By the Commission.
Jonathan G. Katz,
Secretary.
December 1, 1986.

[FR Doc. 86-27739 Filed 12-9-86; 8:45 am]
BILLING CODE 8010-01-M

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

21 CFR Part 520

Oral Dosage Form New Animal Drugs Not Subject to Certification; Ivermectin Paste

AGENCY: Food and Drug Administration.
ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the animal drug regulations to reflect approval of a new animal drug application (NADA) filed by Merck Sharp & Dohme Research Laboratories providing for use of Ivomec® (ivermectin) paste for treating and controlling certain parasites in cattle.

EFFECTIVE DATE: December 10, 1986.

FOR FURTHER INFORMATION CONTACT: Adriano R. Gabuten, Center for Veterinary Medicine (HFV-135), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-4913.

SUPPLEMENTARY INFORMATION: Merck Sharp & Dohme Research Laboratories, Division of Merck & Co., Inc., P.O. Box 2000, Rahway, NJ 07065, has filed a new animal drug application (NADA 137-006) for Ivomec® (ivermectin) Cattle Paste 0.153%. The NADA provides for use of the drug for the control and treatment of certain roundworm, lungworm, grub, and lice infestations in cattle. The NADA is approved and the regulations for ivermectin paste (21 CFR 520.1192 (a) and (c)) are amended by revising paragraph (a), by redesignating paragraph (c)(1) as paragraph (c)(1)(i) and revising it, by redesignating paragraphs (c) (2) and (3) as paragraphs (c)(1) (ii) and (iii), and by adding new paragraph (c)(2) to reflect the approval. The basis for approval is discussed in the freedom of information summary.

In accordance with the freedom of information provisions of Part 20 (21 CFR Part 20) and § 514.11(e)(2)(ii) (21 CFR 514.11(e)(2)(ii)), a summary of safety and effectiveness data and information submitted to support approval of this application may be seen in the Dockets Management Branch (HFA-305), Food and Drug Administration, Rm. 4-62, 5600 Fishers Lane, Rockville, MD 20857, from 9 a.m. to 4 p.m., Monday through Friday.

The agency has determined under 21 CFR 25.24(d)(1)(iii) 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.

List of Subjects in 21 CFR Part 520

Animal drugs.

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, Part 520 is amended as follows:

PART 520—ORAL DOSAGE FORM NEW ANIMAL DRUGS NOT SUBJECT TO CERTIFICATION

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

Authority: Sec. 512(i), 82 Stat. 347 (21 U.S.C. 360b(i)); 21 CFR 5.10 and 5.83.

2. Section 520.1192 is amended by revising paragraph (a), by redesignating paragraph (c)(1) as paragraph (c)(1)(i) and revising it, by redesignating paragraphs (c) (2) and (3) as paragraphs (c)(1) (ii) and (iii), and by adding new paragraph (c)(2) to read as follows:

§ 520.1192 Ivermectin paste.

(a) *Specifications*—(1) *Horses.* Paste contains 1.87 percent ivermectin.

(2) *Cattle.* Paste contains 0.153 percent ivermectin.

* * * * *

(c) *Conditions of use*—(1) Horses—(i) *Amount.* 200 micrograms per kilogram (91 micrograms per pound) of body weight.

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(2) *Cattle*—(i) *Amount.* 23 milligrams per 250 pounds of body weight.

(ii) *Indications for use.* It is used in cattle for the treatment and control of gastrointestinal roundworms (adults and fourth-stage larvae) (*Ostertagia ostertagi* (including inhibited forms), *O. lyrata, Haemonchus placei, Trichostrongylus axei, T. colubriformis, Cooperia oncophora, C. punctata, Nematodirus helvetianus, Bunostomum phlebotomum, Strongyloides papillosus* (adults only), *Oesophagostomum radiatum, Trichuris ovis* (adults only)); lungworms (adults and fourth-stage larvae) (*Dictyocaulus viviparus*); grubs (first, second, and third instars) (*Hypoderma bovis, H. lineatum*); and sucking lice (*Linognathus vituli, Haematopinus eurysternus*).

(iii) *Limitations.* For oral use only. Do not treat cattle within 24 days of slaughter. Because withdrawal time in milk has not been established, do not use in female dairy cattle of breeding age. Consult your veterinarian for assistance in the diagnosis, treatment, and control of parasitism.

Dated: December 4, 1986.
Gerald B. Guest,
Director, Center for Veterinary Medicine.

[FR Doc. 86-27671 Filed 12-9-86; 8:45 am]
BILLING CODE 4160-01-M

21 CFR Part 522

Implantation or Injectable Dosage Form New Animal Drugs Not Subject to Certification; Tripelennamine Hydrochloride Injection

AGENCY: Food and Drug Administration.
ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending the animal drug regulations by codifying an approved new animal drug application (NADA) filed by Solvay Veterinary, Inc. The application provides for safe and effective use of tripelennamine hydrochloride injection as an antihistamine in horses, cattle, dogs, and cats. Codification of this application reflects compliance with the conclusions of the National Academy of Sciences/National Research Council (NAS/NRC) (academy) evaluation of the product. This document also amends the regulations to indicate those conditions of use for which applications for approval of identical products need not include certain types of effectiveness data. These conditions of use were classified as effective as a result of the NAS/NRC review. In lieu of certain effectiveness data, approval may require submission of bioequivalence or similar data.

EFFECTIVE DATE: December 10, 1986.

FOR FURTHER INFORMATION CONTACT: Donald A. Gable, Center for Veterinary Medicine (HFV-130), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-1414.

SUPPLEMENTARY INFORMATION: Solvay Veterinary, Inc., P.O. Box 7348, Princeton, NJ 08540, filed NADA 6-417 that provides for use of tripelennamine hydrochloride injection as an antihistamine in horses, cattle, dogs, and cats. NADA 6-417 was originally approved on January 29, 1948. The drug was the subject of a NAS/NRC report which was published in the **Federal Register** of August 21, 1970 (DESI 6417V,

35 FR 13402). The report covered use of tripelennamine hydrochloride tablets and an injectable product containing 20 milligrams of tripelennamine hydrochloride per milliliter of aqueous solution.

The academy evaluated the drug as probably effective for use in conditions in which antihistaminic therapy may be expected to lead to alleviation of some signs of disease in horses, cattle, sheep, swine, goats, dogs, and cats. The academy stated: (1) The rationale underlying the use of the preparation as a central nervous system stimulant for the "downer cow" syndrome is questioned; consequently, this claim should be deleted trom the label; (2) references to specific diseases should be deleted from the label unless they can be properly substantiated; (3) the documentation of efficacy is inadequate in that it is based primarily upon clinical reports and no controlled data are available in the veterinary medical literature; (4) evidence must be provided to establish that the tablets disintegrate in the gastrointestinal tract of the medicated species to produce the desired therapeutic effect; (5) the labeling should include information on side effects such as: (a) depression of the central nervous system and the incoordination that may occur when the drug is used at therapeutic dose levels; (b) disturbances in gastrointestinal functions that may occur; and (c) the fact that overdosage may give rise to excitement, ataxia, and convulsions; and (6) it is suggested that the labeling limit the indications for use to conditions in which antihistaminic therapy may be expected to lead to the alleviation of some signs of disease. Efficacy is not well established except in the case of exposure to an antigen to which the animal has a preexisting sensitivity. The sedative and antiemetic actions of antihistaminic drugs on the central nervous system may have prophylactic or therapeutic value in selected situations.

The Food and Drug Administration concurred with the academy's findings.

The NAS/NRC evaluation of the drug is concerned only with the effectiveness and safety of the drug for the treated animal and does not take into account safety of food use of drug-treated animals.

The firm submitted a supplemental NADA which brought the application into compliance with the conclusions of the review. The firm indicated that the tablet (bolus) product would be deleted, and the firm only wanted to update the NADA for use of the injectable product in dogs, cats, horses, and cattle. The regulations are amended by adding a new § 522.2615 (21 CFR 522.2615) to reflect the conditions of approval and to indicate those conditions of use which are NAS/NRC approved.

NADA's that pertain to identical products and reflect those conditions of use as set forth in this regulation do not require efficacy data as specified by § 514.1(b)(8)(ii) or § 514.111(a)(5)(ii)(*a*)(*4*) (21 CFR 514.1(b)(8)(ii) or 514.111(a)(5)(ii)(*a*)(*4*)) of the animal drug regulations. In lieu of such data, approval may require bioequivalency or similar data as suggested in the guideline for submitting NADA's for NAS/NRC-reviewed generic drugs. The guideline is available from the Dockets Management Branch (HFA–305), Food and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857.

This document does not involve reevaluation or reaffirmation of the underlying human safety data. Human safety data will be evaluated and affirmed in accordance with the scheduled priorities of the agency.

The agency has determined under 21 CFR 25.24(a)(9) 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.

List of Subjects in 21 CFR Part 522

Animal drugs.

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, Part 522 is amended as follows:

PART 522—IMPLANTATION OR INJECTABLE DOSAGE FORM NEW ANIMAL DRUGS NOT SUBJECT TO CERTIFICATION

1. The authority citation for 21 CFR Part 522 continues to read as follows:

Authority: Sec. 512(i), 82 Stat. 347 (21 U.S.C. 360b(i)); 21 CFR 5.10 and 5.83.

2. New § 522.2615 is added to Part 522 to read as follows:

§ 522.2615 Tripelennamine hydrochloride injection.

(a) *Specifications.* Each milliliter of aqueous solution contains 20 milligrams of tripelennamine hydrochloride.

(b) *Sponsor.* See No. 053501 in § 510.600(c) of this chapter.

(c) *Conditions of use*—(1) *Amount*—(i) *Dogs, cats, and horses.* For intramuscular use only at a dose of 0.5 milligram per pound of body weight.

(ii) *Cattle.* Administer intravenously or intramuscularly at a dose of 0.5 milligram per pound of body weight.

(2) *Indications for use.* For use in treating conditions in which antihistaminic therapy may be expected to lead to alleviation of some signs of disease.

(3) *Limitations.* Federal law restricts this drug to use by or on the order of a licensed veterinarian.

(d) *NAS/NRC status.* These conditions are NAS/NRC reviewed and deemed effective. Applications for these uses need not include effectiveness data as specified by § 514.111 of this chapter, but may require bioequivalency and safety data.

Dated: December 4, 1986.

Gerald B. Guest,

Director, Center for Veterinary Medicine.

[FR Doc. 86–27670 Filed 12–9–86; 8:45 am]

BILLING CODE 4160–01–M

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21 CFR Part 546

Tetracycline Antibiotic Drugs for Animal Use; Tetracycline Soluble Powder

AGENCY: Food and Drug Administration.

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 Medico Industries, Inc., providing for use of tetracycline hydrochloride soluble powder in chickens and turkeys. Approval exists for use of the drug in calves and swine. The supplemental NADA provides for (1) control of chronic respiratory disease, air sac infections, and infectious synovitis in chickens; and (2) control of infectious synovitis and bluecomb in turkeys.

EFFECTIVE DATE: December 10, 1986.

FOR FURTHER INFORMATION CONTACT: Charles E. Haines, Center for Veterinary Medicine (HFV–133), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–443–3410.

SUPPLEMENTARY INFORMATION: Medico Industries, Inc., Elkan Estates, P.O. Box 338, Elwood, KS 66024, has filed a supplement to NADA 65–496 for use of Tetracycline Hydrochloride Soluble Powder-324™ in the drinking water of chickens and turkeys in addition to its currently approved use in the drinking water of calves and swine. Drinking water containing 1,000 milligrams of tetracycline hydrochloride activity per gallon is administered to chickens and turkeys to provide 25 milligrams of drug

per pound of body weight daily. The medicated drinking water is administered to chickens for control of chronic respiratory disease and air sac infection caused by *Mycoplasma gallisepticum* and *Escherichia coli* and infectious synovitis caused by *M. synoviae* susceptible to tetracycline. It is administered to turkeys for control of infectious synovitis caused by *M. synoviae* and bluecomb caused by complicating bacterial organisms susceptible to tetracycline.

The supplemental NADA complies with FDA's accepted conclusions of the National Academy of Sciences/National Research Council (NAS/NRC), Drug Efficacy Study Group evaluation for tetracycline hydrochloride (see 35 FR 10966–10967, July 8, 1970). The supplemental application is approved and 21 CFR 546.180d is amended by adding paragraph (c)(6)(iv)(*c*) to reflect the approval. The basis for approval is discussed in the freedom of information summary. In addition, 21 CFR 546.180d(c)(5) is revised to indicate that these additional claims are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified in 21 CFR 514.111, but may require bioequivalency and safety information.

In accordance with the freedom of information provisions of Part 20 (21 CFR Part 20) and § 514.11(e)(2)(ii) (21 CFR 514.11(e)(2)(ii)), a summary of safety and effectiveness data and information submitted to support approval of this application may be seen in the Dockets Management Branch (HFA–305), Food and Drug Administration, Rm. 4–62, 5600 Fishers Lane, Rockville, MD 20857, from 9 a.m. to 4 p.m., Monday through Friday.

The agency has determined under 21 CFR 25.24(d)(1)(iii) 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.

List of Subjects in 21 CFR Part 546

Animal drugs, Antibiotics.

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, Part 546 is amended as follows:

PART 546—TETRACYCLINE ANTIBIOTIC DRUGS FOR ANIMAL USE

1. The authority citation for 21 CFR Part 546 continues to read as follows:

Authority: Sec. 512, 82 Stat. 343–351 (21 U.S.C. 360b); 21 CFR 5.10 and 5.83.

2. Section 546.180d is amended by revising paragraph (c)(5) and by adding paragraph (c)(6)(iv)(*c*) to read as follows:

§ 546.180d Tetracycline soluble powder.

* * * * *

(c) * * *

(5) *NAS/NRC status.* The conditions of use specified in paragraphs (c)(6)(i)(*c*)(*1*), (iii)(*d*)(*1*), and (iv)(*c*)(*1*) of this section are NAS/NRC reviewed and found effective. Applications for these uses need not include effectiveness data as specified in § 514.111 of this chapter, but may require bioequivalency and safety information.

(6) * * *

(iv) * * *

(*c*) *Amount.* 1,000 milligrams per gallon.

(*1*) *Indications for use.* Chickens: For control of chronic respiratory disease and air sac infection caused by *Mycoplasma gallisepticum* and *Escherichia coli;* infectious synovitis caused by *M. synoviae* susceptible to tetracycline. Turkeys: For control of infectious synovitis caused by *M. synoviae* and bluecomb (transmissible enteritis, coronaviral enteritis) caused by complicating bacterial organisms susceptible to tetracycline.

(*2*) *Limitations.* Administer medicated drinking water to chickens and turkeys to provide a dose of 25 milligrams per pound of body weight daily; administer for not more than 14 consecutive days; do not slaughter birds for food within 4 days of treatment; not for use in chickens and turkeys producing eggs for human consumption; prepare a fresh solution daily; use as sole source of tetracycline.

(*3*) *Sponsor.* See No. 015562 in § 510.600(c) of this chapter.

Dated: December 2, 1986.

Marvin A. Norcross,

Associate Director for New Animal Drug Evaluation.

[FR Doc. 86–27672 Filed 12–9–86; 8:45 am]

BILLING CODE 4160–01–M

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21 CFR Parts 610 and 630

[Docket No. 84N–0051]

General Biological Product Standards; Cell Lines Used for Manufacturing Biological Products, Additional Standards for Viral Vaccines

AGENCY: Food and Drug Administration.

ACTION: Final rule.

SUMMARY: The Food and Drug Administration (FDA) is amending its regulations to establish general requirements for cell lines used for manufacturing any biological product for human use. The regulations will standardize information required to be submitted to FDA in support of license applications regarding cell lines, including cell lines developed using new technologies, such as hybridoma technology or recombinant deoxyribonucleic acid (DNA) technology. FDA also is deleting certain requirements regarding human diploid cell lines used for manufacturing Poliovirus Vaccine Live Oral.

DATE: This regulation becomes effective on January 9, 1987.

FOR FURTHER INFORMATION CONTACT: Michael L. Hooton, Center for Drugs and Biologics (HFN–362), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–295–8049.

SUPPLEMENTARY INFORMATION: In the **Federal Register** of December 6, 1984 (49 FR 47622), FDA proposed to amend its regulations to establish general requirements for cell lines used for manufacturing any biological product for human use. FDA noted that its general biologics regulations in 21 CFR Parts 600, 601, and 610 have not previously contained general standards that apply to all cell lines used to produce viral vaccines and other biological products. FDA's only regulations concerning cell lines were included in the regulations for one product, Poliovirus Vaccine Live Oral (21 CFR 630.12(b) and 630.13(c)), published in the **Federal Register** of October 16, 1971.

In the proposal, FDA identified substrates in which viruses intended for production of viral vaccines are cultivated. The substrates identified included: (1) Primary cell cultures of avian and mammalian species that can be subcultivated for only a limited number of population doublings, and (2) human diploid cell lines.

FDA approved the use of human diploid cell lines for the cultivation of virus on October 16, 1971 (36 FR 20160). Human diploid cell lines that are capable of propagation of viruses in vitro are now being used extensively worldwide for producing viral vaccines. Currently, licensed viral vaccines that are produced in human diploid cell lines include Adenovirus Vaccine Live Oral Type 4, Adenovirus Vaccine Live Oral Type 7, Rubella Virus Vaccine Live, and Rabies Vaccine. Manufacturers of these vaccines produced in human diploid cell lines are required by their approved