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**DEPARTMENT OF HEALTH AND HUMAN SERVICES**

**Food and Drug Administration**

**21 CFR Parts 520 and 556**

**Oral Dosage Form New Animal Drugs; Piperazine**

**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 a supplemental new animal drug application (NADA) filed by Fleming Laboratories, Inc. The supplemental NADA provides for the safe and effective use of piperazine in chickens, turkeys, and swine for the treatment of certain parasitic infections. The approval reflects compliance with the results of the National Academy of Sciences/National Research Council (NAS/NRC) Drug Efficacy Study Implementation (DESI) evaluation of the effectiveness of piperazine and FDA's conclusions concerning that evaluation. FDA also is amending the regulations to provide tolerances for piperazine residues.

**EFFECTIVE DATE:** *(Insert date of publication in the Federal Register.)*

**FOR FURTHER INFORMATION CONTACT:** Dianne T. McRae, Center for Veterinary Medicine (HFV-102), Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301-827-0212.

**SUPPLEMENTARY INFORMATION:** Fleming Laboratories, Inc., P.O. Box 34384, Charlotte, NC 28234, filed a supplement to its approved NADA 10-005 for use of piperazine soluble powder and liquid for oral treatment of chickens and turkeys for roundworm infections and swine for roundworm and nodular worm infections. NADA 10-005 was originally approved on June 9, 1955. The drug was the subject of a NAS/NRC evaluation of effectiveness under FDA's DESI program (DESI 10-005V). The findings of the evaluation were published in the **Federal Register** of February

14, 1969 (34 FR 2213). The NAS/NRC DESI report concluded that the drug is effective as an anthelmintic for dogs, cats, chickens, turkeys, horses, swine, sheep, and cattle. FDA concurred with the conclusions of the report. Fleming Laboratories, Inc., filed a supplemental NADA providing revised labeling that brought its drug into compliance with the results of the NAS/NRC DESI evaluation and FDA's conclusions based on that evaluation.

The supplemental NADA provides for treatment of animals for parasitic infections as follows: (1) Chickens and turkeys, for *Ascaridia* spp., chickens at 50 milligrams (mg)/bird under 6 weeks and 100 mg/bird over 6 weeks; turkeys at 100 mg/bird up to 12 weeks and 200 mg/bird over 12 weeks according to size, at 0.2 to 0.4 percent in feed or 0.1 to 0.2 percent in water for 1 to 2 days; and (2) swine, for *Ascaris suum* and *Oesophagostomum* spp., at 50 mg/pound (lb) body weight, at 0.2 to 0.4 percent in feed or 0.1 to 0.2 percent in water for 1 to 2 days.

The supplement is approved as of March 23, 1999, and the regulations are amended by adding 21 CFR 520.1807 to reflect the approval. The basis of approval is discussed in the freedom of information summary.

In addition, tolerances for residues of piperazine in edible tissues of food-producing animals have been established. The regulations are amended by adding 21 CFR 556.513 to establish the residue tolerances.

In accordance with the freedom of information provisions of 21 CFR part 20 and 514.11(e)(2)(ii), a summary of safety and effectiveness data and information submitted to support approval of this supplemental application may be seen in the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852, between 9 a.m. and 4 p.m., Monday through Friday.

FDA has determined under 21 CFR 25.33(a)(1) that this action is of a type that does not individually or cumulatively have a significant effect on the human environment. Therefore, neither an environmental assessment nor an environmental impact statement is required.

FDA has previously informed manufacturers of piperazine products for food-producing animals not covered by approved applications that such products may be subject to regulatory action. FDA advised sponsors of DESI-reviewed piperazine products to pursue finalization of their NADA's at the earliest possible time. FDA now is providing public notice that it is prepared to take regulatory action against unapproved piperazine products for food-producing animals. In order to provide for an orderly phaseout, the manufacture of piperazine powder and liquid that is not the subject of an approved NADA or abbreviated new animal drug application (ANADA) shall cease by *(insert date 120 days after date of publication in the Federal Register)*, and the distribution of said products not manufactured under an approved application shall also cease by that date.

#### **List of Subjects**

##### *21 CFR Part 520*

Animal drugs.

##### *21 CFR Part 556*

Animal drugs, Foods.

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 parts 520 and 556 are amended as follows:

#### **PART 520—ORAL DOSAGE FORM NEW ANIMAL DRUGS**

1. The authority citation for 21 CFR part 520 continues to read as follows:

**Authority:** 21 U.S.C. 360b.

2. Section 520.1807 is added to read as follows:

**§ 520.1807 Piperazine.**

(a) *Specifications.* A soluble powder or liquid containing piperazine dihydrochloride or dipiperazine sulfate, equivalent to 17, 34, or 230 grams of piperazine per pound or 100 milliliters.

(b) *Sponsor.* See 015565 in § 510.600(c) of this chapter.

(c) *Related tolerances.* See § 556.513 of this chapter.

(d) *Conditions of use*—(1) *Chickens*—(i) *Amount.* 50 milligrams per bird under 6 weeks, 100 milligrams per bird over 6 weeks.

(ii) *Indications for use.* For removal of large roundworm (*Ascaridia* spp.).

(iii) *Limitations.* For use in drinking water or feed. Use as sole source of drinking water. Prepare fresh solution daily. Use as 1-day single treatment. Withdraw 14 days prior to slaughter. Do not use for chickens producing eggs for human consumption. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

(2) *Turkeys*—(i) *Amount.* 100 milligrams per bird up to 12 weeks and 200 milligrams per bird over 12 weeks.

(ii) *Indications for use.* For removal of large roundworm (*Ascaridia* spp.).

(iii) *Limitations.* For use in drinking water or feed. Use as sole source of drinking water. Prepare fresh solution daily. Use as 1-day single treatment. Withdraw 14 days prior to slaughter. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

(3) *Swine*—(i) *Amount.* 50 milligrams per pound of body weight.

(ii) *Indications for use.* For removal of large roundworm (*Ascaris suum*) and nodular worms (*Oesophagostomum* spp.).

(iii) *Limitations.* For use in drinking water or feed. Use as sole source of drinking water. Prepare fresh solution daily. Use as 1-day single treatment. Withdraw 21 days prior to slaughter. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

**PART 556—TOLERANCES FOR RESIDUES OF NEW ANIMAL DRUGS IN FOOD**

3. The authority citation for 21 CFR part 556 continues to read as follows:

Authority: 21 U.S.C. 342, 360b, 371.

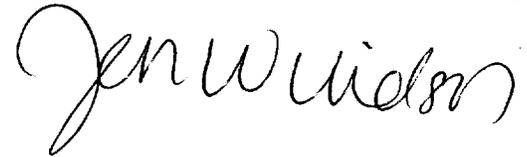
4. Section 556.513 is added to subpart B to read as follows:

**§ 556.513 Piperazine.**

A tolerance of 0.1 part per million piperazine base is established for edible tissues of poultry and swine.

Dated: April 19, 1999  
April 19, 1999

CERTIFIED TO BE A TRUE COPY OF THE ORIGINAL



Margaret Ann Miller

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Evaluation  
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