solution: not more than 0.1% of any individual impurity is found; and not more than 0.3% of total impurities is found.

Ordinary impurities ⟨466⟩**—**

Test solution—Dissolve an accurately weighed quantity of Thalidomide in acetonitrile to obtain a solution having a concentration of about 2 mg per mL.

Standard solution—Dissolve an accurately weighed quantity of glutamine in a mixture of acetonitrile and water (1:1) to obtain a solution having a concentration of about 0.1 mg per mL.

Eluant: a mixture of methylene chloride, methanol, and acetic acid (75:25:0.05).

Application volume: 2 µL (*Standard solution*) and 100 µL (*Test solution*).

Visualization: 4.

Limit: 0.1%.

Assay—

Mobile phase—Prepare a filtered and degassed mixture of water, acetonitrile, and phosphoric acid (85:15:0.1). Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Internal standard preparation—Transfer about 150 mg of phenacetin, accurately weighed, to a 100-mL volumetric flask, dissolve in about 80 mL of acetonitrile, dilute with acetonitrile to volume, and mix.

Standard preparation—Dissolve, with the aid of sonication, an accurately weighed quantity of USP Thalidomide RS in acetonitrile to obtain a solution having a known concentration of about 1 mg per mL. Transfer 10.0 mL of this solution and 5.0 mL of *Internal standard preparation* to a 100-mL volumetric flask, add 10.0 mL of phosphoric acid solution (1 in 100), dilute with water to volume, and mix.

Assay preparation—Transfer about 100 mg of Thalidomide, accurately weighed, to a 100-mL volumetric flask, and dissolve, with the aid of sonication, in 80 mL of acetonitrile. Dilute with acetonitrile to volume, and mix. Pipet 10.0 mL of this solution and 5.0 mL of *Internal standard preparation* into a 100-mL volumetric flask, add 10.0 mL of phosphoric acid solution (1 in 100), dilute with water to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 237-nm detector and a 3.9-mm × 15-cm column that contains 4-µm packing L1. The flow rate is about 1.0 mL per minute. Chromatograph the *Standard preparation*, and record the peak responses as directed for *Procedure:* the resolution, *R,* between thalidomide and phenacetin is not less than 3.0; the column efficiency determined from the thalidomide and phenacetin peaks is not less than 7000 and 9000 theoretical plates, respectively; the tailing factor is not more than 2.0; and the relative standard deviation for replicate injections is not more than 1.0%.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantity, in mg, of $C_{13}H_{10}N_2O_4$ in the portion of Thalidomide taken by the formula:

$$1000C(R_U / R_S)$$

in which *C* is the concentration, in mg per mL, of USP Thalidomide RS in the *Standard preparation;* and R_U and R_S are the peak area ratios obtained from the *Assay preparation* and the *Standard preparation*, respectively.

Thalidomide Capsules

» Thalidomide Capsules contain not less than 90.0 percent and not more than 110.0 percent of the labeled amount of thalidomide ($C_{13}H_{10}N_2O_4$).

Packaging and storage—Preserve in tight containers, protected from light, at controlled room temperature. Do not repackage.

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

Identification—

A: *Thin-Layer Chromatographic Identification Test* ⟨201⟩—

Test solution—Prepare a solution of it in acetonitrile containing about 3000 µg of thalidomide per mL.

Application volume: 5 µL.

Developing solvent system: a mixture of normal butyl acetate, glacial acetic acid, and butyl alcohol (50:25:5).

B: The relative 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.*

Microbial enumeration tests ⟨61⟩ **and Tests for specified microorganisms** ⟨62⟩**—**The total aerobic microbial count using the *Plate Method* is not more than 1000 cfu per g, and the total combined molds and yeasts count is not more than 100 cfu per g. It meets the requirements of the test for absence of *Escherichia coli.*

Dissolution ⟨711⟩**—**

Medium—Add 1.0 mL of polyoxyethylene (23) lauryl ether solution, prepared by dissolving 50 g in 100 mL of water, to 0.225 M hydrochloric acid; 4000 mL.

Apparatus 2: 75 rpm.

Time: 60 minutes.

Determine the amount of $C_{13}H_{10}N_2O_4$ dissolved by employing the following method.

Mobile phase—Prepare as directed in the *Assay* under *Thalidomide.*

Internal standard solution—Prepare a solution of phenacetin in acetonitrile containing about 375 µg per mL. Pipet 20.0 mL of this solution into a 100-mL volumetric flask, add 10.0 mL of phosphoric acid solution (1 in 100), dilute with water to volume, and mix.

Standard solution—Dissolve an accurately weighed quantity of USP Thalidomide RS in acetonitrile to obtain a solution having a known concentration of about 0.25 mg per mL. Pipet 10.0 mL of this solution into a 100-mL volumetric flask, add 10.0 mL of phosphoric acid solution (1 in 100), dilute with water to volume, and mix. Add 5.0 mL of *Internal standard solution* to 20.0 mL of this solution, and mix. This solution contains about 0.02 mg of USP Thalidomide RS per mL.

Test solution—Add 5.0 mL of *Internal standard solution* to each 20.0 mL of filtered solution under test, and mix.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard solution* and the *Test solution* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantity, in mg, of $C_{13}H_{10}N_2O_4$ dissolved by the formula:

$$2500C(R_U / R_S)$$

in which *C* is the concentration, in mg per mL, of USP Thalidomide RS in the *Standard solution;* and R_U and R_S are the peak area ratios of thalidomide to the internal standard obtained from the *Test solution* and the *Standard solution*, respectively.

Tolerances—Not less than 70% *(Q)* of the labeled amount of $C_{13}H_{10}N_2O_4$ is dissolved in 60 minutes.

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

Assay—

Mobile phase, *Internal standard preparation*, *Standard preparation*, and *Chromatographic system*—Prepare as directed in the *Assay* under *Thalidomide.*

Assay preparation—Remove, as completely as possible, the contents of not fewer than 20 Capsules, and weigh accurately. Mix the combined contents, and transfer an accurately weighed portion of the powder, equivalent to about 50 mg of thalidomide, to a 100-mL volumetric flask, add 80 mL of acetonitrile to dissolve, and sonicate for about 20 minutes. Dilute with acetonitrile to volume, and mix. Transfer 20.0 mL of this solution and 5.0 mL of *Internal standard preparation* to a 100-mL volumetric flask, add 10.0 mL of phosphoric acid solution (1 in 100), dilute with water to volume, and mix.

Procedure—Separately inject equal volumes (about 20 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the areas for the major peaks. Calculate the quantity, in mg, of thalidomide ($C_{13}H_{10}N_2O_4$) in the portion of Capsules taken by the formula:

$$1000C(R_U / R_S)$$

in which C is the concentration, in mg per mL, of USP Thalidomide RS in the *Standard preparation;* and R_U and R_S are the peak area ratios of thalidomide to the internal standard obtained from the *Assay preparation* and the *Standard preparation,* respectively.

Thallous Chloride Tl 201 Injection

» Thallous Chloride Tl 201 Injection is a sterile, isotonic, aqueous solution of radioactive thallium (^{201}Tl) in the form of thallous chloride suitable for intravenous administration. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of ^{201}Tl as chloride, expressed in megabecquerels (microcuries or millicuries) per mL, at the time indicated in the labeling. Other chemical forms of radioactivity do not exceed 5.0 percent of the total radioactivity. It may contain a preservative or stabilizer.

Packaging and storage—Preserve in single-dose or multiple-dose containers.

Labeling—Label it to include the following, in addition to the information specified for *Labeling* under *Injections* ⟨1⟩: the time and date of calibration; the amount of ^{201}Tl as labeled thallous chloride expressed as total megabecquerels (microcuries or millicuries) and concentration as megabecquerels (microcuries or millicuries) per mL at the time of calibration; the expiration date and time; and the statement "Caution—Radioactive Material." The labeling indicates that in making dosage calculations, correction is to be made for radioactive decay, and also indicates that the radioactive half-life of ^{201}Tl is 73.1 hours.

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

Radionuclide identification (see *Radioactivity* ⟨821⟩)**—**Its gamma-ray spectrum is identical to that of a specimen of ^{201}Tl of known purity that exhibits a major photopeak at an energy of 167 KeV and a minor photopeak of 135 KeV.

Bacterial endotoxins ⟨85⟩**—**The limit of endotoxin content is not more than 175/V USP Endotoxin Unit per mL of the Injection, when compared with the USP Endotoxin RS, in which V is the maximum recommended total dose, in mL, at the expiration date or time.

pH ⟨791⟩: between 4.5 and 7.5.

Radiochemical purity—Soak a 2.5- × 15.0-cm cellulose polyacetate strip in 0.05 M edetate disodium for 45 to 60 minutes. Remove the strip with forceps, taking care to handle the outer edges only. Place the strip between two absorbent pads, and blot to remove excess solution. Apply not less than 5 µL of a previously mixed solution consisting of equal volumes of Injection and 0.05 M edetate disodium to the center of the blotted strip, and mark the point of application. Attach the strip to the support bridge of an electrophoresis chamber containing equal portions of 0.05 M edetate disodium in each side of the chamber. Ensure that each end of the strip is in contact with the 0.05 M edetate disodium. Attach the chamber cover, and perform the electrophoresis at 250 volts for 30 minutes. Remove the strip from the chamber, and allow to air-dry without blotting. Using a suitable scanner and counting assembly, determine the radioactivity. Not less than 95.0% of the radioactivity on the strip migrates toward the cathode as a single peak.

Radionuclidic purity—Using a suitable counting assembly (see *Selection of a Counting Assembly* under *Radioactivity* ⟨821⟩), determine the radioactivity of each radionuclidic impurity in the Injection by use of a calibrated system. Not less than 95.0% of the total radioactivity is present as thallium 201. In addition, not more than 2.0% of thallium 200 (half-life is 26.1 hours), not more than 0.3% of lead 203 (half-life is 52.02 hours), and not more than 2.7% of thallium 202 (half-life is 12.23 days) are present.

Content of thallium—

Standard thallium solution—Transfer 235 mg of thallous chloride, accurately weighed, to a 1000-mL volumetric flask, dilute with water to volume, and mix. Transfer 1.0 mL of the resulting solution to a 100-mL volumetric flask, dilute with saline TS containing 0.9% benzyl alcohol to volume, and mix. This standard solution contains 2 µg of thallium per mL.

Procedure—Transfer 1.0-mL portions of the *Standard thallium solution* and the Injection to separate screw-cap test tubes. To each tube add 2 drops of a solution, prepared by carefully mixing 18 mL of nitric acid and 82 mL of hydrochloric acid, and mix. Then add to each tube 1.0 mL of sulfosalicylic acid solution (1 in 10), and mix. Add 2 drops of 12 N hydrochloric acid to each tube, and mix. To each tube add 4 drops of rhodamine B solution (50 mg of rhodamine B diluted with hydrochloric acid to 100.0 mL), and mix. Add 1.0 mL of diisopropyl ether. Screw the caps on tightly, shake the tubes by hand for 1 minute, accurately timed, releasing any pressure build-up by loosening the caps slightly. Recap the tubes and allow the phases to separate. Transfer 0.5 mL of the diisopropyl ether layer from each tube to clean tubes. Visually compare the ether layers: the color of the ether layer from the Injection is not darker than that from the *Standard thallium solution.*

Iron—Into separate cavities of a spot plate, place 0.1 mL of the Injection and 0.1 mL of *Standard Iron Solution* (see *Iron* ⟨241⟩) diluted with water to a concentration of 5 µg per mL. Add to each cavity 0.1 mL of hydroxylamine hydrochloride solution (1 in 10), 1 mL of sodium acetate solution (1 in 4), and 0.1 mL of 0.5% dipyridyl solution (0.5 g of 2,2′-dipyridyl dissolved in 100 mL of water containing 0.15 mL of hydrochloric acid), and mix. After 5 minutes, the color of the specimen of Injection is not darker than that of the *Standard Iron Solution.*

Copper—

Standard copper solution—Dissolve 0.982 g of $CuSO_4 \cdot 5H_2O$ in 1000 mL of 0.1 N hydrochloric acid. Transfer 2.0 mL of this solution to a 100-mL volumetric flask, dilute with 0.1 N hydrochloric acid to volume, and mix to obtain a Standard solution containing 5 µg of copper per mL.

Procedure—Into separate cavities of a spot plate, place 0.2 mL of the Injection and 0.2 mL of *Standard copper solution.* Add to each cavity 0.2 mL of water and 0.1 mL of iron thiocyanate solution (1.5 g ferric chloride and 2 g potassium thiocyanate dissolved in water and diluted with water to 100.0 mL). Mix, then add 0.1 mL of sodium thiosulfate solution (1 in 100), and again mix. The time required for the specimen of Thallous