

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 558

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[Docket No. 2003N-0324]

**New Animal Drugs for Use in Animal Feeds; Bacitracin; Nicarbazine;
Oxytetracycline and Neomycin; Penicillin**

AGENCY: Food and Drug Administration, HHS.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the animal drug regulations to reflect approval of four supplemental new animal drug applications (NADAs) filed by Phibro Animal Health. One supplemental NADA provides for the use of fixed-combination Type A medicated articles containing oxytetracycline and neomycin sulfate to formulate two-way fixed-combination drug Type B and Type C medicated feeds for chickens, turkeys, swine, cattle, and sheep. Two of the supplemental NADAs provide for the use of approved, single-ingredient Type A medicated articles containing nicarbazine and penicillin, with or without roxarsone, to formulate two-way or three-way combination drug Type C medicated feeds for broiler chickens. The fourth supplemental NADA provides for the use of approved, single-ingredient Type A medicated articles nicarbazine, bacitracin methylene disalicylate, and roxarsone to formulate three-way combination drug Type C medicated feeds for broiler chickens. These approvals reflect FDA's effectiveness conclusions which relied on the National Academy of Sciences/National Research Council

(NAS/NRC) Drug Efficacy Study Group's evaluation of the effectiveness of these drugs when used in animal feed as single ingredients.

DATES: This rule is effective [*insert date of publication in the Federal Register*].

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SUPPLEMENTARY INFORMATION: In the **Federal Register** of August 8, 2003 (68 FR 47332), as corrected October 7, 2003 (68 FR 57919), as part of the Drug Efficacy Study Implementation (DESI) program, CVM announced the effective conditions of use for several drug products and use combinations listed in 21 CFR 558.15. CVM proposed to withdraw the new animal drug applications (NADAs) for those products or use combinations lacking substantial evidence of effectiveness following a 90-day opportunity to supplement the NADAs with labeling conforming to the relevant findings of effectiveness. Phibro Animal Health, 65 Challenger Rd., 3d Floor, Ridgefield Park, NJ 07660, filed supplements to four of its approved NADAs to revise the labeling of its products to comply with these findings of effectiveness.

Phibro Animal Health filed a supplement to approved NADA 94-975 for NEO-TM 50/50D and NEO-TM 100/100D (oxytetracycline and neomycin sulfate) Type A medicated articles. The supplemental NADA provides for use of these fixed-combination Type A medicated articles to formulate two-way fixed-combination drug Type B and Type C medicated feeds containing oxytetracycline and neomycin sulfate, in a 1:1 ratio, for several production and therapeutic indications in chickens, turkeys, swine, cattle, and sheep.

Phibro Animal Health also filed a supplement to approved NADA 98-371 for use of nicarbazin, procaine penicillin, and roxarsone single-ingredient Type

A medicated articles to make three-way combination drug Type C medicated feeds. This supplemental NADA provides for the use of combination feeds containing NICARBAZIN (nicarbazin) at 90.8 to 181.6 grams per ton (g/ton), PENICILLIN G PROCAINE (procaine penicillin) at 2.4 to 50 g/ton, and 3-NITRO (roxarsone) at 22.7 to 45.4 g/ton of feed in broiler chickens as an aid in preventing outbreaks of cecal (*Eimeria tenella*) and intestinal (*E. acervulina*, *E. maxima*, *E. necatrix*, and *E. brunetti*) coccidiosis; for increased rate of weight gain and improved feed efficiency; and for improved pigmentation.

Phibro Animal Health also filed a supplement to approved NADA 98-374 for use of nicarbazin and procaine penicillin G Type A medicated articles to formulate two-way combination drug Type C medicated feeds. This supplemental NADA provides for the use of combination feeds containing NICARBAZIN (nicarbazin) at 90.8 to 181.6 g/ton and PENICILLIN G PROCAINE (procaine penicillin) at 2.4 to 50 g/ton of feed in broiler chickens as an aid in preventing outbreaks of cecal (*Eimeria tenella*) and intestinal (*E. acervulina*, *E. maxima*, *E. necatrix*, and *E. brunetti*) coccidiosis; and for increased rate of weight gain and improved feed efficiency.

Phibro Animal Health also filed a supplement to approved NADA 100-853 for use of nicarbazin, bacitracin methylene disalicylate, and roxarsone single-ingredient Type A medicated articles to make three-way combination drug Type C medicated feeds. This supplemental NADA provides for the use of combination feeds containing NICARBAZIN (nicarbazin) at 90.8 to 181.6 g/ton, BMD (bacitracin methylene disalicylate) at 4 to 50 g/ton, and 3-NITRO (roxarsone) at 22.7 to 45.4 g/ton of feed in broiler chickens as an aid in preventing outbreaks of cecal (*Eimeria tenella*) and intestinal (*E. acervulina*,

E. maxima, *E. necatrix*, and *E. brunetti*) coccidiosis, and for increased rate of weight gain, improved feed efficiency, and improved pigmentation.

The DESI evaluation is concerned only with the effectiveness of the drug products and use combinations. Nothing in this document constitutes a bar to further proceedings with respect to questions of safety of the subject drugs in treated animals or of the drugs or their metabolites in food products derived from treated animals.

Products that comply with FDA's findings of effectiveness are eligible for copying, as described in the *Generic Animal Drug and Patent Term Restoration Act Policy Letter Eight*, August 21, 1991 (56 FR 41561). Accordingly, sponsors may now obtain approval of abbreviated NADAs for this fixed combination Type A medicated article and three combination drug medicated feeds.

The supplemental NADAs are approved as of February 15, 2006, and the regulations are amended in 21 CFR 558.76, 558.460, and 558.366, and also in 21 CFR part 558 by adding new § 558.455 to reflect these approvals. Approval of these supplemental NADAs did not require review of any new safety or effectiveness data. Therefore, a freedom of information summary was not prepared.

The agency has determined under 21 CFR 25.33(a)(2) that these actions are of a type that do not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

This rule does not meet the definition of "rule" in 5 U.S.C. 804(3)(A) because it is a rule of "particular applicability." Therefore, it is not subject to the congressional review requirements in 5 U.S.C. 801–808.

List of Subjects in 21 CFR Part 558

Animal drugs, Animal feeds.

■ Therefore, under the Federal Food, Drug, and Cosmetic Act and under authority delegated to the Commissioner of Food and Drugs and redelegated to the Center for Veterinary Medicine, 21 CFR part 558 is amended as follows:

PART 558—NEW ANIMAL DRUGS FOR USE IN ANIMAL FEEDS

■ 1. The authority citation for 21 CFR part 558 continues to read as follows:

Authority: 21 U.S.C. 360b, 371.

■ 2. In § 558.76, revise paragraph (d)(3)(xiii) to read as follows:

§ 558.76 Bacitracin methylene disalicylate.

* * * * *

(d) * * *

(3) * * *

(xiii) Nicarbazin alone or with narasin or roxarsone or with narasin and roxarsone as in § 558.366.

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■ 3. In § 558.366, amend the table in paragraph (d) after the entry for “Narasin 27 to 45 and roxarsone 22.7 to 45.4” by adding three entries to read as follows:

§ 558.366 Nicarbazin.

* * * * *

(d) * * *

| Nicarbazin in grams per ton | Combination in grams per ton | Indications for use | Limitations | Sponsor |
|----------------------------------|--|---|--|---------|
| 90.8 to 181.6 (0.01 to 0.02 pct) | Bacitracin methylene disalicylate 4 to 50 and roxarsone 22.7 to 45.4 | Broiler chickens: As an aid in preventing outbreaks of cecal (<i>Eimeria tenella</i>) and intestinal (<i>E. acervulina</i> , <i>E. maxima</i> , <i>E. necatrix</i> , and <i>E. brunetti</i>) coccidiosis, and for increased rate of weight gain and improved feed efficiency, and improved pigmentation | Feed continuously as sole ration from time chicks are placed on litter until past the time when coccidiosis is ordinarily a hazard; do not use as a treatment for outbreaks of coccidiosis. Feed as the sole source of organic arsenic; drug overdose or lack of water may result in leg weakness; do not use in flushing mashers. Discontinue medication 5 days before marketing the birds for human consumption to allow for elimination of the drug from edible tissue. Do not feed to laying hens in production. Nicarbazin as provided by No. 066104; bacitracin methylene disalicylate and roxarsone by No. 046573 in § 510.600(c) of this chapter | 066104 |
| | Penicillin 2.4 to 50 | Broiler chickens: As an aid in preventing outbreaks of cecal (<i>Eimeria tenella</i>) and intestinal (<i>E. acervulina</i> , <i>E. maxima</i> , <i>E. necatrix</i> , and <i>E. brunetti</i>) coccidiosis, and for increased rate of weight gain and improved feed efficiency | Feed continuously as sole ration from time chicks are placed on litter until past the time when coccidiosis is ordinarily a hazard; do not use as a treatment for outbreaks of coccidiosis. Do not use in flushing mashers. Do not feed to chickens producing eggs for human consumption. Discontinue medication 5 days before marketing the birds for human consumption to allow for elimination of the drug from edible tissue. Penicillin as procaine penicillin G. Nicarbazin and penicillin as provided by No. 066104 in § 510.600(c) of this chapter | 066104 |
| | Penicillin 2.4 to 50 and roxarsone 22.7 to 45.4 | Broiler chickens: As an aid in preventing outbreaks of cecal (<i>Eimeria tenella</i>) and intestinal (<i>E. acervulina</i> , <i>E. maxima</i> , <i>E. necatrix</i> , and <i>E. brunetti</i>) coccidiosis, and for increased rate of weight gain and improved feed efficiency, and improved pigmentation | Feed continuously as sole ration from time chicks are placed on litter until past the time when coccidiosis is ordinarily a hazard; do not use as a treatment for outbreaks of coccidiosis. Feed as the sole source of organic arsenic; drug overdose or lack of water may result in leg weakness; do not use in flushing mashers. Discontinue medication 5 days before marketing the birds for human consumption to allow for elimination of the drug from edible tissue. Do not feed to laying hens in production. Penicillin as procaine penicillin G. Nicarbazin and penicillin as provided by No. 066104; roxarsone by No. 046573 in § 510.600(c) of this chapter | 066104 |

■ 4. Add § 558.455 to read as follows:

§ 558.455 Oxytetracycline and neomycin.

(a) *Specifications.* Type A medicated articles containing oxytetracycline equivalent to 50 grams per pound (g/lb) oxytetracycline hydrochloride and 50 g/lb neomycin sulfate or oxytetracycline equivalent to 100 g/lb oxytetracycline hydrochloride and 100 g/lb neomycin sulfate.

(b) *Sponsors.* See No. 066104 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See §§ 556.430 and 556.500 of this chapter.

(d) *Indications for use*—(1) *Chickens.* It is used in feed as follows:

| Oxytetracycline and neomycin sulfate amount in grams per ton of feed | Indications for use | Limitations | Sponsors |
|--|--|---|----------|
| (i) 10 to 50 | Chickens: For increased rate of weight gain and improved feed efficiency | Feed continuously; do not feed to chickens producing eggs for human consumption | 066104 |
| (ii) 100 to 200 | Chickens: For control of infectious synovitis caused by <i>Mycoplasma synoviae</i> ; control of fowl cholera caused by <i>Pasteurella multocida</i> susceptible to oxytetracycline | Feed continuously for 7 to 14 days (d); do not feed to chickens producing eggs for human consumption; in low calcium feed, withdraw 3 d before slaughter | 066104 |
| (iii) 400 | Chickens: For control of chronic respiratory disease (CRD) and air sac infection caused by <i>M. gallisepticum</i> and <i>Escherichia coli</i> susceptible to oxytetracycline | Feed continuously for 7 to 14 d; do not feed to chickens producing eggs for human consumption; in low calcium feeds, withdraw 3 d before slaughter | 066104 |
| (iv) 500 | Chickens: For reduction of mortality due to air sacculitis (air-sac-infection) caused by <i>E. coli</i> susceptible to oxytetracycline | Feed continuously for 5 d; do not feed to chickens producing eggs for human consumption; withdraw 24 hours before slaughter; in low calcium feeds withdraw 3 d before slaughter | 066104 |

(2) *Turkeys*. It is used in feed as follows:

| Oxytetracycline and neomycin sulfate amount | Indications for use | Limitations | Sponsors |
|---|---|---|----------|
| (i) 10 to 50 g/ton of feed | Growing turkeys: For increased rate of weight gain and improved feed efficiency | Feed continuously; do not feed to turkeys producing eggs for human consumption | 066104 |
| (ii) 100 g/ton of feed | Turkeys: For control of hexamitiasis caused by <i>Hexamita meleagridis</i> susceptible to oxytetracycline | Feed continuously for 7 to 14 d; do not feed to turkeys producing eggs for human consumption | 066104 |
| (iii) 200 g/ton of feed | Turkeys: For control of infectious synovitis caused by <i>M. synoviae</i> susceptible to oxytetracycline | Feed continuously for 7 to 14 d; withdraw 5 d before slaughter; do not feed to turkeys producing eggs for human consumption | 066104 |
| (iv) To provide 25 mg/lb of body weight daily | Turkeys: For control of complicating bacterial organisms associated with bluecomb (transmissible enteritis; coronaviral enteritis) susceptible to oxytetracycline | Feed continuously for 7 to 14 d; withdraw 5 d before slaughter; do not feed to turkeys producing eggs for human consumption | 066104 |

(3) *Swine*. It is used in feed as follows:

| Oxytetracycline and neomycin sulfate amount | Indications for use | Limitations | Sponsor |
|---|--|---|---------|
| (i) 10 to 50 g/ton of feed | Swine: For increased rate of weight gain and improved feed efficiency | | 066104 |
| (ii) To provide 10 mg/lb of body weight daily | 1. Swine: For treatment of bacterial enteritis caused by <i>E. coli</i> and <i>Salmonella choleraesuis</i> and treatment of bacterial pneumonia caused by <i>P. multocida</i> susceptible to oxytetracycline; treatment and control of colibacillosis (bacterial enteritis) caused by <i>E. coli</i> susceptible to neomycin | Feed continuously for 7 to 14 d; withdraw 5 d before slaughter | 066104 |
| | 2. Breeding swine: For control and treatment of leptospirosis (reducing the incidence of abortion and shedding of leptospirae) caused by <i>Leptospira pomona</i> susceptible to oxytetracycline | Feed continuously for not more than 14 d; withdraw 5 d before slaughter | 066104 |

(4) *Cattle and sheep*. It is used in feed as follows:

| Oxytetracycline and neomycin sulfate amount | Indications for use | Limitations | Sponsor |
|---|---|--|---------|
| (i) 10 to 20 grams per ton of feed | Sheep: For increased rate of weight gain and improved feed efficiency | | 066104 |
| (ii) To provide 0.05 to 0.1 mg/lb of body weight daily. | Calves (up to 250 lb): For increased rate of weight gain and improved feed efficiency | Feed continuously; in milk replacers or starter feed | 066104 |
| (iii) To provide 10 mg/lb of body weight daily | 1. Calves and beef and nonlactating dairy cattle: For treatment of bacterial enteritis caused by <i>E. coli</i> and bacterial pneumonia (shipping fever complex) caused by <i>P. multocida</i> susceptible to oxytetracycline; treatment and control of colibacillosis (bacterial enteritis) caused by <i>E. coli</i> susceptible to neomycin | Feed continuously for 7 to 14 d; in feed or milk replacers. If symptoms persist after using for 2 or 3 d, consult a veterinarian. Treatment should continue 24 to 48 hours beyond remission of disease symptoms. A withdrawal period has not been established for use in preruminating calves. Do not use in calves to be processed for veal. A milk discard time has not been established for use in lactating dairy cattle. Do not use in female dairy cattle 20 months of age or older. Withdraw 5 d before slaughter | 066104 |

| Oxytetracycline and neomycin sulfate amount | Indications for use | Limitations | Sponsor |
|---|---|--|-----------------------------|
| | <p>2. Calves (up to 250 lb): For treatment of bacterial enteritis caused by <i>E. coli</i> susceptible to oxytetracycline; treatment and control of colibacillosis (bacterial enteritis) caused by <i>E. coli</i> susceptible to neomycin</p> <p>3. Sheep: For treatment of bacterial enteritis caused by <i>E. coli</i> and bacterial pneumonia caused by <i>P. multocida</i> susceptible to oxytetracycline; treatment and control of colibacillosis (bacterial enteritis) caused by <i>E. coli</i> susceptible to neomycin</p> | <p>Feed continuously for 7 to 14 d; in milk replacers or starter feed. If symptoms persist after using for 2 or 3 d, consult a veterinarian. Treatment should continue 24 to 48 hours beyond remission of disease symptoms. A withdrawal period has not been established for use in preruminating calves. Do not use in calves to be processed for veal. A milk discard time has not been established for use in lactating dairy cattle. Do not use in female dairy cattle 20 months of age or older. Withdraw 5 d before slaughter</p> <p>Feed continuously for 7 to 14 d. If symptoms persist after using for 2 or 3 d, consult a veterinarian. Treatment should continue 24 to 48 hours beyond remission of disease symptoms. Withdraw 5 d before slaughter</p> | <p>066104</p> <p>066104</p> |
| (iv) To provide 25 mg/head/day | Calves (250 to 400 lb): For increased rate of weight gain and improved feed efficiency | | 066104 |
| (v) To provide 75 mg/head/day | Growing cattle (over 400 lb): For increased rate of weight gain; improved feed efficiency, and reduction of liver condemnation due to liver abscesses | | 066104 |
| (vi) To provide 0.5 to 2.0 g/head/day | Cattle: For prevention and treatment of the early stages of shipping fever complex | Feed 3 to 5 d before and after arrival in feedlots. A withdrawal period has not been established for use in preruminating calves. Do not use in calves to be processed for veal. A milk discard time has not been established for use in lactating dairy cattle. Do not use in female dairy cattle 20 months of age or older | 066104 |

■ 5. In § 558.460, redesignate paragraphs (d)(2)(vi), (d)(2)(vii), and (d)(2)(viii) as paragraphs (d)(2)(iii), (d)(2)(v), and (d)(2)(vi); and add new paragraph (d)(2)(iv) to read as follows:

§ 558.460 Penicillin.

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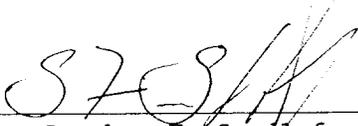
(d) * * *

(2) * * *

(iv) Nicarbazin alone or with roxarsone as in § 558.366.

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Dated: 3/22/06
March 22, 2006.



Stephen F. Sundlof,
Director,
Center for Veterinary Medicine.

[FR Doc. 06-????? Filed ??-??-06; 8:45 am]

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