Assay—Place not fewer than 10 Suppositories in a 250-mL beaker, reduce the mass to the consistency of a paste by crushing with a spatula, and mix. W eigh accurately a portion of the mass, equivalent to about 50 mg of chlorpromazine, place in a beaker, and dissolve in about 40 mL of ether. T ransfer to a 250-mL separator with the aid of three 25-mL portions of ether, and extract with four 75-mL portions of 0.1 N hydrochloric acid, collecting the aqueous extracts in a 500-mL volumetric flask. Add 0.1 N hydrochloric acid to volume, and mix. T ransfer 10.0 mL of this solution to a 200-mL volumetric flask, add 0.1 N hydrochloric acid to volume, and mix. Dissolve an accurately weighed quantity of USP Chlorpromazine Hydrochloride RS in 0.1 N hydrochloric acid, and dilute quantitatively and stepwise with the same solvent to obtain a Standard solution having a known concentration of about 5.5 µg of chlorpromazine hydrochloride per mL. Concomitantly determine the absorbances of both solutions in 1-cm cells at the wavelength of maximum absorbance at about 254 nm and at 277 nm, with a suitable spectrophotometer, using 0.1 N hydrochloric acid as the blank. Calculate the quantity, in mg, of chlorpromazine ($C_{17}H_{19}ClN_2S$) in the portion of Suppositories taken by the formula:

$$10(0.897C)(A_{254} - A_{277})_U / (A_{254} - A_{277})_S$$

in which 0.897 is the ratio of the molecular weight of chlorpromazine to that of chlorpromazine hydrochloride; *C* is the concentration, in µg per mL, of USP Chlorpromazine Hydrochloride RS in the Standard solution; and the parenthetic expressions are the differences in the absorbances of the two solutions at the wavelengths indicated by the subscripts, for the solution from the Suppositories (*U*) and the Standard solution (*S*), respectively.

Chlorpromazine Hydrochloride

$C_{17}H_{19}ClN_2S \cdot HCl$ 355.33

10*H*-Phenothiazine-10-propanamine, 2-chloro-*N*,*N*-dimethyl-, monohydrochloride.

2-Chloro-10-[3-(dimethylamino)propyl]phenothiazine monohydrochloride [69-09-0].

» Chlorpromazine Hydrochloride contains not less than 98.0 per cent and not more than 101.5 percent of $C_{17}H_{19}ClN_2S \cdot HCl$, calculated on the dried basis.

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

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

[NOTE—Throughout the following procedures, protect test or assay specimens, the Reference Standard, and solutions containing them by conducting the procedures without delay, under subdued light, or using low-actinic glassware.]

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: The principal spot found in the test for *Other alkylated phenothiazines* corresponds in R_F to the spot from the *Standard solution*.

C: A solution (1 in 10) responds to the tests for *Chloride* ⟨191⟩.

Melting range ⟨741⟩: between 195° and 198°.

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 0.1%.

Other alkylated phenothiazines—Dissolve 50 mg, previously dried, in methanol to make 10 mL, and mix. Proceed as directed in the test for *Other alkylated phenothiazines* under *Chlorpromazine*, beginning with "Dissolve a suitable quantity of USP Chlorpromazine Hydrochloride RS." The area and intensity of any spot, other than the principal spot, from the solution of Chlorpromazine Hydrochloride are not greater than those of the spot from the *Diluted standard solution* (0.5%).

Assay—Transfer to a beaker about 700 mg of Chlorpromazine Hydrochloride, accurately weighed, and dissolve in 75 mL of glacial acetic acid. Add 10 mL of mer curic acetate TS, and titrate with 0.1 N per chloric acid VS, determining the endpoint potentiometrically. Each mL of 0.1 N per chloric acid is equivalent to 35.53 mg of $C_{17}H_{19}ClN_2S \cdot HCl$.

Chlorpromazine Hydrochloride Oral Concentrate

» Chlorpromazine Hydrochloride Oral Concentrate contains not less than 90.0 per cent and not more than 110.0 per cent of the labeled amount of $C_{17}H_{19}ClN_2S \cdot HCl$.

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

Labeling—Label it to indicate that it must be diluted prior to administration.

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

[NOTE—Throughout the following procedures, protect test or assay specimens, the Reference Standard, and solutions containing them by conducting the procedures without delay, under subdued light, or using low-actinic glassware.]

Identification—

A: It responds to *Identification* test *A* under *Chlorpromazine Hydrochloride Syrup*.

B: Dilute a portion of the Oral Concentrate with an equal volume of water: the resulting solution responds to the tests for *Chloride* ⟨191⟩.

Microbial enumeration tests ⟨61⟩ and **Tests for specified microorganisms** ⟨62⟩**—**It meets the requirements of the tests for the absence of *Escherichia coli*.

pH ⟨791⟩: between 2.3 and 4.1.

Limit of chlorpromazine sulfoxide—Proceed as directed in the test for *Chlorpromazine sulfoxide* under *Chlorpromazine Hydrochloride Syrup*.

Assay—Transfer an accurately measured volume of Oral Concentrate, previously diluted if necessar y, equivalent to about 10 mg of chlorpromazine hydrochloride, to a 50-mL volumetric flask, add 0.1 N hydrochloric acid to volume, and mix. Proceed as directed in the *Assay* under *Chlorpromazine Hydrochloride Injection*, beginning with "Pipet 10 mL of the solution." Calculate the quantity, in mg, of $C_{17}H_{19}ClN_2S \cdot HCl$ in each mL of the Oral Concentrate taken by the formula:

$$1.25C(A_{254} - A_{277})_U / V(A_{254} - A_{277})_S$$

in which *C* is the concentration, in µg per mL, of USP Chlorpromazine Hydrochloride RS in the Standard solution; *V* is the volume, in mL, of Oral Concentrate taken; and the parenthetic expressions are the differences in the absorbances of the two solutions at the wavelengths indicated by the subscripts, for the solution from the Oral Concentrate (*U*) and the Standard solution (*S*), respectively.

Chlorpromazine Hydrochloride Injection

» Chlorpromazine Hydrochloride Injection is a sterile solution of Chlorpromazine Hydrochloride

in Water for Injection. It contains, in each mL, not less than 23.75 mg and not more than 26.25 mg of $C_{17}H_{19}ClN_2S \cdot HCl$.

Packaging and storage—Preserve in single-dose or in multiple-dose containers, preferably of Type I glass, protected from light.

USP Reference standards ⟨11⟩**—**
USP Chlorpromazine Hydrochloride RS
USP Endotoxin RS

[NOTE—Throughout the following procedures, protect test or assay specimens, the Reference Standard, and solutions containing them by conducting the procedures without delay, under subdued light, or using low-actinic glassware.]

Identification—

A: Transfer a volume of Injection, equivalent to about 25 mg of chlorpromazine hydrochloride, to a 10-mL volumetric flask, dilute with methanol to volume, and mix (test solution). Dissolve a suitable quantity of USP Chlorpromazine Hydrochloride RS in dilute methanol (9 in 10) to obtain a Standard solution having a known concentration of 2.5 mg per mL. Apply separately 5-µL portions of each of the two solutions to the starting line of a thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with chromatographic silica gel mixture. Develop the chromatogram in a solvent system consisting of a freshly prepared mixture of equal volumes of ether and ethyl acetate saturated with ammonium hydroxide until the solvent front has moved about 10 cm from the origin. Remove the plate from the developing chamber, air-dry for 20 minutes, then view under short-wavelength UV light: the R_F value of the principal spot obtained from the test solution corresponds to that obtained from the Standard solution.

B: It responds to the tests for *Chloride* ⟨191⟩.

Bacterial endotoxins ⟨85⟩**—**It contains not more than 6.9 USP Endotoxin Units per mg of chlorpromazine hydrochloride.

pH ⟨791⟩: between 3.4 and 5.4.

Limit of chlorpromazine sulfoxide—[NOTE—Conduct this test without exposure to daylight, and with the minimum necessary exposure to artificial light.]

Test preparation—Pipet 4 mL of the test solution prepared with methanol as directed in *Identification* test *A* into a 10-mL volumetric flask, dilute with methanol to volume, and mix.

Standard preparation—Dissolve a suitable quantity of USP Chlorpromazine Hydrochloride RS in methanol to obtain a solution having a concentration of 50 µg per mL.

Procedure—Apply separate 10-µL portions of the *Standard preparation* and the *Test preparation* to the starting line of a thin-layer chromatographic plate coated with a 0.25-mm layer of chromatographic silica gel mixture. Dry the applied solutions with the aid of a stream of nitrogen. Develop the chromatogram, using as the solvent system a freshly prepared mixture of equal volumes of ether and ethyl acetate saturated with ammonium hydroxide, until the solvent front has moved about 13 cm from the origin. Remove the plate from the chamber, and air-dry for 30 minutes. Examine under short-wavelength UV light: the area and intensity of the only other spot in the test specimen chromatogram, other than the principal spot, are not greater than those of the spot from the *Standard preparation* (5.0%).

Other requirements—It meets the requirements under *Injections* ⟨1⟩.

Assay—Transfer an accurately measured volume of Injection, equivalent to about 100 mg of chlorpromazine hydrochloride, to a 500-mL volumetric flask, add 0.1 N hydrochloric acid to volume, and mix. Pipet 10 mL of the solution into a 250-mL separator, add about 20 mL of water, render alkaline with ammonium hydroxide, and extract with four 25-mL portions of ether. Extract the combined ether extracts with four 25-mL portions of 0.1 N hydrochloric acid, collecting the aqueous extracts in a 250-mL volumetric flask. Aerate to remove residual ether, add 0.1 N hydrochloric acid to volume, and mix. Dissolve a suitable quantity, accurately weighed, of USP Chlorpromazine Hydrochloride RS in 0.1 N hydrochloric acid, and dilute quantitatively and stepwise with the same acid to obtain a Standard solution having a known concentration of about 8 µg per mL. Concomitantly determine the absorbances of both solutions in 1-cm cells at the wavelength of maximum absorbance at about 254 nm and at 277 nm, with a suitable spectrophotometer, using 0.1 N hydrochloric acid as the blank. Calculate the quantity, in mg, of $C_{17}H_{19}ClN_2S \cdot HCl$ in each mL of the Injection taken by the formula:

$$12.5C(A_{254} - A_{277})_U / V(A_{254} - A_{277})_S$$

in which C is the concentration, in µg per mL, of USP Chlorpromazine Hydrochloride RS in the Standard solution, V is the volume, in mL, of Injection taken, and the parenthetic expressions are the differences in the absorbances of the two solutions at the wavelengths indicated by the subscripts, for the solution from the Injection (U) and the Standard solution (S), respectively.

Chlorpromazine Hydrochloride Syrup

» Chlorpromazine Hydrochloride Syrup contains, in each 100 mL, not less than 190 mg and not more than 210 mg of $C_{17}H_{19}ClN_2S \cdot HCl$.

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

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

[NOTE—Throughout the following procedures, protect test or assay specimens, the Reference Standard, and solutions containing them by conducting the procedures without delay, under subdued light, or using low-actinic glassware.]

Identification—

A: Transfer a volume of it, equivalent to about 20 mg of chlorpromazine hydrochloride, to a 125-mL separator. Add 10 mL of water, 2 mL of sodium hydroxide solution (1 in 2), and mix. Extract with three 30-mL portions of ether. Filter the combined ether extracts through anhydrous sodium sulfate. With the aid of a stream of nitrogen evaporate the ether to about 5 mL. Quantitatively transfer the solution to a 40-mL centrifuge tube. Evaporate with a stream of nitrogen and mild heat to dryness. Dissolve the residue in 100 mL of methanol to obtain the Test solution. Separately apply 15 µL of this Test solution and 15 µL of a Standard solution, containing 0.2 mg of USP Chlorpromazine Hydrochloride RS per mL of methanol, to a thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 0.25-mm layer of chromatographic silica gel. Develop the chromatogram in a chamber containing a freshly prepared mixture of ethyl acetate that has been saturated with ammonium hydroxide, ether, and methanol (75:25:20) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the chamber, air-dry, and spray with Iodoplatinate reagent prepared by dissolving 100 mg of platinic chloride in 10 mL of 0.1 N hydrochloric acid, adding 25 mL of potassium iodide solution (1 in 25), 0.5 mL of formic acid, and diluting with water to 100 mL: the R_F value of the principal spot from the test solution corresponds to that obtained from the Standard solution.

B: Dilute a portion of the Syrup with an equal volume of water: the resulting solution responds to the tests for *Chloride* ⟨191⟩.

Limit of chlorpromazine sulfoxide—

Chlorpromazine sulfoxide standard solution—Transfer 5 mL of a solution in dilute hydrochloric acid (1 in 100) of USP Chlorpromazine Hydrochloride RS containing 10.6 mg per mL to a 50-mL volumetric flask. Add 2 mL of 30% hydrogen peroxide