

**DEPARTMENT OF HEALTH & HUMAN SERVICES**

Food and Drug Administration
Rockville MD 20857

MAY 26 2004

Norma A. Buckart
Manager, Regulatory Affairs
Phibro Animal Health
710 Rt. 46 East
Suite 401
Fairfield, NJ 07004

Dear Ms. Buckart:

As you are aware, the Center for Veterinary Medicine was charged with examining previously approved antimicrobial products as a result of an amendment to the FY 2001 appropriations sponsored by U.S. Representative Sherrod Brown. As part of that effort, we have completed our review of the administrative file for your Penicillin G Procaine 50% (Type A Medicated Article, NADA 46-668).

Our review included an examination of the correspondence contained in, data submitted to, and master files referenced in, the administrative file. We conducted a qualitative risk assessment in light of the Center's recently published Guidance for Industry #152 entitled, "Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern," using the information contained in the records.

We are taking this opportunity to provide you with a summary of our findings:

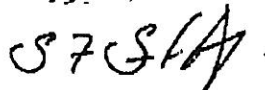
- The codified indications are: "For increased rate of weight gain and improved feed efficiency."
- No data were found to address 21 CFR 558.15 or GFI #152.
- CVM's proposal to withdraw penicillin premixes remains pending. 42 FR 43,770, Aug. 30, 1977 and 42 FR 56,264, Oct. 21, 1977.

The administrative record does not contain sufficient information to alleviate the Center's concern about the use of your product and its possible role in the emergence and dissemination of antimicrobial resistance. We used only that information on penicillin contained in your administrative file to evaluate your product. Where information on your specific product was lacking, we generally took a conservative approach and assessed the risk as high. The outcome of the qualitative risk assessment conducted according to Guidance #152 is that the product is considered Category 1. Production claims for increased rate of weight gain and improved feed efficiency are not considered appropriate for Category 1 or 2 products under Guidance #152.

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The Center for Veterinary Medicine would like to invite you to meet with us and discuss our findings. Please contact my office as soon as possible to arrange this. If you **have** any questions please contact Dr. Linda Tollefson, Deputy Director at 301-827-2950.

Sincerely yours,

A handwritten signature in black ink, appearing to read "S F Sundlof".

Stephen F. Sundlof, D.V.M., Ph.D.
Director, Center for Veterinary Medicine

cc: NADA 046-668
Director, Office of New Animal Drug Evaluation
Division Director, Human Food Safety

Citizen Petition Seeking Withdrawal of Approvals of Certain Herdwide/Flockwide Uses of Critically and Highly Important Antibiotics Pursuant to Guidance #152

Addendum: List of Approvals For Which Withdrawal is Sought

* See below for footnotes

Drug	Class	Dose	Combination (drug(s))	Dose	Section	Animal	Approval	Indications	Usage/Withdrawal Time	Limitations
Chlortetracycline	Tetracycline	0.1 mg/lb bw/day			(e)(4)(i)	Cattle	Revoke	Calves (up to 250 lb) increased rate of weight gain and improved feed efficiency	NS	In milk replacers or starter feed, include on labeling the warning "A withdrawal period has not been established for this product in pre-nursing calves. Do not use in calves to be processed for veal."
Chlortetracycline	Tetracycline	25-70 mg/head/day			(e)(4)(vi)	Cattle	Revoke	Calves (250 to 400 lb) For increased rate of weight gain and improved feed efficiency	NS	In milk replacers or starter feed, include on labeling the warning "A withdrawal period has not been established for this product in pre-nursing calves. Do not use in calves to be processed for veal."
Chlortetracycline	Tetracycline	70 mg/head/day			(e)(4)(vii)	Cattle	Revoke	Growing cattle (over 400 lb) For increased rate of weight gain, improved feed efficiency, and reduction of liver condemnation due to liver abscesses	NS	In milk replacers or starter feed, include on labeling the warning "A withdrawal period has not been established for this product in pre-nursing calves. Do not use in calves to be processed for veal."
Chlortetracycline	Tetracycline	350 mg/head/day			(e)(4)(viii)(1)	Cattle	Revoke	1 Beef cattle For control of bacterial pneumonia associated with shipping fever complex caused by <i>Pasteurella</i> spp. susceptible to chlortetracycline	NS	Withdrawal 48 h prior to slaughter. For sponsor 046573 zero withdrawal time. For sponsor 053389 1 d withdrawal time
Chlortetracycline	Tetracycline	350 mg/head/day	Sulfamethazine	350 mg/head/day	ALL	Cattle	Revoke	Aid in the maintenance of weight gains in the presence of respiratory disease such as shipping fever	28 days	Feed for 28 days, withdraw 7 days prior to slaughter
Chlortetracycline	Tetracycline	500-1000 g/ton	Decoquinat	13.6-27.2 g/ton	(e)(2)(i)***	Cattle	Amend	Calves, beef and non-lactating dairy cattle For the prevention of coccidiosis caused by <i>Eimeria bovis</i> and <i>E. zuernii</i> , for treatment of bacterial enteritis caused by <i>Escherichia coli</i> , for bacterial pneumonia caused by <i>Pasteurella multocida</i> organisms susceptible to chlortetracycline	???	???
Chlortetracycline	Tetracycline	400 g/ton	Decoquinat	13.6-27.2 g/ton	(e)(2)(iii)	Cattle	Amend	Calves, beef and non-lactating dairy cattle For prevention of coccidiosis caused by <i>Eimeria bovis</i> and <i>E. zuernii</i> , for treatment of bacterial enteritis caused by <i>Escherichia coli</i> , for bacterial pneumonia caused by <i>Pasteurella multocida</i> organisms susceptible to chlortetracycline	5-28 days	Feed Type C lead to provide 22.7 mg decoquinat and 1 gram (g) chlortetracycline per 100 lb body weight (0.5 mg/kg) per day for not more than 5 days. Type C lead may be prepared from Type B feed containing 535.8 to 5,440 g/ton decoquinat and 8,700 to 80,000 g/ton chlortetracycline. When consumed, feed 22.7 mg decoquinat per 100 lb body weight/day for a total of 28 days to prevent coccidiosis. Withdraw 24 hours prior to slaughter when manufactured from CTC (chlortetracycline) Type A medicated article under NADA 141-147. Zero withdrawal time when manufactured from ALPREONICIN (chlortetracycline) Type A medicated article under NADA 141-185. Do not feed to calves to be processed for veal. Do not feed to animals producing milk for food
Tylosin	Macrolide	8-10 g/ton	Decoquinat, monensin	13.6-27.2, 5-50 g/ton	(e)(2)(v)	Cattle	Revoke	Cattle fed in confinement for slaughter For prevention of coccidiosis caused by <i>Eimeria bovis</i> and <i>E. zuernii</i> , for improved feed efficiency, and for reduction of incidence of liver abscesses caused by <i>Fusobacterium necrophorum</i> and <i>Actinomyces</i> (<i>Corynebacterium</i>) <i>pyogenes</i>	C	Feed only to cattle fed in confinement for slaughter. Feed continuously as the sole ration to provide 22.7 mg of decoquinat per 100 lb body weight per day, 50 to 360 mg of monensin per head per day, and 60 to 90 mg of tylosin per head per day. Feed at least 28 days during period of exposure to coccidiosis or when it is likely to be a hazard. Do not feed to animals producing milk for food. Also see paragraph (d)(1) of this section and Sec 508.355(d)(8). Monensin and tylosin as provided by No. 000986 in Sec 510.600(c) of this chapter
Erythromycin	Macrolide	37 mg/head/day			(d)(2)	Cattle	Revoke	In feed for feedlot beef cattle at 37 milligrams per head per day as an aid in stimulating growth and improving feed efficiency	NS	
Chlortetracycline	Tetracycline	10 mg/lb bw	Laidlomycin	5 g/ton	(e)(2)	Cattle	Amend	For improved feed efficiency and increased rate of weight gain, treatment of bacterial enteritis caused by <i>Escherichia coli</i> and bacterial pneumonia caused by <i>Pasteurella multocida</i> organisms susceptible to chlortetracycline	5 days	Feed continuously at a rate of 30 to 75 mg laidlomycin propionate potassium per head per day for not more than 5 days. A withdrawal period has not been established for this product in pre-nursing calves. Do not use in calves to be processed for veal

Drug	Dose	Concentration	Form	Species	Section	Section	Section	Section	Section	Section
Chlortetracycline	350 mg/head/day	Laidlomycin	5 g/ton	305	(e)(3)	Cattle	Revoke	For improved feed efficiency and increased rate of weight gain, control of bacterial pneumonia associated with shipping fever complex caused by <i>Pasteurella</i> spp. susceptible to chlortetracycline	C	Feed continuously at a rate of 30 to 75 mg laddiomycin propionate potassium per head per day. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.
Chlortetracycline	10 mg/lb bw	Laidlomycin	5-10 g/ton	305	(e)(5)	Cattle	Amend	For improved feed efficiency, and for treatment of bacterial enteritis caused by <i>E. coli</i> and bacterial pneumonia caused by <i>P. multocida</i> organisms susceptible to chlortetracycline	5 days	Feed continuously at a rate of 30 to 150 mg laddiomycin propionate potassium per head per day for not more than 5 days. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.
Chlortetracycline	350 mg/head/day	Laidlomycin	5-10 g/ton	305	(e)(6)	Cattle	Revoke	For improved feed efficiency, and for control of bacterial pneumonia associated with shipping fever complex caused by <i>Pasteurella</i> spp. susceptible to chlortetracycline	C	Feed continuously at a rate of 30 to 150 mg laddiomycin propionate potassium per head per day. A withdrawal period has not been established for this product in pre-ruminating calves. Do not use in calves to be processed for veal.
Oxytetracycline	7.5 g/ton	Lasalocid	10-30 g/ton	311	(e)(1)(vi)	Cattle	Revoke	Cattle for improved feed efficiency and reduction of incidence and severity of liver abscesses	C	In Type C feeds, for beef cattle fed in confinement for slaughter, feed continuously at 100 to 360 mg/head/day lasalocid and 75 mg/head/day oxytetracycline As monoalkyl (C8-C18) trimethyl ammonium oxytetracycline
Oxytetracycline	7.5 g/ton	Lasalocid	25-30 g/ton	311	(e)(1)(vii)	Cattle	Revoke	Cattle for improved feed efficiency, increased rate of weight gain, and reduction of incidence and severity of liver abscesses	C	In Type C feeds, for beef cattle fed in confinement for slaughter, feed continuously at 250 to 360 mg/head/day lasalocid and 75 mg/head/day oxytetracycline As monoalkyl (C8-C18) trimethyl ammonium oxytetracycline
Oxytetracycline	75 g/ton	Melengestrol	0.25-0.5 g/ton	342	(e)(1)(viii)	Cattle	Revoke	Heifers fed in confinement for slaughter. For increased rate of weight gain, improved feed efficiency, and suppression of estrus (heat). For reduction of liver condemnation due to liver abscesses	NS	Add at the rate of 0.5 to 2.0 lb/head/day a medicated feed (liquid or dry) containing 0.125 to 1.0 mg melengestrol acetate per pound to a feed containing 0.5 to 2.0 lb/head/day a dry medicated feed containing 0.125 to 1.0 mg melengestrol acetate plus 37.5 to 150 mg oxytetracycline to provide 0.25 to 0.5 mg melengestrol acetate and 75 mg oxytetracycline/head/day. Oxytetracycline as provided by No. 066104 in Sec 510.600(c) of this chapter
Tylosin	90 g/ton	Melengestrol, lasalocid	0.25-0.5, 100-360 g/ton	342	(e)(1)(iv)	Cattle	Revoke	Heifers fed in confinement for slaughter. For increased rate of weight gain, improved feed efficiency, and suppression of estrus (heat). For reduced incidence of liver abscesses	NS	To administer 0.25 to 0.5 mg melengestrol acetate plus 100 to 360 mg lasalocid plus 90 mg tylosin/head/day 1. Add 0.5 to 2.0 lb/head/day of a liquid or dry medicated feed containing 0.125 to 1.0 mg melengestrol acetate to a medicated feed containing 10 to 30 g lasalocid and 8 to 10 g tylosin per ton, or 2. Add 0.5 to 2.0 lb/head/day of a liquid or dry medicated feed containing 0.125 to 1.0 mg melengestrol acetate plus 50 to 720 mg lasalocid to 4.5 to 18 lb of a dry medicated feed containing 10 to 40 g tylosin per ton, or 3. Add 0.5 to 2.0 lb/head/day of a dry pelleted medicated feed containing 0.125 to 1.0 mg melengestrol acetate (from a dry Type A article), 50 to 720 mg lasalocid, and 45 to 180 mg tylosin to a ration of nonmedicated feed Lasalocid provided by No. A1pharma and tylosin as Tylosin phosphate by No. 000986 in Sec 510.600(c) of this chapter

Drug	Class	Dose	Combination (mg/lb)	Dose	Precautions	Section	Animal	Action	Indications	Usage Time	Warnings
Tylosin	Macrolide	60-80 g/ton	Melengestrol, monensin	0.25-0.5, 50-360 g/ton	342	(e)(1)(vii)	Cattle	Revoke	Heifers fed in confinement for slaughter. For increased rate of weight gain, improved feed efficiency, and suppression of esthus (heat). For the prevention and control of coagulose due to E. bovis and E. zuraui, and for reduced incidence of liver abscesses caused by Fusobacterium necrophorum and Actinomyces (Corynebacterium) pyogenes.	NS	To administer 0.25 to 0.5 mg melengestrol acetate plus 50 to 360 mg lasalocid plus 60 to 90 mg Tylosin/head/day 1. Add 0.5 to 2.0 lb/head/day of a liquid or dry medicated feed containing 0.125 to 1.0 mg melengestrol acetate/lb to a medicated feed containing 5 to 30 g monensin and 8 to 10 g Tylosin per ton, or 2. Add 0.5 to 2.0 lb/head/day of a liquid or dry medicated feed containing 0.125 to 1.0 mg melengestrol acetate plus 25 to 750 g monensin/lb to 4.5 to 18 lb of a dry medicated feed containing 10 to 40 g Tylosin per ton; or 3. Add 0.5 to 2.0 lb/head/day of a dry pelleted medicated feed containing 0.125 to 1.0 mg melengestrol acetate (from a dry Type A article), 25 to 600 mg monensin, and 45 to 180 mg Tylosin/lb to a ration of nonmedicated feed. Monensin and Tylosin as Tylosin phosphate by No. 000988 in Sec. 510.600(c) of this chapter.
Tylosin	Macrolide	60-90 g/ton	Melengestrol	0.25-0.5 g/ton	342	(e)(1)(x)	Cattle	Revoke	Heifers fed in confinement for slaughter. For increased rate of weight gain, improved feed efficiency, and suppression of esthus (heat). For reduced incidence of liver abscesses caused by F. necrophorum and Actinomyces (Corynebacterium) pyogenes.	NS	To administer 0.25 to 0.5 mg melengestrol acetate with 60 to 90 mg Tylosin/head/day 1. Add 0.5 to 2.0 lb/head/day of a liquid or dry medicated feed containing 0.125 to 1.0 mg melengestrol acetate/lb to a medicated feed containing 8 to 10 g Tylosin per ton, or 2. Add 0.5 to 2.0 lb/head/day of a liquid or dry medicated feed containing 0.125 to 1.0 mg melengestrol acetate/lb to 4.5 to 18 lb of a dry medicated feed containing 10 to 40 g Tylosin per ton, or 3. Add 0.5 to 2.0 lb/head/day of a dry pelleted medicated feed containing 0.125 to 1.0 mg melengestrol acetate (from a dry Type A article) plus 45 to 180 mg Tylosin/lb to a ration of nonmedicated feed. Tylosin as Tylosin phosphate by No. 000986 in Sec. 510.600(c) of this chapter.
Tylosin	Macrolide	8-10 g/ton	Monensin	5-30 g/ton	355	(f)(3)(i)	Cattle	Revoke	Improved feed efficiency, for reduction of incidence of liver abscesses caused by Fusobacterium necrophorum and Actinomyces (Corynebacterium) pyogenes.	C	Feed only to cattle being fed in confinement for slaughter. Feed continuously as sole ration at the rate of 50 to 360 milligrams of monensin and 60 to 90 milligrams of Tylosin per head per day, as monensin sodium, as Tylosin phosphate. Combined with liquid Type B medicated feeds may be used in conjunction with dry Type C medicated feeds and shall conform to mixing instructions as in Sec. 559.625 (c).
Tylosin	Macrolide	150 g/ton	Monensin	400 g/ton	355	(f)(3)(x)	Cattle	Revoke	Improved feed efficiency, for reduction of incidence of liver abscesses caused by Fusobacterium necrophorum and Actinomyces (Corynebacterium) pyogenes.	C	Feed only to cattle being fed in confinement for slaughter. Feed continuously at the rate of 8.2 to 10.2 kilograms (18 to 22.5 pounds) of Type C medicated feed per head per day to supply 240 milligrams of monensin and 90 milligrams of Tylosin per head per day, as monensin sodium, as Tylosin phosphate. Do not allow horses or other equines access to feeds containing monensin. Ingestion of monensin by equines has been fatal. Safe use in unapproved equine breeding cattle has not been established. The liquid Type B medicated feed must bear an expiration date of 14 days after date of manufacture. The mixing directions for this liquid Type B medicated feed should be followed in recirculation or agitation tank systems. Feeds should be agitated immediately prior to use for not less than 10 minutes, moving at least 1 percent of the tank's contents per minute from the bottom of the tank to the top. Recirculate or agitate as directed daily, even when the Type B medicated feed is not used. Inadequate mixing (recirculation or agitation) of liquid Type B medicated feeds may result in increased monensin

Drug	Class	Dose	Combination (g/kg)	Dose	Species	Animal	Action	Precautions	Withdrawal	Residue	
Tylosin	Macrolide	8-10 g/ton	Monensin	10-30 g/ton	355	(f)(3)(xii)	Cattle	Revoke	For improved feed efficiency, prevention and control of coccidiosis due to <i>Eimeria bovis</i> and <i>E. zuernii</i> , and reduction of incidence of liver abscesses caused by <i>Fusobacterium necrophorum</i> and <i>Achromonyx</i> (<i>Corynebacterium</i>) progenies	C	Feed only to cattle being fed in confinement for slaughter. Feed continuously to provide 50 to 360 milligrams monensin per head per day. For prevention and control of coccidiosis, feed at a rate of 0.14 to 0.42 milligram monensin per pound of body weight per day, depending upon the severity of challenge, up to a maximum of 360 milligrams per head per day, and 60 to 90 milligram of tylosin per head per day.
Oxytetracycline	Tetracycline	0.05 to 0.1 mg/lb bw/day			450	(d)(1)(viii)	Cattle	Revoke	Calves (up to 250 lb), for increased rate of weight gain and improved feed efficiency	C	Feed continuously, in milk replacers or starter feed
Oxytetracycline	Tetracycline	25 mg/head/day			450	(d)(1)(xi)	Cattle	Revoke	Calves (250 to 400 lb), increased rate of weight gain and improved feed efficiency	NS	
Oxytetracycline	Tetracycline	75 mg/head/day			450	(d)(1)(xii)	Cattle	Revoke	Growing cattle (over 400 lb), increased rate of weight gain, improved feed efficiency, and reduction of liver condemnation due to liver abscesses	NS	
Tylosin	Macrolide	8-10 g/ton	Ractopamine, monensin	8-24 6, 10-30 g/ton	500	(e)(2)(iv)	Cattle	Revoke	Cattle fed in confinement for slaughter. For increased rate of weight gain and improved feed efficiency during the last 28 to 42 days on feed; for prevention and control of coccidiosis due to <i>E. bovis</i> and <i>E. zuernii</i> , and for reduction of incidence of liver abscesses caused by <i>Fusobacterium necrophorum</i> and <i>Achromonyx</i> (<i>Corynebacterium</i>) progenies	28-42 days	Feed continuously as sole ration during the last 28 to 42 days on feed. Not for animals intended for breeding.
Tylosin	Macrolide	8-10 g/ton	Ractopamine, monensin, melengestrol acetate	9.8-24.6, 10-30 g/ton, 0.25-0.5 mg/head/day	500	(e)(2)(v)***	Cattle	Revoke	For prevention and control of coccidiosis due to <i>Eimeria bovis</i> and <i>E. zuernii</i> ; for reduction of liver abscesses caused by <i>Fusobacterium necrophorum</i> and <i>Achromonyx</i> (<i>Corynebacterium</i>) progenies; improved feed efficiency, increased rate of weight gain, for increased carcass leanness, and for suppression of estrus (heat)	28-42 days	Feed continuously as sole ration during the last 28 to 42 days on feed. Not for animals intended for breeding.
Tylosin	Macrolide	8-10 g/ton	Ractopamine, monensin	9.8-24.6, 10-30 g/ton	500	(e)(2)(ix)	Cattle	Revoke	Cattle fed in confinement for slaughter. For increased rate of weight gain and improved feed efficiency during the last 28 to 42 days on feed; for prevention and control of coccidiosis due to <i>E. bovis</i> and <i>E. zuernii</i> , and for reduction of incidence of liver abscesses caused by <i>Fusobacterium necrophorum</i> and <i>Achromonyx</i> (<i>Corynebacterium</i>) progenies	28-42 days	Feed continuously as sole ration during the last 28 to 42 days on feed. Not for animals intended for breeding.
Tylosin	Macrolide	8-10 g/ton			625	(f)(1)(i)	Cattle	Revoke	For reduction of incidence of liver abscesses caused by <i>Fusobacterium necrophorum</i> and <i>Achromonyx</i> (<i>Corynebacterium</i>) progenies	C	As tylosin phosphate, each animal must receive not more than 90 milligrams per day and not less than 60 milligrams per day; feed continuously as sole ration
Virginiamycin	Streptogramin	16-22.5 g/ton			635	(d)(3)(i)	Cattle	Revoke	For increased rate of weight gain	C	Feed continuously as sole ration to cattle fed in confinement for slaughter. Not for use in animals intended for breeding.
Virginiamycin	Streptogramin	13.5-16 g/ton			635	(d)(3)(ii)	Cattle	Revoke	For reduction of incidence of liver abscesses	C	Feed continuously as sole ration to cattle fed in confinement for slaughter. Not for use in animals intended for breeding.
Virginiamycin	Streptogramin	11-16 g/ton			635	(d)(3)(iii)	Cattle	Revoke	For improved feed efficiency	C	Feed continuously as sole ration to cattle fed in confinement for slaughter. Not for use in animals intended for breeding.
Sulfantran	Sulfonamide	181.6 g/ton	Aklamide	227 g/ton	35	(c)(2)	Poultry	Revoke	Chickens. As an aid in the prevention of coccidiosis caused by <i>E. tenella</i> , <i>E. necatrix</i> , and <i>E. acervulina</i>	NS	Not to be fed to laying chickens, withdraw 5 days before slaughter.
Sulfantran	Sulfonamide	181.6 g/ton	Aklamide, roxarsone	227, 22.7-45.4 g/ton	35	(c)(3)	Poultry	Revoke	Chickens. As an aid in the prevention of coccidiosis caused by <i>E. tenella</i> , <i>E. necatrix</i> , and <i>E. acervulina</i> , growth promotion and feed efficiency, improving parentability	NS	Not to be fed to laying chickens, withdraw 5 days before slaughter, as sole source of organic arsenic, chickens should have access to drinking water at all times.
Chlortetracycline	Tetracycline	100-200 g/ton	Amprolium	36.3-113.5 g/ton	55	(d)(2)(i)	Poultry	Amend	Chickens, development of active immunity to coccidiosis, control of infectious synovitis caused by <i>Mycoplasma synoviae</i> susceptible to chlortetracycline	7-14 days	Do not feed to chickens producing eggs for human consumption. Feed for 7 to 14 d
Chlortetracycline	Tetracycline	200-400 g/ton	Amprolium	36.3-113.5 g/ton	55	(d)(2)(i)	Poultry	Amend	Chickens, development of active immunity to coccidiosis, control of chronic respiratory disease (CRD) and air sac infection caused by <i>M. gallisepticum</i> and <i>E. coli</i> susceptible to chlortetracycline	7-14 days	Do not feed to chickens producing eggs for human consumption. Feed for 7 to 14 d