

concentration of 400 units of nystatin per milliliter (estimated). Further dilute with 10 percent potassium phosphate buffer, pH 6.0 (solution 6), to the reference concentration of 20 units of nystatin per milliliter (estimated).

(ii) *Neomycin content.* Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows: Place an accurately weighed representative portion of the ointment into a separatory funnel containing 50 milliliters of peroxide-free ether. Shake the sample and ether until homogenous. Add 20 to 25 milliliters of 0.1M potassium phosphate buffer, pH 8.0 (solution 3), and shake well. Allow the layers to separate. Remove the buffer layer and repeat the extraction with new portions of the buffer at least three times and any additional times necessary to insure complete extraction of the antibiotic. Combine the extractives and adjust to an appropriate volume to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 3 to the reference concentration of 1.0 microgram of neomycin per milliliter (estimated).

(iii) *Gramicidin content.* Proceed as directed in §436.106 of this chapter, preparing the sample for assay as follows: Accurately weigh and dissolve a representative portion of the sample in approximately 50 milliliters of petroleum ether in a separatory funnel. Extract with 20 milliliters of 80 percent alcohol prepared from alcohol U.S.P. XX. Repeat the extraction three times. Combine the extractives in a suitable volumetric flask, bring to volume with alcohol U.S.P. XX, and mix well. Further dilute with alcohol U.S.P. XX to the reference concentration of 0.04 microgram of gramicidin per milliliter (estimated).

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

[39 FR 19134, May 30, 1974, as amended at 47 FR 23710, June 1, 1982; 50 FR 19920, May 13, 1985]

§ 449.550d Nystatin cream.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Nystatin cream is composed of nystatin and suitable and harmless emulsifiers, perfumes, buffers, preserv-

atives, and a protectant in a suitable and harmless cream base. Each gram contains 100,000 units of nystatin. Its potency is satisfactory if it is not less than 90 percent and not more than 130 percent of the number of units of nystatin that it is represented to contain. The nystatin used conforms to the standards prescribed by §449.50(a)(1) (i), (iii), (iv), and (v).

(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 the requirements of §431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The nystatin used in making the batch for potency, loss on drying, pH, and identity.

(b) The batch for potency.

(ii) Samples required:

(a) The nystatin used in making the batch: 10 containers, each consisting of 300 milligrams.

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

(b) *Tests and methods of assay; potency.* Proceed as directed in §436.105 of this chapter, preparing the sample for assay as follows: Using sufficient dimethylformamide to give an estimated concentration of 400 units of nystatin per milliliter, blend an accurately weighed representative portion in a high-speed blender for 3 to 5 minutes. Further dilute with 10 percent potassium phosphate buffer, pH 6.0 (solution 6), to the reference concentration of 20 units of nystatin per milliliter (estimated).

§ 449.550e Nystatin-neomycin sulfate-gramicidin-triamcinolone acetamide cream.

(a) *Requirements for certification—(1) Standards of identity, strength, quality, and purity.* Nystatin-neomycin sulfate-gramicidin-triamcinolone acetamide cream is composed of nystatin, neomycin sulfate, gramicidin, triamcinolone acetamide, and suitable and harmless emulsifiers, solvents, perfumes, buffers, preservatives, and a protectant in a suitable cream base. Each gram contains 100,000 units of nystatin, 2.5 milligrams of neomycin, 0.25 milligram of gramicidin, and 1 milligram of

triamcinolone acetonide. Its nystatin content is satisfactory if it is not less than 90 percent and not more than 140 percent of the number of units of nystatin that it is represented to contain. Its neomycin content is satisfactory if it is not less than 90 percent and not more than 140 percent of the number of milligrams of neomycin that it is represented to contain. Its gramicidin content is satisfactory if it is not less than 90 percent and not more than 140 percent of the number of milligrams of gramicidin that it is represented to contain. The nystatin used conforms to the standards prescribed by § 449.50(a)(1) (i), (iii), (iv), and (v). The neomycin sulfate used conforms to the standards prescribed by § 444.42(a)(1) of this chapter. The gramicidin used conforms to the standards prescribed by § 448.25(a)(1) (i), (iii), (iv), (v), and (vi) of this chapter.

(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 the requirements of § 431.1 of this chapter, each such request shall contain:

(i) Results of tests and assays on:

(a) The nystatin used in making the batch for potency, loss on drying, pH, and identity.

(b) The neomycin sulfate used in making the batch for potency, loss on drying, pH, and identity.

(c) The gramicidin used in making the batch for potency, loss on drying, residue on ignition, melting point, crystallinity, and identity.

(d) The batch for nystatin content, neomycin content, and gramicidin content.

(ii) Samples required:

(a) The nystatin used in making the batch: 10 packages, each consisting of 300 milligrams.

(b) The neomycin sulfate used in making the batch: 10 packages, each consisting of 300 milligrams.

(c) The gramicidin used in making the batch: 10 packages, each consisting of 500 milligrams.

(d) The batch: A minimum of seven immediate containers.

(b) *Tests and methods of assay*—(1) *Potency*—(i) *Nystatin content.* Proceed as directed in § 436.105 of this chapter, pre-

paring the sample for assay as follows: Using sufficient dimethylformamide to give a concentration of 400 units of nystatin (estimated) per milliliter, blend an accurately weighed representative portion in a high-speed glass blender for 3 to 5 minutes. Further dilute with 10 percent potassium phosphate buffer, pH 6.0 (solution 6), to the reference concentration of 20 units of nystatin per milliliter (estimated).

(ii) *Neomycin content.* Proceed as directed in § 436.105 of this chapter, preparing the sample for assay as follows: Place an accurately weighed representative portion of the cream in a separatory funnel containing 50 milliliters of peroxide-free ether. Shake the sample and either until homogeneous. Add 20 to 25 milliliters of 0.1M potassium phosphate buffer, pH 8.0 (solution 3), and shake well. Allow the layers to separate. Remove the buffer layer and repeat the extraction with new portions of the buffer at least three times and any additional times necessary to ensure complete extraction of the antibiotic. Combine the extractives and adjust to an appropriate volume to give a stock solution of convenient concentration. Further dilute an aliquot of the stock solution with solution 3 to the reference concentration of 1.0 microgram of neomycin per milliliter (estimated).

(iii) *Gramicidin content.* Proceed as directed in § 436.106 of this chapter, preparing the sample for assay as follows: Accurately weigh a representative portion of the sample and dissolve in approximately 50 milliliters of petroleum ether in a separatory funnel. Extract with 20 milliliters of 80 percent alcohol prepared from alcohol U.S.P. XX. Repeat the extraction three times. Combine the extractives in a suitable volumetric flask, bring to volume with alcohol U.S.P. XX, and mix well. Further dilute with alcohol U.S.P. XX to the reference concentration of 0.04 microgram of gramicidin per milliliter (estimated).

[39 FR 19134, May 30, 1974, as amended at 47 FR 23710, June 1, 1982; 50 FR 19920, May 13, 1985]

§ 449.550f Nystatin topical powder.

(a) *Requirements for certification*—(1) *Standards of identity, strength, quality,*