Technetium Tc 99m Sulfur Colloid Injection

Type of Posting	Notice of Intent to Revise
Posting Date	25-Feb-2022
Targeted Official Date	To Be Determined, Revision Bulletin
Expert Committee	Small Molecules 4

In accordance with the Rules and Procedures of the Council of Experts and the Pending Monograph Guideline, this is to provide notice that the Small Molecules 4 Expert Committee intends to revise the Technetium Tc 99m Sulfur Colloid Injection monograph.

Based on the supporting documentation received from a manufacturer awaiting FDA approval, the Expert Committee proposes the following revision:

Revise the number of animals used from "3" to "The number of animals under test should be pre-determined prior to testing and must be a multiple of 3" and the *Acceptance criteria* from "In NLT 2 mice, NLT 80% of the radioactivity is found in the liver, and NMT 5% of the radioactivity is found in the lungs" to "In NLT 2/3 of mice, NLT 80% of the radioactivity is found in the liver, and NMT 5% of the radioactivity is found in the lungs" in the *Biological Distribution* test.

Additionally, minor editorial changes have been made to update the monograph to current *USP* style.

The proposed revision is contingent on FDA approval of a product that meets the proposed monograph specifications. The proposed revision will be published as a Revision Bulletin and an official date will be assigned to coincide as closely as possible with the FDA approval of the associated product.
See below for additional information about the proposed text.[1]

Should you have any questions, please contact Gerald J. Hsu, Principal Scientist (240-221-2097 or gdh@usp.org).

[1] This text is not the official version of a *USP–NF* monograph and may not reflect the full and accurate contents of the currently official monograph. Please refer to the current edition of the *USP–NF* for official text.

USP provides this text to indicate changes that we anticipate will be made official once the product subject to this proposed revision under the Pending Monograph Program receives FDA approval. Once FDA approval is granted for the associated revision request, a Revision Bulletin will be posted that will include the changes indicated herein, as well as any changes indicated in the product's final approval, combined with the text of the monograph as effective on the date of approval. Any revisions made to a monograph under the Pending Monograph Program that are posted without prior publication for comment in the *Pharmacopeial Forum* must also meet the requirements outlined in the USP Guideline on Use of Accelerated Processes for Revisions to the *USP–NF*.

Notice of Intent to Revise
Official: To Be Determined

Technetium Tc 99m Sulfur Colloid Injection

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

DEFINITION

Technetium Tc 99m Sulfur Colloid Injection is a sterile, colloidal dispersion of sulfur labeled with radioactive technetium [^{99m}Tc], suitable for intravenous administration. It contains NLT 90.0% and NMT 110.0% of the labeled concentration of ^{99m} Tc as sulfur colloid expressed in MBq (mCi or µCi)/mL at the time indicated in the labeling. It may contain chelating agents, buffers, and stabilizing agents. Other chemical forms of radioactivity are NMT 8% of the total radioactivity. [Note—Agitate the container before withdrawing the Injection into a syringe.]

IDENTIFICATION

- **A. Radionuclidic Identity**

(See *Radioactivity,* ⟨821⟩ *Identification of Radionuclides*)

Acceptance criteria: Its gamma-ray spectrum is identical to that of a specimen of ^{99m}Tc that exhibits a major photopeak having an energy of 0.140 MeV.

ASSAY

- **Radioactive Concentration (Strength)**

Analysis: Using a suitable counting assembly (see *Radioactivity* ⟨821⟩), determine the radioactivity, in MBq (or µCi) per mL, of the Injection by use of a calibrated system.

Acceptance criteria: 90.0%–110.0% of the labeled concentration of ^{99m}Tc at the time indicated on the label

PURITY

- **Radionuclidic Purity**

(See *Radioactivity* ⟨821⟩.)

Analysis: Using a suitable counting assembly, determine the radioactivity of each radionuclidic impurity in kBq/MBq (µCi/mCi) of technetium 99m, in the Injection by use of a calibrated system as directed under *Radioactivity* ⟨821⟩.

For Injection prepared from technetium 99m derived from parent molybdenum 99 formed as a result of neutron bombardment of stable molybdenum:

Radionuclidic impurity	Most prominent photopeaks	Half-life	Acceptance Criteria NMT[a]
Molybdenum 99	0.181 MeV gamma 0.740 MeV gamma 0.780 MeV gamma	66.0 h	0.15 kBq/MBq (µCi/mCi)
Total of all other gamma-emitting radionuclides	—	—	0.5 kBq/MBq (µCi/mCi)[b]

[a] Radioactivity of radionuclidic impurity/radioactivity of Tc99m per administered dose of Injection at the time of administration.
[b] Does not exceed 92 kBq (2.5 µCi) per administered dose of the Injection, at the time of administration.

For Injection prepared from technetium 99m derived from parent molybdenum 99 formed as a result of uranium fission—Gamma- and beta-emitting impurities

Radionuclidic impurity	Most prominent/maximum photopeaks	Half-life	Acceptance criteria, NMT[a]
Molybdenum 99	0.181 MeV gamma 0.740 MeV gamma 0.780 MeV gamma	66.0 h	0.15 kBq/MBq (µCi/mCi)
Iodine 131	0.364 MeV	8.08 d	0.05 kBq/MBq (µCi/mCi)
Ruthenium 103	0.497 MeV	39.5 d	0.05 kBq/MBq (µCi/mCi)
Strontium 89[b]	1.463 MeV beta	52.7 d	0.0006 kBq/MBq (µCi/mCi)
Strontium 90[b]	0.546 MeV beta	27.7 y	0.00006 kBq/Mbq (µCi/mCi)
Gross alpha impurity	—	—	0.001 Bq/Mbq (nCi/mCi)
All other beta and gamma emitting radionuclidic impurities	—	—	0.01%

[a] Radioactivity of radionuclidic impurity/radioactivity of Tc99m present at the time of administration.
[b] Use a counting system appropriate for the detection of particulate radiations.

- **Radiochemical Purity**

Chromatographic system

(See *Chromatography* ⟨621⟩*, General Procedures, Paper Chromatography*.)

Mode: Paper chromatography

Absorbent: 25-mm × 300-mm strip of chromatographic paper

Application volume: A volume of the Injection, appropriately diluted, to provide a count rate of about 20,000 counts/min

Developing solvent system: Methanol and water (85:15)

Analysis: Place the appropriately diluted Injection about 25 mm from one end of the chromatographic paper and allow to dry. Develop the chromatogram over a suitable period by ascending chromatography using the *Developing solvent system* and air-dry. Determine the radioactivity distribution by scanning the chromatogram with a suitable collimated radiation detector.

Acceptance criteria: NLT 92% of the total radioactivity is found as sulfur colloid (at the point of application).

SPECIFIC TESTS

Change to read:

- **Biological Distribution**

Animals: Mice

Number of animals: ▲The number of animals under test should be pre-determined prior to testing and must be a multiple of 3.▲ (TBD)

Weight of animals: 20–25 g

Injection volume: Inject intravenously 0.075–0.75 MBq (2–20 µCi) of the Injection in a volume NMT 0.2 mL.

Site of administration: Into the caudal vein

Analysis: Ten to 30 min 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/min, in each container in an appropriate scintillation well counter, using the same counting geometry.

Calculate the percentage of radioactivity in the liver and the lungs:

$$\text{Result} = (A/B) \times 100$$

A = net radioactivity in the organ (counts/min)

B = total radioactivity in the lungs, liver, and carcass (counts/min)

Acceptance criteria: In NLT ▲2/3 of mice▲ (TBD), NLT 80% of the radioactivity is found in the liver, and NMT 5% of the radioactivity is found in the lungs.

- **pH** ⟨791⟩**:** 4.5-7.5
- **Bacterial Endotoxins Test** ⟨85⟩**:** The limit of endotoxin content is NMT 175/V USP Endotoxin Unit/mL of the Injection, when compared with the *USP Endotoxin RS*, in which V is the maximum recommended total dose, in milliliters, at the expiration date or time.
- **Other Requirements:** It meets the requirements under *Injections and Implanted Drug Products* ⟨1⟩, except that the injection may be distributed or dispensed before completion of the test for *Sterility*, the latter test being started on the day of manufacture, and except that it is not subject to the recommendation of *Container Content*.

ADDITIONAL REQUIREMENTS

- **Packaging and Storage:** Store in single-dose or multiple-dose containers.
- **Labeling:** Label the Injection to include the following, in addition to the information specified under *Labeling* ⟨7⟩*, Labels and Labeling for Injectable Products*: the time and date of calibration; the amount of ^{99m}Tc as sulfur colloid expressed as total MBq (µCi or mCi) and concentration as MBq (µCi or mCi)/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 h. 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.

Page Information:

Not Applicable

Current DocID: