

granted if the objections are supported by grounds legally sufficient to justify the relief sought. Objections may be accompanied by a memorandum or brief in support thereof.

**Effective date.** This order shall become effective on its date of publication in the FEDERAL REGISTER.

(Sec. 409(c)(1), 72 Stat. 1786; 21 U.S.C. 348(c)(1))

Dated: June 2, 1970.

R. E. DUGGAN,  
Acting Associate Commissioner  
for Compliance.

[F.R. Doc. 70-7148; Filed, June 9, 1970;  
8:46 a.m.]

SUBCHAPTER C—DRUGS

**PART 141b—STREPTOMYCIN (OR DIHYDROSTREPTOMYCIN) AND STREPTOMYCIN- (OR DIHYDROSTREPTOMYCIN-) CONTAINING DRUGS; TESTS AND METHODS OF ASSAY**

**PART 146b—CERTIFICATION OF STREPTOMYCIN (OR DIHYDROSTREPTOMYCIN) AND STREPTOMYCIN- (OR DIHYDROSTREPTOMYCIN-) CONTAINING DRUGS**

**Antibiotic Drugs for Parenteral Use Containing Dihydrostreptomycin Sulfate and Dihydrostreptomycin Sulfate With Streptomycin Sulfate**

In the FEDERAL REGISTER of February 6, 1970 (35 F.R. 2670), the Commissioner of Food and Drugs announced (DESI 60109) the conclusions of the Food and Drug Administration following evaluation of reports received from the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, regarding the following anti-infective drugs offered for intramuscular use in man:

1. Dihydrostreptomycin sulfate powder, equivalent to 1.0 gram dihydrostreptomycin base per vial; by Chas. Pfizer & Co., Inc., 235 East 42d Street, New York, N.Y. 10017.

2a. Dihydrostreptomycin sulfate powder, equivalent to 1.0 gram and 5.0 grams dihydrostreptomycin base per vial; and

b. Dihydrostreptomycin sulfate solution 2.5 cc. (1 gram) and 12.5 cc. (5 grams); both by Merck & Co., Inc., Rahway, N.J. 07065.

3a. Dihydrostreptomycin sulfate powder, equivalent to 1.0 gram and 5.0 grams dihydrostreptomycin base per vial; and

b. Dihydrostreptomycin sulfate solution, equivalent to 0.4 gram or 0.5 gram dihydrostreptomycin base per cc.; both by Philadelphia Labs., 9815 Roosevelt Boulevard, Philadelphia, Pa. 19114.

4. Dihydrostreptomycin sulfate powder, equivalent to 1.0 gram and 5.0 grams dihydrostreptomycin base per vial; by E. R. Squibb & Sons, Inc., Georges Road, New Brunswick, N.J. 08903.

5a. Dihydrostreptomycin sulfate powder, equivalent to 1.0 gram and 5.0 grams dihydrostreptomycin base per vial; and

b. Dihydrostreptomycin sulfate solution, equivalent to 0.5 gram dihydrostreptomycin base per cc.; both by Pure Laboratories, Inc., 50 Intervale Road, Parsippany, N.J. 07054.

6. Dihydrostreptomycin sulfate powder with streptomycin sulfate powder, equivalent to 0.5 gram dihydrostreptomycin base and 0.5 gram streptomycin base per vial; by Merck & Co., Inc., Rahway, N.J. 07065.

7. Dihydrostreptomycin sulfate powder with streptomycin sulfate powder, equivalent to 0.5 gram dihydrostreptomycin base and 0.5 gram streptomycin base per vial, or 2.5 grams dihydrostreptomycin base and 2.5 grams streptomycin base per vial; by E. R. Squibb & Sons, Inc., Georges Road, New Brunswick, N.J. 08903.

Although these drugs had been evaluated by the Academy as effective for certain indications, the Commissioner concluded that the risks involved in their use outweigh any benefits that might be derived from such use and that provision for their certification should be repealed. Also announced was that dihydrostreptomycin sulfate, alone or in combination, is regarded as unsafe for its recommended uses because such uses expose patients to the drug's ototoxic hazard.

No comments were received in response to the proposal to amend the antibiotic drug regulations to repeal provision for certification of these drugs and to revoke certificates of safety heretofore issued for them.

Therefore, pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (secs. 502, 507, 52 Stat. 1050-51, as amended; 59 Stat. 463, as amended; 21 U.S.C. 352, 357) and under authority delegated to the Commissioner (21 CFR 2.120), Parts 141b and 146b are amended:

1. By revising the section headings of §§ 141b.111, 141b.118, and 141b.122 to read as follows:

§ 141b.111 Streptomycin sulfate injection: dihydrostreptomycin sulfate injection veterinary; crystalline dihydrostreptomycin sulfate injection veterinary.

§ 141b.118 Dihydrostreptomycin-streptomycin sulfates veterinary.

§ 141b.122 Dihydrostreptomycin-streptomycin sulfates solution veterinary.

§ 141b.125 [Revoked]

2. By revoking § 141b.125 *Dihydrostreptomycin-streptomycin sulfates with isonicotinic acid hydrazide.*

§ 146b.103 [Amended]

3. In § 146b.103 *Dihydrostreptomycin sulfate, crystalline dihydrostreptomycin sulfate, dihydrostreptomycin hydrochloride:*

a. By adding to paragraph (a) a new subparagraph reading as follows:

(3) Its labeling shall conform to the requirements of § 146b.101(c) (2) or (3).

b. By deleting paragraph (b).

4. In § 146b.106:

a. By revising the section heading and paragraphs (b) and (c) (1) to read as follows:

§ 146b.106 Streptomycin sulfate injection: dihydrostreptomycin sulfate injection (crystalline dihydrostreptomycin sulfate injection) veterinary.

(b) *Packaging.* In all cases the immediate container shall be a tight container as defined by the U.S.P., shall be sterile at the time of filling and closing, shall be so sealed that the contents cannot be used without destroying the seal, and shall be of such composition as will not cause any change in the strength, quality, or purity of the contents beyond any limit therefor in applicable standards, except that minor changes so caused which are normal and unavoidable in good packaging, storage, and distribution practice shall be disregarded.

(c) *Labeling.*—(1) If it is intended for use by man. It does not contain dihydrostreptomycin and in addition to the labeling requirements prescribed by § 1.106 (b) of this chapter (regulations issued under section 502(f) of the act), each package shall bear on its label or labeling, as hereinafter indicated, the following:

(i) On the outside wrapper or container and the immediate container, the statement "Expiration date....." the blank being filled in with the date that is 12 months after the month during which the batch was certified except that the blank may be filled in with the date that is 18 months, 24 months, 36 months, 48 months, or 60 months after the month during which the batch was certified if the person who requests certification has submitted to the Commissioner results of tests and assays showing that after having been stored for such period such drug as prepared by him complies with the standards prescribed by paragraph (a) of this section.

(ii) On the outside wrapper or container the statement "Store in refrigerator not above 15° C. (59° F.)" or "Store below 15° C. (59° F.)" unless the person who requests certification has submitted to the Commissioner results of tests and assays showing that such drug as prepared by him complies with the standards prescribed by paragraph (a) of this section after having been stored at room temperature.

b. By deleting "(i) (a) and (ii)" from paragraph (c) (2).

c. By deleting "(i) (a) and (1) (ii)" from paragraph (c) (3) (iv).

d. By changing in the second sentence of paragraph (d) (3) (iii) the phrase "requirements of" to "requirements for veterinary use of".

5. In § 146b.113, by revising the section heading and paragraphs (c) and (d) (4) to read as follows:

§ 146b.113 Dihydrostreptomycin-streptomycin sulfates veterinary.

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(c) *Labeling*. It shall be labeled in accordance with § 146b.101(c) (2) or (3), except that each package shall bear on the outside wrapper or container the number of grams of dihydrostreptomycin, the number of grams of streptomycin, and the total number of grams of both salts in the immediate container.

(d) . . . .

(4) If such batch is packaged for repackaging, such person shall submit with his request a sample consisting of the following:

(i) For all tests except sterility: 6 packages.

(ii) For sterility testing: 20 packages.

Each such package shall contain not less than 0.5 gram of dihydrostreptomycin and 0.5 gram of streptomycin taken from different parts of such batch, and each shall be packaged in accordance with the requirements for veterinary use of § 146b.101(b).

6. In § 146b.117, by deleting paragraph (a) (1) and by revising the section heading and paragraph (c) to read as follows:

§ 146b.117 Dihydrostreptomycin-streptomycin sulfates solution veterinary.

(a) . . . .

(1) [Deleted]

(c) *Labeling*. It shall be labeled in accordance with the requirements of § 146b.101(c) (2) or (3).

§ 146b.120 [Revoked]

7. By revoking § 146b.120 *Dihydrostreptomycin-streptomycin sulfates with isonicotinic acid hydrazide*.

Any person who will be adversely affected by the removal of any such drug from the market may file objections to this order, within 30 days after its publication in the FEDERAL REGISTER, stating reasonable grounds and requesting a hearing on such objections. A statement of reasonable grounds and request for a hearing shall identify the claimed errors in the NAS-NRC evaluation and the Administration's conclusions as to risk involved in the parenteral use of dihydrostreptomycin sulfate alone or in combination with streptomycin sulfate. It shall identify and provide a well-organized and full-factual analysis of any adequate and well-controlled investigations the objector is prepared to prove in support of his objections. A request for a hearing must set forth specific facts showing there is a genuine and substantial issue of fact that requires a hearing. If a hearing is requested and justified by the objections, the issues will be defined and a hearing examiner named to conduct the hearing. (35 F.R. 7259; May 3, 1970). Objections should be filed, preferably in quintuplicate, with the Hearing Clerk, Department of Health, Education, and Welfare, Room 8-32, 5600 Fishers Lane, Rockville, Md. 20852, and may be accompanied by a memorandum or brief in support thereof.

*Effective date*. This order shall become effective 40 days after its date of publica-

tion in the FEDERAL REGISTER to allow time for recall to be completed.

(Secs. 502, 507, 52 Stat. 1050-51, as amended; 59 Stat. 463, as amended; 21 U.S.C. 352, 357)

Dated: May 28, 1970.

SAM D. FINE.

Acting Associate Commissioner  
for Compliance.

[F.R. Doc. 70-7149; Filed, June 9, 1970;  
8:16 a.m.]

FEDERAL REGISTER, VOL. 35, NO. 112—WEDNESDAY, JUNE 10, 1970

**Title 21—FOOD AND DRUGS**

**Chapter I—Food and Drug Administration, Department of Health, Education, and Welfare**

**SUBCHAPTER C—DRUGS**

[DESI 60108]

**PART 141b—STREPTOMYCIN (OR DIHYDROSTREPTOMYCIN) AND STREPTOMYCIN- (OR DIHYDROSTREPTOMYCIN-) CONTAINING DRUGS; TESTS AND METHODS OF ASSAY**

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**Antibiotic Drugs for Parenteral Use Containing Dihydrostreptomycin Sulfate and Dihydrostreptomycin Sulfate With Streptomycin Sulfate; Confirmation of Effective Date**

An order was published in the FEDERAL REGISTER of June 10, 1970 (35 F.R. 8931), amending the antibiotic drug regulations to repeal provision for certification of dihydrostreptomycin sulfate and dihydrostreptomycin sulfate with streptomycin sulfate. The order amended §§ 141b.111, 141b.118, 141b.122, 146b.103, 146b.106, 146b.113, and 146b.117 and revoked §§ 141b.125 and 146b.120.

Pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (secs. 502, 507, 52 Stat. 1050-51, as amended, 59 Stat. 463, as amended; 21 U.S.C. 352, 357) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 2.120), notice is given that no objections were filed to the above-identified order. Accordingly, the amendments promulgated thereby became effective July 20, 1970.

Dated: August 21, 1970.

SAM D. FINE,  
Associate Commissioner  
for Compliance.

[F.R. Doc. 70-11632; Filed, Sept. 2, 1970;  
8:46 a.m.]