

moisture, residue on ignition, crystallinity, and identity.

(b) The batch for potency, loss on drying, and disintegration time.

(i) Samples required:

(a) The erythromycin stearate used in making the batch: 10 containers, each consisting of not less than 500 milligrams.

(b) The batch: A minimum of 36 tablets.

(b) *Tests and methods of assay*—(1) *Potency*. Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Blend a representative number of tablets in a high-speed glass blender with 200 milliliters of methyl alcohol for 3 to 5 minutes. Add 300 milliliters of 0.1M potassium phosphate buffer, pH 8.0 (solution 3), and blend again for 3 to 5 minutes. Further dilute with solution 3 to the reference concentration of 1.0 microgram of erythromycin base per milliliter (estimated).

(2) *Loss on drying*. Proceed as directed in § 436.200(b) of this chapter.

(3) *Disintegration time*. Proceed as directed in § 436.212 of this chapter, using the procedure described in paragraph (e)(2) of that section.

[39 FR 19149, May 30, 1974, as amended at 42 FR 59068, Nov. 15, 1977; 50 FR 19921, May 13, 1985]

**§ 452.135b Erythromycin stearate oral suspension.**

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Erythromycin stearate oral suspension is erythromycin stearate with suitable and harmless buffer substances, dispersing agents, diluents, colorings, and flavorings. It contains the equivalent of 25 milligrams of erythromycin per milliliter. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of erythromycin that it is represented to contain. Its pH is not less than 7.0 and not more than 8.5. The erythromycin stearate used conforms to the standards prescribed by § 452.35(a)(1).

(2) *Labeling*. It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples*. In addition to complying with the re-

quirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The erythromycin stearate used in making the batch for potency, moisture, pH, residue on ignition, identity, and crystallinity.

(b) The batch for potency and pH.

(ii) Samples required:

(a) The erythromycin stearate used in making the batch: 10 packages, each containing approximately 500 milligrams.

(b) The batch: A minimum of 5 immediate containers.

(b) *Tests and methods of assay*—(1) *Potency*. Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place an accurately measured representative volume of the suspension into a high-speed glass blender jar. Add sufficient methyl alcohol to the jar to give a concentration of 1.25 milligrams of erythromycin base per milliliter (estimated). Blend for 2 to 3 minutes. Add sufficient 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to give a concentration of 0.5 milligrams of erythromycin base per milliliter (estimated) and blend again for 2 to 3 minutes. Further dilute with solution 3 to the reference concentration of 1.0 microgram of erythromycin base per milliliter (estimated).

(2) *pH*. Proceed as directed in § 436.202 of this chapter, using the undiluted suspension.

[39 FR 19149, May 30, 1974, as amended at 50 FR 19921, May 13, 1985]

**§ 452.135c Erythromycin stearate for oral suspension.**

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity*. Erythromycin stearate for oral suspension is a dry mixture of erythromycin stearate with suitable and harmless buffer substances, dispersing agents, diluents, colorings, and flavorings. It contains the equivalent of 25 or 50 milligrams of erythromycin per milliliter of the reconstituted suspension. Its potency is satisfactory if it is not less than 90 percent and not more than 120 percent of the number of milligrams of erythromycin that it is represented to contain. Its moisture content is not more than 2 percent. When reconstituted as directed in the

labeling, its pH is not less than 6.0 and not more than 9.0. The erythromycin stearate used conforms to the standards prescribed by § 452.35(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification; samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The erythromycin stearate used in making the batch for potency, moisture, pH, residue on ignition, identity, and crystallinity.

(b) The batch for potency, moisture, and pH.

(ii) Samples required:

(a) The erythromycin stearate used in making the batch: 10 packages, each containing approximately 500 milligrams.

(b) The batch: A minimum of 6 immediate containers.

(b) *Tests and methods of assay*—(1) *Potency.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Reconstitute as directed in the labeling. Place an accurately measured representative portion of the suspension into a high-speed glass blender jar with sufficient methyl alcohol to give a concentration of 1.0 milligram of erythromycin base per milliliter (estimated). Blend for 3 to 5 minutes. Further dilute with 0.1M potassium phosphate buffer, pH 8.0 (solution 3), to the reference concentration of 1.0 microgram of erythromycin base per milliliter (estimated).

(2) *Moisture.* Proceed as directed in § 436.201 of this chapter.

(3) *pH.* Proceed as directed in § 436.202 of this chapter, using the suspension obtained when the drug is reconstituted as directed in the labeling.

[40 FR 49083, Oct. 21, 1975, as amended at 41 FR 24884, June 21, 1976; 50 FR 19921, May 13, 1985]

#### **§ 452.150 Clarithromycin oral dosage forms.**

##### **§ 452.150a Clarithromycin tablets.**

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality, and purity.* Clarithromycin tablets are composed of clarithromycin and one or

more suitable and harmless diluents, binders, lubricants, colorings, and flavorings. Each tablet contains 250 milligrams or 500 milligrams of clarithromycin activity. Its clarithromycin content is satisfactory if it is not less than 90 percent and not more than 110 percent of the number of milligrams of clarithromycin that it is represented to contain. The loss on drying is not more than 6.0 percent. It passes the dissolution test. It passes the identity test. The clarithromycin used conforms to the standards prescribed by § 452.50(a)(1).

(2) *Labeling.* It shall be labeled in accordance with the requirements of § 432.5 of this chapter.

(3) *Requests for certification samples.* In addition to complying with the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(A) The clarithromycin used in making the batch for potency, moisture, pH, residue on ignition, heavy metals, specific rotation, identity, and crystallinity.

(B) The batch for content, loss on drying, dissolution, and identity.

(ii) Samples, if required by the Director, Center for Drug Evaluation and Research:

(A) The clarithromycin used in making the batch: 10 packages, each containing approximately 500 milligrams.

(B) The batch: A minimum of 100 tablets.

(b) *Tests and methods of assay*—(1) *Clarithromycin content.* Proceed as directed in § 452.50(b)(1), preparing the sample solution and calculating the clarithromycin content as follows:

(i) *Preparation of sample solution.* Grind and composite five whole tablets in a glass mortar and pestle and quantitatively transfer the powder to a 500-milliliter volumetric flask with 50 milliliters of distilled water and shake mechanically until the tablets are well dispersed (approximately 5 to 10 minutes). Add 300 milliliters of methanol and shake mechanically for 30 minutes. Dilute with methanol to volume and mix. Allow the excipients to settle. Quantitatively transfer and dilute a convenient aliquot of the supernatant with mobile phase (described in § 452.50(b)(1)(i)) to obtain a solution