pH ⟨791⟩: between 2.0 and 3.0.

Radiochemical purity—Activate a 65- × 95-mm silicic acid thin-layer chromatographic plate by heating at 100-110° for 30 minutes. Cool over silica gel and immediately apply 1 µL of Injection, appropriately diluted, if necessary, to a radioactive concentration of 18.5 to 370 MBq (0.5 to 10 mCi) per mL, about 17 mm from one end of the chromatographic plate, and allow to dry. Develop the chromatogram over a period of about 30 to 45 minutes by ascending chromatography, using *n*-butanol saturated with 0.3 N hydrochloric acid, and air-dry. Determine the radioactive distribution by scanning the chromatogram with a suitable collimated radiation detector. Not less than 85% of the total radioactivity is found as succimer at an R_F between 0.45 and 0.70. Hydrolyzed ^{99m}Tc is located at the origin (R_F 0 to 0.15) and the unbound ^{99m}Tc is located at the solvent front (R_F 1.0).

Biological distribution—Inject intravenously between 3.7 MBq and 92.5 MBq (100 µCi and 2500 µCi) of Injection, in a volume of 0.2 to 0.25 mL, into the caudal vein of each of three 125-g to 225-g anesthetized Sprague-Dawley female rats. Clamp the opening of the urethra with a hemostat. Sacrifice the animals 1 hour after the injection, and carefully remove the kidneys, bladder, and liver and spleen of each as *three* separate organs by dissections. Place each organ and the remaining carcass (excluding the tail) in separate, suitable counting containers, and determine the radioactivity, in counts per minute, in each container with an appropriate detector, using the same counting geometry. Determine the percentage of administered radioactive dose in each organ: not less than 40% of the administered radioactive dose is found in the kidneys and a ratio of not less than 6:1 of the administered dose is found in the ratio kidneys/(liver and spleen), in not fewer than two of the animals.

Other requirements—It meets the requirements of the tests for *Radionuclide identification* and *Radionuclidic purity* under *Sodium Pertechnetate Tc 99m Injection.* It meets also the requirements under *Injections* ⟨1⟩, except that it may be distributed or dispensed prior to completion of the test for *Sterility*, the latter test being started on the day of final manufacture, and except that it is not subject to the recommendation on *Volume in Container.*

Assay for radioactivity ⟨821⟩**—**Using a suitable counting assembly (see *Selection of a Counting Assembly*), determine the radioactivity, in MBq (µCi) per mL, of Injection by use of a calibrated system.

Technetium Tc 99m Sulfur Colloid Injection

Sulfur, colloidal, metastable technetium-99 labeled [7704-34-9].

» Technetium Tc 99m Sulfur Colloid Injection is a sterile, colloidal dispersion of sulfur labeled with radioactive ^{99m}Tc, suitable for intravenous administration.

Technetium Tc 99m Sulfur Colloid Injection contains not less than 90.0 percent and not more than 110.0 percent of the labeled concentration of ^{99m}Tc as sulfur colloid expressed in megabecquerels (microcuries or millicuries) per mL at the time indicated in the labeling. It may contain chelating agents, buffers, and stabilizing agents. Other chemical forms of radioactivity do not exceed 8 percent of the total radioactivity.

NOTE—Agitate the container before withdrawing the Injection into a syringe.

Packaging and storage—Store 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 ^{99m}Tc as sulfur colloid 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 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 ^{99m}Tc is 6.0 hours; in addition, the labeling states that it is not to be used if flocculent material is visible and directs that the container be agitated before the Injection is withdrawn into a syringe.

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

Radionuclide identification (see *Radioactivity* ⟨821⟩)**—**It meets the requirements of the test for *Radionuclide identification* under *Sodium Pertechnetate Tc 99m Injection.*

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.

Radionuclidic purity—It meets the requirements of the test for *Radionuclidic purity* under *Sodium Pertechnetate Tc 99m Injection.*

Radiochemical purity—Place a measured volume of Injection, appropriately diluted, such that it provides a count rate of about 20,000 counts per minute, about 25 mm from one end of a 25- × 300-mm strip of chromatographic paper (see *Chromatography* ⟨621⟩), and allow to dry. Develop the chromatogram over a suitable period by ascending chromatography, using dilute methanol (8.5 in 10), and air-dry. Determine the radioactivity distribution by scanning the chromatogram with a suitable collimated radiation detector. Not less than 92% of the total radioactivity is found as sulfur colloid (at the point of application).

Biological distribution—Inject intravenously between 0.075 MBq and 0.75 MBq (2 µCi and 20 µCi) of the Injection in a volume not exceeding 0.2 mL into the caudal vein of each of three 20-g to 25-g mice. Ten to 30 minutes after the injection, sacrifice the animals, and carefully remove the liver and lungs of each by dissection. Place each organ and remaining carcass in separate, suitable counting containers, and determine the radioactivity, in counts per minute, in each container in an appropriate scintillation well counter, using the same counting geometry. Determine the percentage of radioactivity in the liver and the lungs taken by the formula:

$$100(A/B)$$

in which A is the net radioactivity, in counts per minute, in the organ, and B is the total radioactivity, in counts per minute, in the lungs, liver, and carcass. Not less than 80% of the radioactivity is found in the liver and not more than 5% of the radioactivity is found in the lungs, in two of the mice.

Other requirements—It meets the requirements under *Injections* ⟨1⟩, except that the Injection may be distributed or dispensed prior to completion of the test for *Sterility*, the latter test being started on the day of final manufacture, and except that it is not subject to the recommendation on *Volume in Container.*

Assay for radioactivity ⟨821⟩**—**Using a suitable counting assembly (see *Selection of a Counting Assembly*), determine the radioactivity, in MBq (µCi) per mL, of Injection by use of a calibrated system.

Technetium Tc 99m Tetrofosmin Injection

» Technetium Tc 99m Tetrofosmin Injection is a sterile aqueous solution, suitable for intravenous injection, that contains ^{99m}Tc in the form of a complex of tetrofosmin. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of ^{99m}Tc as tetrofosmin complex expressed in MBq (or mCi) per mL at the date and time indicated in the labeling. It may contain reducing agents, stabilizers, and buffers. It contains no antimicrobial agents. Other chemical forms of radioactivity do not exceed 10.0 percent of the total.

Packaging and storage—Preserve in adequately shielded single-dose or in multiple-dose containers. Protect from light. Store at a temperature not exceeding 25°.

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 ^{99m}Tc as labeled tetrofosmin expressed as total MBq (or mCi) and the concentration as megabecquerels per mL (or as mCi per mL) on the date and time of calibration; the expiration date and time; and a 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 ^{99m}Tc is 6.0 hours.

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

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 USP Endotoxin RS, in which *V* is the maximum recommended total dose, in mL, at the expiration date or time.

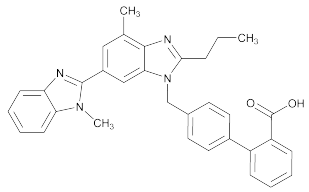
pH ⟨791⟩: between 8.3 and 9.1.

Radiochemical purity—To determine the amount of free technetium, apply a 10- to 20-µL volume of Injection about 3.0 cm from the bottom of a 2- × 20-cm instant thin-layer chromatographic silica gel strip (see *Chromatography* ⟨621⟩). Immediately develop the chromatogram by ascending chromatography to a height of 15 cm using a solvent system consisting of a mixture of acetone and dichloromethane (35:65). Allow the chromatogram to air-dry. Determine the radioactivity distribution of the chromatogram by scanning with a suitable radiation detector. The R_F value of the technetium Tc 99m tetrofosmin spot is approximately 0.5: the sum of radioactivity at the solvent front (unbound pertechnetate) and the origin (reduced hydrolyzed technetium and hydrophilic impurities) is not more than 10%.

Other requirements—It meets the requirements for *Radionuclide identification* and *Radionuclidic purity* under *Sodium Pertechnetate Tc 99m Injection.* It meets also the requirements under *Injections* ⟨1⟩, except that it may be distributed or dispensed prior to completion of the test for *Sterility*, the latter test being started on the date of manufacture.

Assay for radioactivity ⟨821⟩**—**Using a suitable counting assembly (see *Selection of a Counting Assembly*), determine the radioactivity, in MBq (µCi) per mL, of the Injection by use of a calibrated system.

Telmisartan



$C_{33}H_{30}N_4O_2$ 514.62

[1,1′-Biphenyl]-2-carboxylic acid, 4′-[(1,4′-dimethyl-2′-propyl [2,6′-bi-1*H*-benzimidazol]-1′-yl)methyl-];
4′-[[4-Methyl-6-(1-methyl-2-benzimidazolyl)-2-propyl-1-benzimidazolyl]methyl]-2-biphenylcarboxylic acid [144701-48-4].

DEFINITION
Telmisartan contains NLT 98.0% and NMT 101.0% of $C_{33}H_{30}N_4O_2$, calculated on the dried basis.

IDENTIFICATION
- **A. Infrared Absorption ⟨197K⟩:** If the spectra obtained shows differences, proceed with the samples prepared as follows. Separately dissolve a quantity of USP Telmisartan RS and the Telmisartan sample in alcohol. [Note—Heating the solution may be necessary for complete dissolution.] Cool the solution in an ice bath, filter the crystals, and dry at 105°.
- **B.** The retention time of the major peak from the *Sample solution* corresponds to that from the *Standard solution*, as obtained in the test for *Organic Impurities*.

ASSAY
- **Procedure**

(See *Titrimetry* ⟨541⟩.)
Sample solution: 190 mg of Telmisartan in 5 mL of anhydrous formic acid. Dilute with 75 mL of acetic anhydride.
Analysis: Titrate with 0.1 M perchloric acid versus a blank determination under the same conditions. Each mL of 0.1 M perchloric acid is equivalent to 25.73 mg of $C_{33}H_{30}N_4O_2$.
Acceptance criteria: 98.0%–101.0% on the dried basis

IMPURITIES
- **Residue on Ignition ⟨281⟩:** NMT 0.1%. A 1-g sample is used.

Change to read:

- **Heavy Metals,** ▲*Method II*▲*USP35* ⟨**231**⟩**:** NMT 10 ppm
▲ ▲*USP35*
- **Organic Impurities**

[Note—Freshly prepare sample solutions, and protect from light.]
Solution A: 2.0 g of monobasic potassium phosphate and 3.8 g of sodium 1-pentanesulfonate in 1 L of water. Adjust with 1 M phosphoric acid to a pH of 3.0.
Solution B: Acetonitrile and methanol (4:1)
Mobile phase: See *Table 1*.

Table 1

Time (min)	Solution A (%)	Solution B (%)
0	70	30
2	70	30
27	20	80
32	20	80
32.1	70	30
37	70	30