upper ethyl acetate phase to a suitable glass container. Evaporate the solvent, dry the residue at 105 ° for 10 minutes, and use the residue.

B: 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*.

Bacterial endotoxins ⟨85⟩**—**It contains not more than 0.5 USP Endotoxin Unit per mg of dantrolene sodium.

Sterility ⟨71⟩**:** meets the requirements.

Uniformity of dosage units ⟨905⟩**:** meets the requirements.

pH ⟨791⟩**—**Dissolve the contents of 1 vial in 60 mL of USP Water for Injection: the pH is between 8.8 and 11.0.

Water, *Method Ia* ⟨921⟩**:** not more than 3.0%.

Related compounds—

Mobile phase and *Diluent*—Proceed as directed in the *Assay.*

Standard solution—Transfer 10 mg of USP Dantrolene Related Compound B RS, accurately weighed, into a 50-mL volumetric flask, and dissolve in 2.5 mL of dimethylformamide. Add 2.5 mL of glacial acetic acid, and dilute with acetone to volume to obtain a solution having a known concentration of about 0.2 mg per mL. Dilute with *Diluent* to obtain a solution having a known concentration of about 0.002 mg per mL of dantrolene related compound B.

Test solution—Use the *Assay preparation.*

Chromatographic system—Proceed as directed in the *Assay.* Chromatograph the *Standard solution,* and record the peak responses as directed for *Procedure:* the relative standard deviation for replicate injections for dantrolene related compound B is not more than 5.0%.

Procedure—Separately inject equal volumes (about 10 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 dantrolene related compound B in the portion of Dantrolene Sodium for Injection taken by the formula:

$$100(r_U/r_S)(C_S/C_T)$$

in which r_U is the peak response for dantrolene related compound B obtained from the *Test solution;* r_S is the corresponding peak response in the *Standard solution*; C_S is the concentration, in mg per mL, of dantrolene related compound B in the *Standard solution*; and C_T is the concentration, in mg per mL, of dantrolene sodium hydrate in the *Test solution*. Not more than 8% of dantrolene related compound B is found.

Other requirements: meets the requirements under *Injections* ⟨1⟩.

Assay—

Buffer—Dissolve 3.3 g of ammonium acetate in 1 L of water, and adjust with acetic acid to a pH of 4.5 ± 0.1.

Solution A—Prepare a filtered and degassed mixture of *Buffer,* acetonitrile, and glacial acetic acid (120:80:7).

Solution B—Prepare a filtered and degassed mixture of acetonitrile and water (70:30).

Mobile phase—Use variable mixtures of *Solution A* and *Solution B,* as directed for *Chromatographic system.* Make adjustments if necessary (see *System Suitability* under *Chromatography* ⟨621⟩).

Diluent—Prepare a mixture of acetonitrile and water (60:40).

Standard preparation—Transfer 40 mg of USP Dantrolene RS, accurately weighed, into a 50-mL volumetric flask, and dissolve in 2.5 mL of dimethylformamide. Add 2.5 mL of glacial acetic acid, and dilute with acetone to volume to obtain a solution having a known concentration of about 0.8 mg per mL. Dilute this solution with *Diluent* to obtain a solution having a known concentration of about 0.08 mg per mL of dantrolene.

Assay preparation—Using 70 mL of water for each vial, transfer the entire contents of the required number of vials to a suitable flask necessary to obtain a solution having a known concentration of about 0.1 mg of dantrolene sodium hydrate per mL. Sonicate for 2 to 5 minutes to dissolve the sample. Dilute with *Diluent* to volume.

Chromatographic system (see *Chromatography* ⟨621⟩)—The liquid chromatograph is equipped with a 365-nm detector and a 4.6-mm × 15-cm column that contains 5- µm packing L1. The flow rate is about 1.5 mL per minute. The chromatograph is programmed as follows.

Time (minutes)	*Solution A* (%)	*Solution B* (%)	Elution
0–8	100	0	isocratic
8–8.1	100→0	0→100	linear gradient
8.1–13	0	100	isocratic
13–13.1	0→100	100→0	linear gradient
13.1–20	100	0	re-equilibration

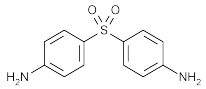
Chromatograph the *Standard preparation,* and record the peak responses as directed for *Procedure:* the tailing factor is not more than 1.5; and the relative standard deviation for replicate injections for dantrolene is not more than 1.5%.

Procedure—Separately inject equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph, record the chromatograms, and measure the peak responses for dantrolene. Calculate the per centage of $C_{14}H_9N_4NaO_5 \cdot 3^1/_2H_2O$ in the portion of Dantrolene Sodium for Injection taken by the formula:

$$(399.29/314.25)(r_U/r_S)(C_S/C_U)$$

in which 399.29 and 314.25 are the molecular weights of dantrolene sodium hydrate and dantrolene, respectively; r_U and r_S are the peak responses for dantrolene obtained from the *Assay preparation* and the *Standard preparation*, respectively; C_S is the concentration, in mg per mL, of dantrolene in the *Standard preparation*; and C_U is the concentration, in mg per mL, of dantrolene sodium hydrate in the *Assay preparation.*

Dapsone



$C_{12}H_{12}N_2O_2S$ 248.30
Benzenamine, 4,4′-sulfonylbis-.
4,4′-Sulfonyldianiline [80-08-0].

» Dapsone contains not less than 98.0 per cent and not more than 102.0 per cent of $C_{12}H_{12}N_2O_2S$, calculated on the dried basis.

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

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

Identification—

A: *Infrared Absorption* ⟨197K⟩.

B: *Ultraviolet Absorption* ⟨197U⟩—

Solution: 5 µg per mL.

Medium: methanol.

Melting range ⟨741⟩: between 175 ° and 181 °.

Loss on drying ⟨731⟩**—**Dry it at 105 ° for 3 hours: it loses not more than 1.5% of its weight.

Residue on ignition ⟨281⟩: not more than 0.1%.

Selenium ⟨291⟩: 0.003%, a 100-mg test specimen, mixed with 100 mg of magnesium oxide, being used.

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Chromatographic purity—

Standard solutions—Dissolve USP Dapsone RS in methanol and mix to obtain *Standard solution A* having a known concentration of 12.5 mg per mL. Dilute quantitatively with methanol to obtain *Standard solution B,* containing 125 µg of the USP Reference Standard per mL, and *Standard solution C,* containing 62.5 µg of the USP Reference Standard per mL.

Test solution—Dissolve an accurately weighed quantity of Dapsone in methanol to obtain a solution containing 12.5 mg per mL.

Procedure—[NOTE—Prepare the solvent system fresh daily. Equilibrate the chromatographic chamber with the solvent system for 30 minutes prior to development of the chromatographic plate.] Separately apply 4 µL of the *Test solution* and each of the *Standard solutions* to a suitable high-performance thin-layer chromatographic plate (see *Chromatography* ⟨621⟩) coated with a 150- to 200- µm layer of chromatographic silica gel. Dry the applications with the aid of a stream of nitrogen. Position the plate in a chromatographic chamber, and develop the chromatograms in a solvent system consisting of a mixture of chloroform, acetone, *n*-butyl alcohol, and formic acid (60:15:15:10) until the solvent front has moved about three-fourths of the length of the plate. Remove the plate from the developing chamber and air-dry. Spray the plate lightly with a 0.1% (w/v) solution of 4-dimethylaminocinnamaldehyde in a mixture of equal volumes of glacial acetic acid and water. Examine the spots that are developed immediately, and compare the intensities of any secondary spots observed in the chromatogram of the *Test solution* with those of the principal spots in the chromatogram of the *Standard solutions:* no secondary spot from the chromatogram of the *Test solution* is larger or more intense than the principal spot obtained from *Standard solution C* (0.5%), and the sum of the intensities of all the secondary spots obtained from the *Test solution* corresponds to not more than 1.0%.

Assay—

Mobile phase—Transfer 100 mL of isopropyl alcohol, 100 mL of acetonitrile, and 100 mL of ethyl acetate to a 1000-mL volumetric flask. Add hexane to volume without mixing, then mix, and allow the mixture to cool to room temperature.

Standard preparation—Dissolve an accurately weighed quantity of USP Dapsone RS in *Mobile phase* to obtain a solution having a known concentration of about 250 µg per mL. Pipet 5 mL of this solution into a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix to obtain a *Standard preparation* having a known concentration of about 25 µg per mL.

Assay preparation—Transfer about 50 mg of Dapsone, accurately weighed, to a 200-mL volumetric flask. Dissolve in and dilute with *Mobile phase* to volume, and mix. Pipet 5 mL of this solution into a 50-mL volumetric flask, dilute with *Mobile phase* to volume, and mix.

Chromatographic system (see *Chromatography* ⟨621⟩)—The chromatograph is equipped with a 254-nm detector and a 4-mm × 30-cm column that contains 10- µm diameter packing L3. Chromatograph a sufficient number of injections of the *Standard preparation* as directed for *Procedure:* the relative standard deviation is not more than 2%.

Procedure—Separately introduce equal volumes (about 10 µL) of the *Standard preparation* and the *Assay preparation* into the chromatograph by means of a suitable microsyringe or sampling valve, adjusting the specimen size and other operating parameters to obtain satisfactory chromatograms. Measure the responses for the major peaks obtained at corresponding retention times with the *Assay preparation* and the *Standard preparation*. Calculate the quantity, in mg, of $C_{12}H_{12}N_2O_2S$ in the portion of Dapsone taken by the formula:

$$2C(P_U / P_S)$$

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

Dapsone Tablets

» Dapsone Tablets contain not less than 92.5 percent and not more than 107.5 per cent of the labeled amount of $C_{12}H_{12}N_2O_2S$.

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

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

Identification—

A: Transfer a quantity of finely powdered Tablets, equivalent to about 100 mg of dapsone, to a suitable container, add 5 mL of acetone, shake for 5 minutes, filter, and evaporate the filtrate to dryness. Dry this residue at 105 ° for 1 hour: the residue so obtained responds to *Identification* test *A* under *Dapsone*.

B: Triturate a quantity of finely powdered Tablets, equivalent to about 100 mg of dapsone, with 50 mL of methanol, and filter. Dilute a portion of the filtrate with methanol to make approximately a 1 in 200,000 solution: this solution responds to *Identification* test *B* under *Dapsone*.

Dissolution ⟨711⟩**—**

Medium: dilute hydrochloric acid (2 in 100); 1000 mL.

Apparatus 1: 100 rpm.

Time: 60 minutes.

Procedure—Withdraw and filter a portion of the solution under test. Transfer an accurately measured portion of the filtrate, estimated to contain about 0.2 mg of dapsone, to a 25-mL volumetric flask, add 5 mL of 1 N sodium hydroxide, dilute with water to volume, and mix. Determine the amount of $C_{12}H_{12}N_2O_2S$ dissolved from UV absorbances at the wavelength of maximum absorbance at about 290 nm of the solutions so obtained from the solution under test in comparison with a Standard solution having a known concentration of USP Dapsone RS in the same medium.

Tolerances—Not less than 75% *(Q)* of the labeled amount of $C_{12}H_{12}N_2O_2S$ is dissolved in 60 minutes.

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

Procedure for content uniformity—Transfer 1 Tablet to a 100-mL volumetric flask, add 2.0 mL of water, and allow to stand for 30 minutes, swirling occasionally. Add about 70 mL of methanol, and place the flask in an ultrasonic bath until the specimen is completely dispersed. Add methanol to volume, mix, and centrifuge a portion of the mixture. Quantitatively dilute an accurately measured volume of the clear supernatant with methanol to obtain a solution having a concentration of about 8 µg of dapsone per mL. Dissolve an accurately weighed quantity of USP Dapsone RS in methanol to obtain a Standard solution having a known concentration of about 8 µg per mL. Concomitantly determine the absorbances of the test solution and the Standard solution in 1-cm cells at the wavelength of maximum absorbance at about 296 nm, with a suitable spectrophotometer, using methanol as the blank. Calculate the quantity, in mg, of $C_{12}H_{12}N_2O_2S$ in the Tablet taken by the formula:

$$(TC / D)(A_U / A_S)$$

in which T is the labeled quantity, in mg, of dapsone in the Tablet, C is the concentration, in µg per mL, of USP Dapsone RS in the Standard solution, D is the concentration, in µg per mL, of dapsone in the solution from the Tablet, based upon the labeled quantity per Tablet and the extent of dilution, and A_U and A_S are the absorbances of the solution from the Tablet and the Standard solution, respectively.

Assay—

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

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