Wavelength: UV 258 nm
Path length: 0.2 cm
Blank: *Medium*
Tolerances: NLT 75% (Q) of the labeled amount of cilostazol is dissolved.

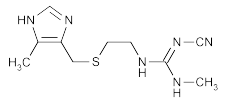
Test 3: If the product complies with this test, the labeling indicates that it meets USP *Dissolution Test 3*.
Medium: 0.3% sodium laur yl sulfate in water; 900 mL
Apparatus 2: 75 rpm
Time: 60 min
Standard solution, Sample solution, Wavelength, Path length, and **Blank:** Proceed as directed for *Test 1*.
Tolerances: NLT 70% (Q) of the labeled amount of cilostazol is dissolved.

- **UNIFORMITY OF DOSAGE UNITS** ⟨**905**⟩**:** Meet the requirements

ADDITIONAL REQUIREMENTS

- **PACKAGING AND STORAGE:** Preserve in tight and light-resistant containers. Store at controlled room temperature.
- **LABELING:** When more than one *Dissolution* test is given, the labeling states the *Dissolution* test used only if *Test 1* is not used.
- **USP REFERENCE STANDARDS** ⟨**11**⟩
  USP Cilostazol RS

Cimetidine



$C_{10}H_{16}N_6S$ 252.34
Guanidine, *N* ′′-cyano-*N*-methyl-*N*′-[2-[[(5-methyl-1*H*-imidazol-4-yl)methyl]thio]ethyl]-.
2-Cyano-1-methyl-3-[2-[[(5-methylimidazol-4-yl)methyl]thio] ethyl]guanidine [51481-61-9].

» Cimetidine contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{10}H_{16}N_6S$, calculated on the dried basis.

Packaging and storage—Preserve in tight, light-resistant containers.

USP Reference standards ⟨11⟩**—**
USP Cimetidine RS

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: The UV absorption spectrum of a solution (1 in 80,000) in 0.1 N sulfuric acid exhibits maxima and minima at the same wavelengths as that of a similar solution of USP Cimetidine RS , concomitantly measured.

Melting range ⟨741⟩: between 139° and 144°.

Loss on drying ⟨731⟩**—**Dry it at 110° for 2 hours: it loses not more than 1.0% of its weight.

Residue on ignition ⟨281⟩: not more than 0.2%.

Heavy metals, *Method II* ⟨231⟩: 0.002%.

Chromatographic purity—

Mobile phase—Mix 240 mL of methanol, 0.3 mL of phosphoric acid (85%), 940 mg of sodium 1-hexanesulfonate, and sufficient water to make 1 L. Filter before use. Make adjustments if necessar y (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard solution—Prepare a solution of USP Cimetidine RS in *Mobile phase* having a concentration of 0.80 µg per mL.

Test solution—Transfer 100.0 mg of Cimetidine, accurately weighed, to a 250-mL volumetric flask, dissolve in about 50 mL of *Mobile phase*, and dilute with *Mobile phase* to volume. Mix, sonicate for 15 minutes, and mix again.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 220-nm detector and a 4.6-mm × 25-cm column that contains packing L1. The flow rate is about 2.0 mL per minute. Chromatograph the *Standard solution,* and record the peak response as directed for *Procedure:* the capacity factor, k', is not less than 3.0; the number of theoretical plates, n, is not less than 2000; and the relative standard deviation of the response for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 50 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the per centage of each impurity in the portion of Cimetidine taken by the formula:

$$100(0.001C_S)/C_U)(r_U / r_S)$$

in which C_S is the concentration, in µg per mL, of cimetidine in the *Standard solution,* the multiplier of 0.001 is for conversion of µg per mL to mg per mL; C_U is the concentration, in mg per mL, of Cimetidine in the *Test solution;* r_U is the peak response for each impurity obtained from the *Test solution;* and r_S is the response of the cimetidine peak obtained from the *Standard solution:* not more than 0.2% of any single impurity is found, and not more than 1.0% of total impurities is found.

Assay—

Mobile phase—Transfer 200 mL of methanol and 0.3 mL of phosphoric acid to a 1000-mL volumetric flask, dilute with water to volume, mix, and filter. Make adjustments if necessar y (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Cimetidine RS in a mixture of water and methanol (4:1) to obtain a stock solution having a known concentration of about 0.4 mg per mL by initially dissolving the Reference Standard in one part of methanol and diluting the methanolic solution quantitatively with about 4 parts of water to volume in a volumetric flask. Transfer 5.0 mL of this stock solution to a 200-mL volumetric flask, dilute with *Mobile phase* to volume, and mix to obtain a solution having a known concentration of about 10 µg per mL.

Assay preparation—Transfer an accurately weighed quantity of about 100 mg of Cimetidine to a 250-mL volumetric flask, add 50 mL of methanol to dissolve the specimen, dilute with water to volume, and mix. T ransfer 5.0 mL of this solution to a 200-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 220-nm detector, and a 3.9-mm × 30-cm column that contains packing L1. The flow rate is about 2.0 mL per minute. Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the capacity factor, k', is not less than 0.6; the column efficiency determined from the analyte peak is not less than 1000 theoretical plates; and the relative standard deviation of the response for replicate injections is not more than 2.0%.

Procedure—Separately inject equal volumes (about 50 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the quantity, in mg, of $C_{10}H_{16}N_6S$ in the portion of Cimetidine taken by the formula:

$$10C(r_U / r_S)$$

in which C is the concentration, in µg per mL, of USP Cimetidine RS in the *Standard preparation*; and r_U and r_S are the Cimetidine peak responses obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Cimetidine Tablets

» Cimetidine Tablets contain not less than 90.0 percent and not more than 110.0 per cent of the labeled amount of cimetidine ($C_{10}H_{16}N_6S$).

Packaging and storage—Preserve in tight, light-resistant containers, at controlled room temperature.

USP Reference standards ⟨11⟩**—**
USP Cimetidine RS

Identification—The retention time of the major peak in the chromatogram of the *Assay preparation* corresponds to that in the chromatogram of the *Standard preparation,* as obtained in the *Assay*.

Dissolution ⟨711⟩**—**

Medium: 0.01 N hydrochloric acid; 900 mL.

Apparatus 1: 100 rpm. A 20-mesh basket may be used for 800-mg strength Tablets.

Time: 15 minutes.

Procedure—Determine the amount of $C_{10}H_{16}N_6S$ dissolved by employing UV absorption at the wavelength of maximum absorbance at about 218 nm on filtered portions of the solution under test, suitably diluted with *Dissolution Medium*, in comparison with a Standard solution having a known concentration of USP Cimetidine RS in the same *Medium*.

Tolerances—Not less than 80% *(Q)* of the labeled amount of $C_{10}H_{16}N_6S$ is dissolved in 15 minutes.

Uniformity of dosage units ⟨905⟩: meet the requirements.

Assay—

Mobile phase, *Standard preparation,* and *Chromatographic system*—Proceed as directed in the *Assay* under *Cimetidine.*

Assay preparation—Weigh and finely powder not fewer than 20 Tablets. Transfer an accurately weighed portion of the powder, equivalent to about 100 mg of cimetidine, to a 250-mL volumetric flask. Add 50 mL of methanol, shake for 2 minutes, add 40 mL of water, sonicate for 15 minutes, dilute with water to volume, and mix. Transfer 5.0 mL of this solution to a 200-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Procedure—Separately inject equal volumes (about 50 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the responses for the major peaks. Calculate the quantity, in mg, of cimetidine ($C_{10}H_{16}N_6S$) in the portion of Tablets taken by the formula:

$$10C(r_U / r_S)$$

in which the terms are as defined in the *Assay* under *Cimetidine.*

Cimetidine Hydrochloride

$C_{10}H_{16}N_6S \cdot HCl$ 288.81

Guanidine, *N*′′-cyano-*N*-methyl-*N*′-[2-[[(5-methyl-1*H*-imidazol-4-yl)methyl]thio]ethyl]-, monohydrochloride.

2-Cyano-1-methyl-3-[2-[[(5-methylimidazol-4-yl)methyl]thio]ethyl]guanidine monohydrochloride [70059-30-2].

» Cimetidine Hydrochloride contains not less than 98.0 percent and not more than 102.0 percent of $C_{10}H_{16}N_6S \cdot HCl$, calculated on the dried basis.

Packaging and storage—Preserve in tight, light-resistant containers.

USP Reference standards ⟨11⟩**—**
USP Cimetidine Hydrochloride RS

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: *Ultraviolet Absorption* ⟨197U⟩**—**

Solution: 14 µg per mL.

Medium: 0.1 N sulfuric acid.

Loss on drying ⟨731⟩**—**Dry it at 105 ° for 2 hours: it loses not more than 0.5% of its weight.

Residue on ignition ⟨281⟩: not more than 0.2%.

Heavy metals, *Method II* ⟨231⟩: 0.002%.

Chromatographic purity—

Mobile phase—Transfer about 940 mg of sodium 1-hexanesulfonate to a 1000-mL volumetric flask, add 240 mL of methanol followed by 0.3 mL of phosphoric acid, and dilute with water to volume. Mix, and filter. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Test solution 1—Transfer about 100 mg of Cimetidine Hydrochloride, accurately weighed, to a 250-mL volumetric flask, dissolve in and dilute with *Mobile phase* to volume, and mix.

Test solution 2—Transfer 1.0 mL of *Test solution 1* to a 500-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Resolution solution—Dissolve about 50 mg of Cimetidine Hydrochloride in 10 mL of 1 N hydrochloric acid, and heat on a steam bath for about 10 minutes (or boil on a hot plate for about 2 minutes), and allow to cool. Dilute a suitable volume of this solution with *Mobile phase* to obtain a solution having a concentration of about 2 µg per mL. [NOTE—Use this solution within 24 hours of its preparation. Adjustment of the heating step may be necessary to achieve a satisfactory amide analog peak response for the measurement of the resolution between the cimetidine and the amide analog peaks.]

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 220-nm detector and a 4.6-mm × 25-cm column that contains packing L1. The flow rate is about 2 mL per minute. Chromatograph the *Resolution solution*, and record the peak responses as directed for *Procedure:* the resolution, *R,* between the cimetidine and the amide analog peaks is not less than 4.0. Chromatograph *Test solution 2*, and record the peak responses as directed for *Procedure:* the capacity factor, *k*′, is not less than 3.0; the column efficiency is not less than 2000 theoretical plates; and the relative standard deviation for replicate injections is not more than 7.0%.

Procedure—Separately inject equal volumes (about 50 µL) of *Test solution 1* and *Test solution 2* into the chromatograph, record the chromatograms, and measure the peak responses. Calculate the percentage of each impurity in the portion of Cimetidine Hydrochloride taken by the formula:

$$0.2(r_i / r_S)$$

in which r_i is the peak response for an individual impurity observed in the chromatogram obtained from *Test solution 1*, and r_S is the peak response of cimetidine in the chromatogram obtained from *Test solution 2:* no single impurity is greater than 0.2%, and the sum of all impurities is not more than 1.0%.

Assay—

Mobile phase—Transfer 200 mL of methanol and 0.3 mL of phosphoric acid to a 1000-mL volumetric flask, dilute with water to volume, mix, and filter. Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Standard preparation—Dissolve an accurately weighed quantity of USP Cimetidine Hydrochloride RS in a mixture of water and methanol (80:20) to obtain a solution having a known concentration of about 0.5 mg per mL. Transfer 5.0 mL of this solution to a 200-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Assay preparation—Transfer about 115 mg of Cimetidine Hydrochloride, accurately weighed, to a 250-mL volumetric flask, dissolve in about 50 mL of water, add 50 mL of methanol, and