples During the 28 Day Dosing Period at 3 Feeding Levels		
Day	10 ppb	30 ppb	100 ppb
1	ND	ND	ND
2	ND	ND	ND - 1 ppb (ave. = 0.5 ppb)
3	ND	ND	ND - 1 ppb (ave. = 0.5 ppb)
5	ND	ND - 1 ppb (ave. = 0.5 ppb)	ND - 1 ppb (ave. = 0.5 ppb)
7	ND	ND	1 - 2 ppb (ave. = 1.3 ppb)
14	ND	ND	1 - 4 ppb (ave. = 2.3 ppb)
28	ND	ND	1 ppb (ave. = 1 ppb)
Average	0.25 ppb	0.36 ppb	0.91 ppb

ND - not detected down to the lower limit that adequate method recoveries were achieved (0.5 ppb). For the purposes of the risk assessment, an ND value of ½ X 0.5 ppb, or 0.25 ppb will be used.

Since milk from various cows is mixed and composited, an average residue value during the 28 day dosing period from the 100 ppb feeding level was chosen to best correspond to the cow consuming a theoretical 43 ppb of residue in its diet. Therefore, from feeding 43 ppb of residues, residues in milk would be estimated to be 1 ppb. **CBTS recommends that a value of 0.001 ppm be used as the acute anticipated residue for milk.** Avermectin is intermediate in polarity (very soluble in chloroform, not as soluble in hexane or water). The normal concentration factors that would be applied to the DRES entries for non-fat milk solids and milk fat are 8X. Based on its solubility, for risk assessment purposes, CBTS will assume that ½ of the residue will go into each fraction (concentration factors of 4X for each). **Therefore, the following residue values should be used for estimating the acute anticipated residues for the following DRES milk entries.**

CAMR - calculated acute milk residue = 0.001 ppm

milk fat 4 X CAMR = 0.004 ppm
non-fat milk solids 4 X CAMR = 0.004 ppm
milk sugar CAMR = 0.001 ppm

Chronic

Based on a production figure of 50 pounds of milk per day, a realistic cow diet was established based on our in-house Spartan Dairy Ration Evaluator program. The residue levels used for the feed items in Table 11 are taken from those developed in the memo of G.J. Herndon dated 12/21/94 concerning PP#9F3787.

Table 11

Maximum Avermectin Residues in Dairy Cattle from Various Crops

Ingredients	pounds of dry matter	pounds (as fed)	% in diet (based on dry matter)	% in diet (as fed)	Maximum Avermectin Residues (ppb) In Feed Items	Maximum Avermectin Residues (ppb) In the Diet (normalized to 100% total of all feed items)
alfalfa hay	13	14.8	32.5%	33.26%	N/A	N/A
almond hulls	6	6.7	15%	15.06%	39.0	5.873
cotton hulls	6	6.6	15%	14.83%	0.5	0.0742
cottonseed meal	3	3.2	7.5%	7.19%	0.5	0.0360
tomato pomace (dried)	4	4.3	10%	10%	11	1.10
citrus pulp (dried)	8	8.9	20%	20%	18	3.60
TOTAL	40	44.5	100%	100%		10.7

Using the feed factor (dose) for dairy cattle at 11 ppb, the potential maximum residues of avermectin B^1 in milk can be estimated. Data from the same 28 day feeding study that was used for the acute dietary risk assessment (see Table 10 above) was used. An average residue value from the 10 ppb feeding level was chosen to best correspond to the cow consuming a theoretical 11 ppb of residue in its diet. Therefore, from feeding 11 ppb of residues, residues in milk would be estimated to be 0.25 ppb. **CBTS recommends that a value of 0.00025 ppm be used as the chronic anticipated residue for milk.** Avermectin is intermediate in polarity (very soluble in chloroform, not as soluble in hexane or water). The normal concentration factors that would be applied to the DRES entries for non-fat milk solids and milk fat are 8X. Based on its solubility, for risk assessment purposes, CBTS will assume that ½ of the residue will go into each fraction (concentration factors of 4X for each). **Therefore, the following residue values should be used for estimating the chronic anticipated residues for the following DRES milk entries.**

CCMR - calculated acute milk residue = 0.00025 ppm

milk fat 4 X CCMR = 0.001 ppm
non-fat milk solids 4 X CCMR = 0.001 ppm
milk sugar CCMR = 0.00025 ppm

Other Considerations

Avermectin tolerances on various commodities are under consideration by Codex, but have not been officially adopted. No Canadian or Mexican tolerances are established for avermectin and therefore no compatibility problem exists between the proposed U.S. and Codex tolerances.

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