collect the washings into the volumetric flask. Dilute the sample with *Diluent* to volume.

**Chromatographic system**

(See *Chromatography* ⟨621⟩, *System Suitability*.)

**Mode:** LC

**Detector:** 240 nm

**Column:** 4.6-mm × 25-cm; 5-µm packing L1

**Column temperature:** 50°

**Flow rate:** 1.5 mL/min

**Injection size:** 50 µL

**System suitability**

**Samples:** *System suitability solution* and *Standard solution*

**Suitability requirements**

**Resolution:** NLT 1.4 between fluticasone propionate and fluticasone propionate related compound D, *System suitability solution*

**Tailing factor:** NMT 1.4, *Standard solution* (calculated using the width of the peak at 10% of the height)

**Relative standard deviation:** NMT 2.0%, *Standard solution*

**Analysis**

**Samples:** *Standard solution* and *Sample solution*

Calculate the percentage of fluticasone propionate ($C_{25}H_{31}F_3O_5S$) in the portion of Ointment taken:

$$\text{Result} = (r_U/r_S) \times (C_S/C_U) \times 100$$

$r_U$ = peak response of fluticasone propionate from the *Sample solution*

$r_S$ = peak response of fluticasone propionate from the *Standard solution*

$C_S$ = concentration of USP Fluticasone Propionate RS in the *Standard solution* (µg/mL)

$C_U$ = *nominal concentration of fluticasone* propionate in the *Sample solution* (µg/mL)

**Acceptance criteria:** 90.0%–110.0%

## SPECIFIC TESTS

- **Microbial Enumeration Tests** ⟨61⟩ and **Tests for Specified Microorganisms** ⟨62⟩**:** Meets the requirements of the tests for absence of *Staphylococcus aureus* and *Pseudomonas aeruginosa*. The total aerobic microbial count is NMT 100 cfu/g, and the total combined molds and yeasts count is NMT 10 cfu/g.

## ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Preserve in collapsible tubes or tight containers, protected from light. Store between 2° and 30°.
- **USP Reference Standards** ⟨11⟩

USP Fluticasone Propionate RS

USP Fluticasone Propionate Nasal Spray Resolution Mixture RS

This Reference Standard is a mixture of fluticasone propionate and fluticasone propionate related compound D, and the chemical names for both are given below:

*Fluticasone propionate:* *S*-Fluoromethyl 6α,9α-difluoro-11β-hydroxy-16α-methyl-3-oxo-17α-propionyloxyandrosta-1,4-diene-17β-carbothioate.

*Fluticasone propionate related compound D:* *S*-Methyl-6α,9α-difluoro-11β-hydroxy-16α-methyl-3-oxo-17α-propionyloxy-androsta-1,4-diene-17β-carbothioate.

# Fluticasone Propionate and Salmeterol Inhalation Aerosol

## DEFINITION

Fluticasone Propionate and Salmeterol Inhalation Aerosol is a suspension of Fluticasone Propionate and Salmeterol with suitable propellants in a pressurized container. The mean content per actuation contains NLT 88% and NMT 112% of the labeled amount of fluticasone propionate ($C_{25}H_{31}F_3O_5S$). The mean content per actuation contains NLT 88% and NMT 112% of the labeled amount of salmeterol ($C_{25}H_{37}NO_4$) as salmeterol xinafoate.

## IDENTIFICATION

- **A. Infrared Absorption** ⟨197A⟩

**Wavenumber range:** 4000 –600 $cm^{-1}$

**Sample:** Discharge an appropriate number of actuations from two containers into an agate mortar. Allow the propellant to evaporate and dry if necessary. Transfer the residue to the sample window.

**Acceptance criteria:** Meets the requirements. In addition, the ratio of the fluticasone propionate band at 833 $cm^{-1}$ to that of the salmeterol band at 744 $cm^{-1}$ meets the requirements in *Table 1*.

**Table 1**

| Fluticasone Propionate/ Salmeterol (µg/µg for each dose) | Ratio (band at 833 $cm^{-1}$/band at 744 $cm^{-1}$) |
|---|---|
| 45/21 | NMT 2.5 |
| 115/21 | 2.5–4.0 |
| 230/21 | NLT 4.0 |

- **B.** The retention time of the major peak of the *Sample solution* corresponds to that of the *Standard solution*, as obtained in the test for *Delivered-Dose Uniformity*.

## ASSAY

- **Procedure**

**Buffer:** 0.01 M sodium dodecyl sulfate containing 0.1% glacial acetic acid

**Solution A:** Methanol and *Buffer* (20:80)

**Mobile phase:** Acetonitrile and *Solution A* (50:50)

**Diluent:** Methanol and water (70:30)

**Standard solution:** 50 µg/mL of USP Fluticasone Propionate RS and 15 µg/mL of USP Salmeterol Xinafoate RS in *Diluent*

**Sample solution:** Nominally 20–110 µg/mL of fluticasone propionate and 10 µg/mL of salmeterol prepared as follows. Shake the canister vigorously, and cool for 10 min in a dry ice–methanol bath. Remove the canister from the bath, and shake vigorously. Using a suitable device, carefully remove and keep the valve, and pour the contents into a suitable container. Allow the propellant to evaporate. Dissolve the canister contents in a minimum amount of methanol and quantitatively transfer to a suitable volumetric flask containing 30% of the flask volume of water. Rinse the canister and valve with methanol into the same volumetric flask. Allow the flask to come to room temperature and dilute with methanol to volume.

**Chromatographic system**

(See *Chromatography* ⟨621⟩, *System Suitability*.)

**Mode:** LC

**Detectors**

**Fluticasone propionate:** UV 239 nm

**Salmeterol:** Fluorescence with excitation at 225 nm and emission at 305 nm. Use emission response for quantification.

**Column:** 4.6-mm × 5-cm; 3.5-µm packing L1

**Column temperature:** 40°

**Flow rate:** 2 mL/min

**Injection volume:** 5 µL

**Run time:** NLT 1.5 times the retention time of salmeterol

**System suitability**

**Sample:** *Standard solution*

[NOTE—The relative retention times for fluticasone propionate and salmeterol are 0.6 and 1.0, respectively.]

**Suitability requirements**

**Resolution:** NLT 3.5 between fluticasone propionate and salmeterol