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

OFFICE OF
PREVENTION, PESTICIDES
AND TOXIC SUBSTANCES

MEMORANDUM

Date:01/27/09.

Subject: **Abamectin. Revised** Review of the Section 3 Registration Request for Ear Tag Use on Beef Cattle and Non-Lactating Dairy Cattle. EPA File Symbol: 39039-RT.

PC Code: 122804 & 067501
Decision No.: 380725
Petition No.: 8F7454
Risk Assessment Type: Residue Chemistry
TXR No.: Non Applicable
MRID No.: 47164011, 47164012, 47164016, 47185502, 47185503, 47623901, 47623902, 47623903, 47623904, 47623905, and 47623906

DP Barcode: 357192, 360418 & 360699
Registration No.: 39039-RT
Regulatory Action: Section 3 Registration Request
Case No.: Not applicable
CAS No.: 71751-41-2
40 CFR: 180.449

From: Thurston G. Morton, Chemist
Risk Assessment Branch IV
Health Effects Division (7509P)

Through: Susan V. Hummel, Branch Senior Scientist
Risk Assessment Branch IV
Health Effects Division (7509P)

To: Nancy Dodd, Risk Assessor
Risk Assessment Branch III
Health Effects Division (7509P)

and

Thomas Harris
Insecticide/Rodenticide Branch
Registration Division (7505P)

This memorandum updates the previous memorandum (T. Morton, D354910, 8/06/08). This memorandum includes the residues of piperonyl butoxide in the tissues of cattle, summarizes data submitted for the dermal metabolism study requirement, along with removing the reference stating the tolerance for the meat byproducts of hog, horse, and sheep need increased.

This document was originally prepared under contract by Dynamac Corporation (2275 Research Blvd, Suite 300; Rockville, MD 20850; submitted 01/21/2008). The document has been reviewed by the Health Effects Division (HED) and revised to reflect current Office of Pesticide Programs (OPP) policies.

Executive Summary

Abamectin includes the combined residues of avermectin B_1 [a mixture of avermectins containing greater than or equal to 80% avermectin B_{1a} (5-*O*-demethyl avermectin A_1) and less than or equal to 20% avermectin B_{1b} (5-*O*-demethyl-25-de(1-methylpropyl)-25-(1-methylethyl) avermectin A_1)] and its delta-8,9-isomer. Abamectin is a natural fermentation product of the soil bacterium *Streptomyces avermitilis.* Abamectin is an insecticide/miticide used to control mites, leafminers, and other insects in commercially important crops; it is also used as a seed protectant against nematodes. Abamectin acts by interfering with the nervous system of the pest, causing the pest to become paralyzed. Available mechanistic data indicate a neurotoxic mechanism of action, related to interference with GABA-mediated neurotransmission.

Y-TEX Corporation has submitted an application for the use of abamectin to beef cattle and non-lactating dairy cattle as ear tags for protection against blood-feeding pests such as horn flies and ticks. The end-use product (EP) proposed for this use is Bovamec™ (YT-2508) Cattle Ear Tags (EPA Reg. No. 39039-RT) which is an injection-molded, plastic cattle ear tag with an average weight of 9 grams per tag that contains two active ingredients in the following nominal concentrations: abamectin (8.0%, w/w) and piperonyl butoxide (20.0%, w/w). A maximum of two ear tags (one on each ear) for up to four months may be applied. The proposed preslaughter interval (PSI) is 21 days.

No tolerances have been proposed in connection with the proposed cattle ear tag use. Tolerances have been established in 40 CFR §180.449(a) for the combined residues of the insecticide avermectin B_1 [a mixture of avermectins containing greater than or equal to 80% avermectin B_{1a} (5-*O*-demethyl avermectin A_1) and less than or equal to 20% avermectin B_{1b} (5-*O*-demethyl-25-de(1-methylpropyl)-25-(1-methylethyl) avermectin A_1)] and its delta-8,9-isomer in: milk at 0.005 ppm; meat and meat byproducts of cattle, hog, horse, and sheep at 0.02 ppm each; and cattle fat at 0.015 ppm. These tolerances were established based on expected secondary transfer of residues from oral dosing of livestock animals. Higher tolerances for cattle fat, and cattle meat byproducts are needed to support the proposed ear tag use.

The qualitative nature of abamectin residues in ruminants reflecting oral dosing is adequately understood based on a goat metabolism study. The residues of concern in orally dosed ruminants for the tolerance expression and risk assessment are the parent compounds (avermectin B_{1a} and B_{1b}) and their delta-8,9-isomers. 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 stuffs, the 2,4-hydroxymethyl metabolite may need to be included in the tolerance expression and appropriate enforcement methods developed.

The qualitative nature of abamectin residues in ruminants reflecting dermal treatment is adequately understood for the cattle ear tag use only. Sufficient non-guideline data have been submitted to support the waiving of the requirement of the dermal metabolism study for the ear tag use. . The residues of concern in cattle from the ear tag use for the tolerance expression and risk assessment are the parent compounds (avermectin B_{1a} and B_{1b}) and their delta-8,9-isomers. If additional dermal uses are requested in the future, a dermal metabolism study will be required.

An analytical enforcement method for abamectin is available in the Pesticide Analytical Manual (PAM Volume II) for bovine tissues and milk (Method II). The data-collection method used for

the analysis of samples from a beef cattle ear tag study is an HPLC method with fluorescence detection (Method AATM-R-53), which is similar to the enforcement method.

The 1990 Pestrak data base indicates that abamectin and its metabolites are not recovered or not likely to be recovered by FDA multiresidue methods. Therefore, the multiresidue methods can not be used to determine residues for dietary exposure assessment and can not be used as the primary enforcement method.

The submitted magnitude of the residue study, depicting magnitude of the residue reflecting application of abamectin to beef cattle as ear tags, is adequate to determine that quantifiable abamectin residues of concern were detected in liver, kidney, back fat, and perirenal fat when the proposed product formulation is applied according to label directions (1x). The residue data suggest that the established tolerances for fat and meat byproducts of ruminant will need to be raised to cover residues resulting from ear tag use; no change is required to the established tolerance for ruminant meat as a result of the ear tag use. No residue data were submitted for milk since the proposed ear tag use is restricted to beef cattle and non-lactating dairy cattle. The majority of samples collected from this study were stored frozen for less than 30 days prior to completion of residue analysis. No supporting storage stability data were submitted and none are required because of the relatively short storage period of samples.

Regulatory Recommendations and Residue Chemistry Deficiencies

A petition is required including the following: (i) a revised Directions for Use in Section B (see requirements under Directions for Use); and (ii) a Section F as specified below. Following submission of the petition, there are no residue chemistry issues that would preclude granting an unconditional registration for the requested use of abamectin to beef cattle and non-lactating dairy cattle as ear tags.

The proposed uses and the submitted data support the following tolerances for the combined residues of the insecticide avermectin B_1 [a mixture of avermectins containing greater than or equal to 80% avermectin B_{1a} (5-*O*-demethyl avermectin A_1) and less than or equal to 20% avermectin B_{1b} (5-*O*-demethyl-25-de(1-methylpropyl)-25-(1-methylethyl) avermectin A_1)] and its delta-8,9-isomer in:

Cattle, fat	0.03 ppm
Cattle, meat*	0.02 ppm
Goat, meat*	0.02 ppm
Hog, meat*	0.02 ppm
Horse, meat*	0.02 ppm
Poultry, meat*	0.02 ppm
Milk*	0.005 ppm
Sheep, meat*	0.02 ppm
Cattle, meat byproducts	0.06 ppm
Goat, meat byproducts*	0.02 ppm
Hog, meat byproducts*	0.02 ppm
Horse, meat byproducts*	0.02 ppm
Poultry, meat byproducts*	0.02 ppm
Sheep, meat byproducts*	0.02 ppm

*Tolerances of asterisked commodities need not be raised.

860.1200 Directions for Use

The label statement "Do not apply within 21 days of slaughter for human consumption" should be changed to "For optimum use of the product, do not apply within 21 days of slaughter". In addition, "Remove the cattle ear tags before slaughter" should be added to the label.

860.1300 Nature of the Residue - Livestock

The nature of the residue in livestock reflecting dermal metabolism is adequately understood for the cattle ear tag use only. Sufficient non-guideline data have been submitted to support the waiving of the requirement of the dermal metabolism study for the ear tag use. Any additional dermal uses will require a dermal metabolism study. . The residues of concern in cattle from the ear tag use for the tolerance expression and risk assessment are the parent compounds (avermectin B_{1a} and B_{1b}) and their delta-8,9-isomers.

860.1550 Proposed Tolerances

The petitioner is required to submit a petition to increase the tolerance levels to those presented in Table 4.

A human health risk assessment is forthcoming in a separate document.

Background

Table 1 lists the test compound nomenclature and Table 2 the physicochemical properties of the technical grade test compound abamectin.

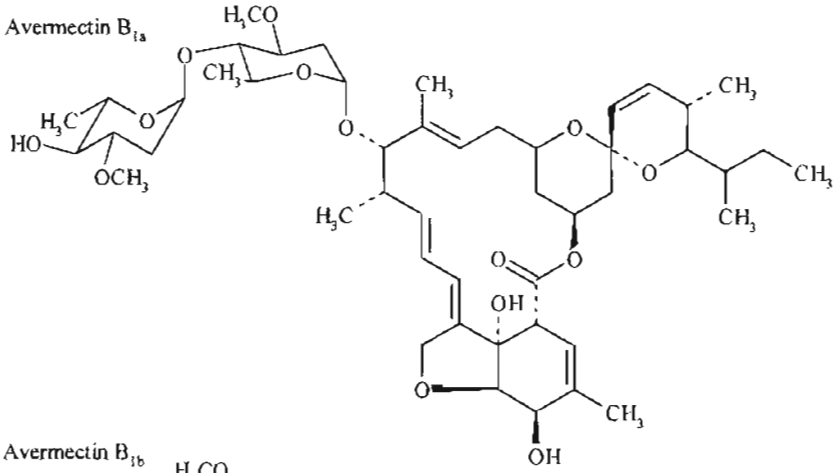
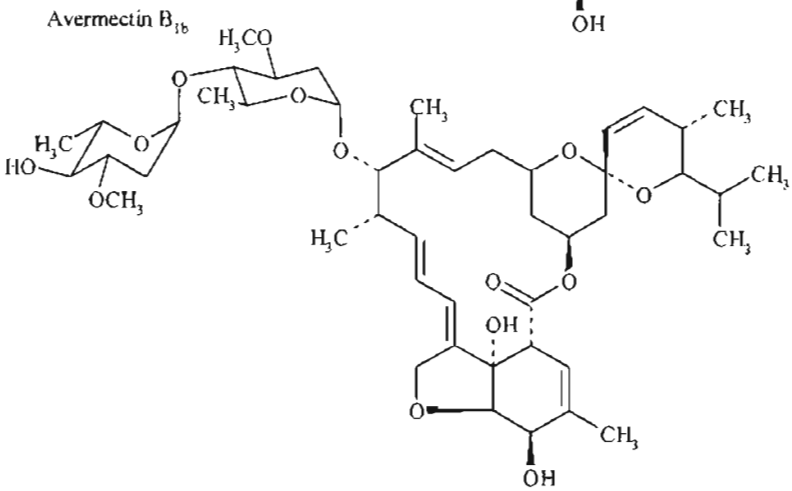
Table 1. Test Compound Nomenclature.	
Compound	Avermectin B_{1a}  Avermectin B_{1b} 
Common name	Abamectin; Avermectin B_1
Company experimental name	MK-0936
IUPAC name	mixture of (10*E*,14*E*,16*E*,22*Z*)-(1*R*,4*S*,5 '*S*,6*S*,6 '*R*,8*R*,12*S*,13*S*,20*R*,21*R*,24*S*)-6 '-[(*S*)-*sec*-butyl]-21,24-dihydroxy-5 ',11,13,22-tetramethyl-2-oxo-(3,7,19-trioxatetracyclo[15.6.1.1^{4,8}.0^{20,24}]pentacosa-10,14,16,22-tetraene)-6-spiro-2 '-(5 ',6 '-dihydro-2 '*H*-pyran)-12-yl 2,6-dideoxy-4-*O*-(2,6-dideoxy-3-*O*-methyl-α-L-*arabino*-hexopyranosyl)-3-*O*-methyl-α-L-*arabino*-hexopyranoside and (10*E*,14*E*,16*E*,22*Z*)-(1*R*,4*S*,5 '*S*,6*S*,6 '*R*,8*R*,12*S*,13*S*,20*R*,21*R*,24*S*)-21,22-dihydroxy-6 '-isopropyl-5 ',11,13,22-tetramethyl-2-oxo-(3,7,19-trioxatetracyclo[15.6.1.1^{4,8}.0^{20,24}]pentacosa-10,14,16,22-tetraene)-6-spiro-2 '-(5 ',6 '-dihydro-2 '*H*-pyran)-12-yl 2,6-dideoxy-4-*O*-(2,6-dideoxy-3-*O*-methyl-α-L-*arabino*-hexopyranosyl)-3-*O*-methyl-α-L-*arabino*-hexopyranoside
CAS name	Avermectin B_1
CAS registry number	71751-41-2
End-use product (EP)	Bovamec™ (YT-2508) Cattle Ear Tags (EPA Reg. No. 39039-RT) which contains two active ingredients in the following nominal concentrations: abamectin (8.0%, w/w) and piperonyl butoxide (20.0 %, w/w)

Table 2. Physicochemical Properties of the Technical Grade Test Compound Abamectin.

Parameter	Value	Reference[1]
Melting point/range	155-157 C	MRID 155627
pH	Not available	
Density/specific gravity	1.16 g/cm^3 at 21 C	MRID 155627
Water solubility (20 C)	< 0.01 mg/mL in distilled water < 0.001 mg/mL in tap water < 0.001 mg/mL in buffer system pH 6, 7.4 & 9.0 < 0.001 mg/mL in 0.9% NaCl	MRID 155627
Solvent solubility (mg/mL at 20 C)	> 3 mg/mL in ethanol; >2 mg/mL in isopropyl myristate, chloroform, dimethylacetamide, dimethylformamide, glycerol formal & polyethylene dycol 400.	MRID 155627
Vapor pressure at 25 C	1.5 x 10^{-9} mm Hg	MRID 155627
Dissociation constant (pK_a)	Not available	
Octanol/water partition coefficient, Log(K_{OW})	9.9 x 10^{-3}	MRID 155627
UV/visible absorption spectrum	Not available	

[1] Product Chemistry data were reviewed by L. Cheng (Accession No. 260785, RCB No. 388, 5/1/1986).

860.1200 Directions for Use

MRID Reference List: 47164011 (no der generated)

The end-use product relevant to this registration request is Bovamec™ (YT-2508) Cattle Ear Tags (EPA Reg. No. 39039-RT) which is an injection-molded, plastic cattle ear tag with an average weight of 9 grams per tag. It contains two active ingredients in the following nominal concentrations: abamectin (8.0%, w/w) and piperonyl butoxide (20.0 %, w/w). The product will be packed in laminated foil pouches of 20 tags each, and these will be packed in shelf cartons of 20 and 100 tags. The EP may be applied to beef cattle and non-lactating dairy cattle including calves. Non-lactating dairy cattle includes dairy breed animals of the following types: bulls, steers, replacement heifers (immature females) and dry cows.

The specimen label specifies the application of one tag per head for control of horn flies (*Haematobia irritans*) for up to three months. Two tags per head (one on each ear) may be applied for control of horn flies (*Haematobia irritans*) for up to four months, for control of ear ticks (Gulf Coast ticks and spinose ear ticks) and to aid in control of other ticks and face flies (*Musca autumnalis*). Tags may be applied to the front or back of each ear for horn fly control. With Brahman or Brahman-crossed cattle that have large ears, it is recommended to put the tag on the back of the ear for optimum efficacy against horn flies. For ear ticks, it is recommended to put a tag on the front of each ear.

The label specifies "Do not tag cattle within 21 days of slaughter for human consumption" as residues in liver (meat byproducts) or in perirenal fat may exceed tolerances during 7 to 14 days after tagging with fresh tags at the rate of two tags per animal. There is no need for a withdrawal period of used tags after at least 21 days of use due to declines in the detected residues of

abamectin". The label further specifies "Do not tag lactating dairy cows producing milk for human consumption' as a milk residue study has not yet been conducted with this product.

Conclusions. The label statement "Do not apply within 21 days of slaughter for human consumption" should be changed to "For optimum use of the product, do not apply within 21 days of slaughter". In addition, "Remove the cattle ear tags before slaughter" should be added to the label.

860.1300 Nature of the Residue - Plants

The residue chemistry data requirements for nature of the residue in plants are not pertinent to this review.

860.1300 Nature of the Residue - Livestock

Residue Chemistry Memo DP# 311383, N. Dodd, 2/10/05
MRID Reference List: 47164012, 47164016, 47623901, 47623902, 47623903, 47623904, 47623905, 47623906 (no der generated)

A goat metabolism study reflecting oral dosing of radiolabeled abamectin test substance has previously been submitted. HED review of this study concluded that the residues of concern in ruminants for the tolerance expression and risk assessment are the parent compounds (avermectin B_{1a} and B_{1b}) and their delta-8,9-isomers. 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.

Supplemental study submissions

A dermal ruminant metabolism study with abamectin was not included in this application. However, the petitioner submitted supplemental data from published scientific reports. Most of the reports submitted had supplemental information that was not directly related to dermal application or ear tag use. Only the pertinent information is summarized here.

MRID 47164012. 1982) The Metabolism of Avermectins B(1a), H(2)B(1a), and H(2)B(1b) by Liver Microsomes Drug Metabolism and Disposition 10(2): 268-274.

MRID 47164016. Baynes, R. (2004) "In Vitro Dermal Disposition of Abamectin (Avermectin B(1) in Livestock": YT-2508 Cattle Ear Tag. Research in Veterinary Science 76: 235-242.

MRID 47623901. Farnsworth, B. (2007) A Regulatory Study to Determine the Depletion of Abamectin Residues from the Plasma of Beef Cattle Following Treatment with Y-TEX YT-2508 Cattle Ear Tags - Analytical Phase. Project Number: Y/TEX/GLP/06/01, 06/0443, 06/0508. Unpublished study prepared by Agrisearch Services Pty. Ltd. 20 p.

MRID 47623902. Kellerby, J. (2008) Bovamec (YT-2508) Cattle Ear Tags: Summary of Residue Disposition and Ruminant Metabolism of Abamectin B1 After Dermal and Other Routes of Administration. Project Number: Y/TEX/2508/08/3. Unpublished study prepared by Y-Tex

Corporation. 291 p.

This submission contained a number of appendices one of which was the Australian Pesticides and Veterinary Medicines Authority's summary of the ear tag use. Residues of concern for the Australian regulatory agency are the same for oral and dermal application.

MRID 47623903. Jacob, T.; Buhs, R.; Carlin, J.; et al. (1983) YT-2508 (Bovamec) Cattle Ear Tag: "The Metabolism and Tissue Profiles of Ivermectin", Proceedings of the MSD AGVET Symposium on Recent Developments in the Control of Animal Parasites, XXII World Veterinary Congress, Perth, Australia, August 25 and 26, 1983: (Cattle). Project Number: 2508/PUBLIC/LIT/3. Unpublished study prepared by Merck, Sharp & Dohme Research Labs. 47 p.

Subcutaneous dosing of ivermectin which is a closely related compound revealed unchanged H_2B_{1a} and H_2B_{1b} as the major residue in cattle tissue ranging from 50% to 86% of the TRR.

MRID 47623904. Lee Chiu, S.; Sestokas, E.; Taub, R.; et al. (1986) YT-2508 (Bovamec) Cattle Ear Tag: Metabolic Disposition of Ivermectin in Tissues of Cattle, Sheep, and Rats. The American Society for Pharmacology and Experimental Therapeutics. 14(5): 590-600.

This was an article summarizing the same study as MRID 47623903.

MRID 47623905. Lee Chiu, S.; Carlin, J.; Taub, R.; et al. (1988) YT-2508 (Bovamec) Cattle Ear Tag: Comparative Metabolic Disposition of Ivermectin in Fat Tissues of Cattle, Sheep, and Rats. The American Society for Pharmacology and Experimental Therapeutics. 16(5): 728-736.

This submission appears to be the same study as 47623903 and 47623904.

MRID 47623906. Laffont, C.; Melou, A.; Bralet, D.; et al. (2003) YT-2508 (Bovamec) Cattle Ear Tag: A Pharmacokinetic Model to Document the Actual Disposition of Topical Ivermectin in Cattle. Veterinary Research. 34: 445-460.

Conclusions: The qualitative nature of abamectin residues in ruminants reflecting dermal treatment is adequately understood for the cattle ear tag use only. Sufficient non-guideline data have been submitted to support the waiving of the dermal metabolism study for the ear tag use. Any additional dermal uses will require a dermal metabolism study.

860.1340 Residue Analytical Methods

DER Reference List: 47185502.der.doc

Y-TEX Corporation has submitted an HPLC method with fluorescence detection (Method AATM-R-53) for the determination of residues of abamectin (total avermectin B1a and avermectin B1b) in bovine (cattle) and ovine (sheep) tissues. Method AATM-R-53 was the analytical method used for the analysis of samples collected from a beef cattle ear tag study (see DER for MRID 47185503; DP# 344808). A similar enforcement method (32A) is available for determination of abamectin residues in bovine milk and tissues.

Briefly, minced samples of animal tissue are extracted by maceration with acetonitrile (ACN), filtered and partitioned with hexane. The ACN extract/phase is evaporated to dryness and residues are redissolved in ACN:water (1:4, v:v). For sheep tissues, the extract is then partitioned into hexane and the hexane fraction evaporated to dryness. For cattle tissues, magnesium sulfate and sodium chloride are added to the extract causing partitioning between ACN and water; the ACN phase is evaporated to dryness. The evaporated fraction of sheep or cattle extracts is then diluted with 1-methylimidazole:ACN (1:1, v:v), and the residues converted to the anhydro derivative with the addition of trifluoroacetic anhydride. The derivatized residues are quantitated using HPLC with fluorescence detection.

Acceptable method validation recoveries were obtained for abamectin from samples of sheep and cattle muscle, fat, kidney and liver fortified at the LOQ (0.005 ppm), 10x LOQ (0.05 ppm for sheep kidney and liver, and cattle muscle, fat, kidney and liver), and/or up to 0.1 ppm (sheep fat only). Average recoveries were within the acceptable range of 70-120% and RSDs were <20% for abamectin in all matrices; individual recoveries were not reported. The fortification levels used in method validation are adequate to bracket expected residue levels in cattle commodities from the ear tag study.

Concurrent recovery data were generated in conjunction with the magnitude of the residue in cow studies submitted. Fortification levels for the concurrent recovery investigations were approximately 5 and 50 ppm in cattle fat, muscle, liver and kidney. Concurrent method validation data were not adequate to bracket expected residue levels in cattle tissues.

Confirmatory analysis procedures or an interference study is not required for the data-collection method. In addition, radiovalidation data are not required because the data-collection method is similar to the enforcement method for abamectin residues in bovine tissues and milk.

Conclusions: An analytical enforcement method for abamectin is available in the Pesticide Analytical Manual (PAM Volume II) for bovine tissues and milk (Method II). The data-collection method used for the analysis of samples from a beef cattle ear tag study is an HPLC method with fluorescence detection (Method AATM-R-53), which is similar to the enforcement method.

860.1360 Multiresidue Methods

The 1990 Pestrak data base indicates that abamectin and its metabolites are not recovered or not likely to be recovered by FDA multiresidue methods. Therefore, the multiresidue methods can not be used to determine residues for dietary exposure assessment and can not be used as the primary enforcement method.

860.1380 Storage Stability

The storage conditions and durations of samples collected from the cattle ear tag study are summarized in Table 3. Samples were stored frozen for up to 3.5 months prior to analysis, with the majority of the samples stored for less than 30 days. Only samples from treated groups 6 and 7 were stored for >30 days. No storage stability data were included in the study report, and these data may not be required considering that most samples were analyzed within 30 days.

Table 3. Summary of Storage Conditions.			
Matrix	Storage Temperature (°C)	Actual Storage Duration [1]	Interval of Demonstrated Storage Stability[2]
Bovine tissues	-15	2 – 107 days (0.1 – 3.5 months)	None

[1] Duration from sample collection to analysis; durations are estimated based on study termination and sample shipment dates.
[2] Storage stability data were not submitted.

860.1400 Water, Fish, and Irrigated Crops

The residue chemistry data requirements for water, fish, and irrigated crops are not pertinent to this review.

860.1460 Food Handling

The residue chemistry data requirements for food-handling establishments are not pertinent to this review.

860.1480 Meat, Milk, Poultry, and Eggs

Magnitude of the Residue Study Reflecting Application of Abamectin to Beef Cattle as Ear Tags

DER Reference List: 47185503.der.doc

Agrisearch Services Pty. Ltd. has submitted a magnitude of the residue study reflecting application of abamectin to beef cattle as ear tags. Twenty-eight mature beef cattle were divided into six treatment groups and one control group, with each group consisting of four cows. The test substance, Y-TEX YT-2508 CATTLE EAR TAGS, a 9-gram ear tag containing 8% abamectin and 20% piperonyl butoxide, was applied at a rate of 2 tags per animal (one per ear) (1x the maximum proposed use pattern). The six treatment groups were exposed to the ear tags for 1, 3, 7, 14, 21, or 42 days. Animal sacrifice of treated cattle was designed such that each exposure period is represented. Four control cows were sacrificed after 1 (2 cows), 14 (1 cow) or 42 (1 cow) days of exposure. The following tissue samples were collected for analysis at animal sacrifice: subcutaneous fat (lumbar region), muscle (rump), liver, perirenal fat, and kidney.

The study report included residue data for abamectin and piperonyl butoxide (PBO). Since the review instruction requests for abamectin data only, the analytical results from PBO determination are not reported herein. Cattle tissues were analyzed for residues of abamectin (total avermectin B1a and avermectin B1b) using an HPLC method with fluorescence detection (Method AATM-R-53). The method is adequate for the analysis of abamectin based on acceptable recovery data. The LOQ was 0.005 ppm, and LOD was 0.002 ppm for all cattle commodities.

A tabular summary of the beef cattle ear tag study is presented below. Quantifiable residues of abamectin (>0.005 ppm) were found in some liver, kidney, and fat samples from treated animals.

Residues of Abamectin in Tissues of Cattle Treated with Y-TEX YT-2508 CATTLE EAR TAGS, a 9-Gram Ear Tag Containing 8% Abamectin and 20% PBO, at a Rate of 2 Tags per Animal (One per Ear).					
Exposure Period (Days)	Abamectin (ppm)				
	Muscle	Liver	Kidney	Back Fat	Perirenal Fat
1	<LOD	<LOD	<LOD	<LOD	<LOD
3	<LOD	<LOD – 0.007	<LOD – 0.006	<LOD	<LOD - <LOQ
7	<LOD - <LOQ	0.012 – 0.031	<LOD – 0.017	<LOD - <LOQ	<LOQ – 0.018
14	<LOD - <LOQ	<LOQ – 0.043	<LOD – 0.010	<LOD – 0.006	<LOD – 0.017
21	<LOD	<LOD – 0.007	<LOQ	<LOD – 0.007	0.005-0.011
42	NA	<LOD - <LOQ	<LOD - <LOQ	<LOD - <LOQ	<LOD - <LOQ

LOD = 0.002 ppm; LOQ = 0.005 ppm; NA = not analyzed.

Residues of Piperonyl Butoxide in Tissues of Cattle Treated with Y-TEX YT-2508 CATTLE EAR TAGS, a 9-Gram Ear Tag Containing 8% Abamectin and 20% PBO, at a Rate of 2 Tags per Animal (One per Ear).					
Exposure Period (Days)	Piperonyl Butoxide (ppm)				
	Muscle	Liver	Kidney	Back Fat	Perirenal Fat
1	<LOD	<LOD	<LOD	<LOD	<LOD
3	<LOD	<LOD	<LOD	<LOD	<LOD
7	<LOD	<LOD	<LOD	<LOD	<LOD – 0.021
14	<LOD	<LOD	<LOD	<LOD	<LOD – 0.023
21	NA	NA	NA	NA	<LOD-0.027
42	NA	NA	NA	NA	NA

LOD = 0.01 ppm; LOQ = 0.02 ppm; NA = not analyzed.

Conclusions: The submitted study, depicting magnitude of the residue reflecting application of abamectin to beef cattle as ear tags, is adequate to determine that quantifiable abamectin residues of concern were detected in liver, kidney, back fat, and perirenal fat when the proposed product formulation is applied according to label directions (1x). The residue data suggest that the established tolerances for fat and meat byproducts of ruminant will need to be adjusted to cover residues resulting from ear tag use; no change is required to the established tolerance for ruminant meat as a result of the ear tag use. No residue data were submitted for milk since the proposed ear tag use is restricted to beef cattle and non-lactating dairy cattle.

860.1500 Crop Field Trials

The residue chemistry data requirements for crop field trials are not pertinent to this review.

860.1520 Processed Food and Feed

The residue chemistry data requirements for processed food and feed are not pertinent to this review.

860.1650 Submittal of Analytical Reference Standards

Analytical standards for abamectin and its metabolites are currently available in the EPA National Pesticide Standards Repository (personal communication with Dallas Wright, ACB, 1/08). Analytical reference standards of abamectin and its metabolites must be replenished when requested by the Repository. The reference standards should be sent to the Analytical Chemistry Lab, which is located at Fort Meade, to the attention of either Theresa Cole or William Chism at the following address:

USEPA
National Pesticide Standards Repository/Analytical Chemistry Branch/OPP
701 Mapes Road
Fort George G. Meade, MD 20755-5350

(Note that the mail will be returned if the extended zip code is not used.)

860.1850 Confined Accumulation in Rotational Crops

The residue chemistry data requirements for confined accumulation in rotational crops are not pertinent to this review.

860.1900 Field Accumulation in Rotational Crops

The residue chemistry data requirements for field accumulation in rotational crops are not pertinent to this review.

860.1550 Proposed Tolerances

No tolerances have been proposed in connection with the proposed cattle ear tag use.

Tolerances have been established in 40 CFR §180.449(a) for the combined residues of the insecticide avermectin B_1 [a mixture of avermectins containing greater than or equal to 80% avermectin B_{1a} (5-*O*-demethyl avermectin A_1) and less than or equal to 20% avermectin B_{1b} (5-*O*-demethyl-25-de(1-methylpropyl)-25-(1-methylethyl) avermectin A_1)] and its delta-8,9-isomer in: milk at 0.005 ppm; meat and meat byproducts of cattle, hog, horse, and sheep at 0.02 ppm each; and cattle fat at 0.015 ppm. These tolerances were established based on expected secondary transfer of residues from oral dosing of livestock animals.

The qualitative nature of abamectin residues in ruminants reflecting dermal treatment is adequately understood. Sufficient non-guideline data have been submitted to support the waiving of the dermal metabolism study for the ear tag use. Any additional dermal uses will require a dermal metabolism study.

The submitted study, depicting magnitude of the residue reflecting application of abamectin to beef cattle as ear tags, indicates that quantifiable abamectin residues of concern were detected in liver, kidney, back fat, and perirenal fat when the proposed product formulation is applied according to label directions. The residue data suggest that the established tolerances for fat and meat byproducts of cattle will need to be adjusted to cover residues resulting from ear tag use; no change is required to the established tolerance for ruminant meat as a result of the ear tag use. No residue data were submitted for milk since the proposed ear tag use is restricted to beef cattle and non-lactating dairy cattle.

A summary of the reassessed tolerances, which includes residues expected from ear tag use, is presented in Table 4.

Table 4. Tolerance Summary for Abamectin

Commodity	Established Tolerance (ppm)	Recommended Tolerance (ppm)	Comments; *Correct Commodity Definition*
Cattle, fat	0.015	0.03	
Cattle, meat Goat, meat Hog, meat Horse, meat Poultry, meat Sheep, meat	0.02	0.02	
Goat, meat byproducts Hog, meat byproducts Horse, meat byproducts Poultry, meat byproducts Sheep, meat byproducts	0.02	0.02	
Cattle, meat byproducts	0.02	0.06	
Milk	0.005	0.005	

The maximum residues from the ear tag study were added to the existing tolerance for each animal matrix.

References

DP Barcode: D311383
Date: 2/10/05
From: N. Dodd
To: J. Hebert
Subject: Abamectin. Seed Treatment of Cotton. Summary of Analytical Chemistry and Residue Data
MRIDs: None

Template Version September 2005