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Technetium Tc 99m Albumin Aggregated Injection

Albumins, blood serum, metastable technetium-99 labeled.

» Technetium Tc 99m Albumin Aggregated Injection is a sterile, aqueous suspension of Albumin Human that has been denatured to produce aggregates of controlled particle size that are labeled with ^{99m}Tc. It is suitable for intravenous administration. It contains not less than 90.0 percent and not more than 110.0 percent of the labeled amount of ^{99m}Tc as aggregated albumin expressed in megabecquerels (microcuries or millicuries) per mL at the time indicated in the labeling. It may contain antimicrobial, reducing, chelating, and stabilizing agents, buffers, and nonaggregated albumin human. Other chemical forms of radioactivity do not exceed 10 percent of the total radioactivity. Its production and distribution are subject to federal regulations (see Biologics ⟨1041⟩ and Radioactivity ⟨821⟩).

Packaging and storage—Preserve in single-dose or in multiple-dose containers, at a temperature between 2° and 8°.

Labeling—Label it to include the following, in addition to the information specified for *Labeling ⟨7⟩, Labels and Labeling for Injectable Products*: the time and date of calibration; the amount of ^{99m}Tc as aggregated albumin expressed as total megabecquerels (millicuries or microcuries) 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to be used if clumping of the albumin is observed and directs that the container be agitated before the contents are withdrawn into a syringe.

Particle size—Shake the Injection well, and determine the dimension of not less than 100 particles of a representative test specimen, using a suitable counting chamber, such as a hemacytometer grid, by optical microscopy. Not less than 90.0% of the observed aggregated particles have a diameter between 10 µm and 90 µm, and none of the observed particles have a diameter greater than 150 µm.

Bacterial Endotoxins Test ⟨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 3.8 and 8.0.

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 period of about 3 to 4 hours by ascending chromatography, using dilute methanol (7 in 10), and air-dry. Determine the radioactivity distribution by scanning the chromatogram with a suitable collimated radiation detector. Not less than 90% of the total radioactivity is found as aggregated albumin (at the point of application).

Place a measured volume of Injection in a centrifuge tube, and determine the net radioactivity in a suitable counting assembly. Centrifuge at approximately 2000 rpm for 5 to 10 minutes. Separate the supernatant by aspiration, and determine its net radioactivity in a suitable counting assembly. Determine the percentage of radioactivity in the supernatant taken by the formula:

$$100(A/B)$$

in which *A* is the net radioactivity, in counts per minute, in the supernatant aliquot, and *B* is the total radioactivity, in counts per minute, in the tube prior to centrifugation. Not more than 10.0% of the radioactivity is found in the supernatant, which contains soluble and dispersed radiochemical impurities, following centrifugation.

Protein concentration—

Test preparation—Transfer 2.0 mL of Injection to a suitable centrifuge tube, and centrifuge at about 2000 rpm for 5 to 10 minutes. Decant the supernatant, and add 2.0 mL of Sodium Chloride Injection to wash the centrifuged aggregate. Centrifuge again at 2000 rpm for 5 to 10 minutes, decant the supernatant, and add 2.0 mL of Sodium Chloride Injection.

Standard preparation—To a second test tube add 2.0 mL of a solution containing 2.0 mg of Albumin Human per mL in 0.9 percent sodium chloride solution.

Procedure—To a third test tube add 2.0 mL of Sodium Chloride Injection to provide a blank. To each of the three tubes containing the *Test preparation*, *Standard preparation*, and blank, add 4.0 mL of biuret reagent TS, mix, and allow to stand for 30 minutes, accurately timed, for maximum color development. Additional mixing or slight heating may be required to dissolve the aggregated albumin completely, but the *Test preparation*, *Standard preparation*, and blank are to be treated identically. Determine the absorbances of the solutions from the *Test*

preparation and the *Standard preparation* in 1-cm cells at the wavelength of maximum absorbance at about 540 nm, with a suitable spectrophotometer, against the blank. Calculate the quantity, in mg, of aggregated albumin in each mL of the Injection taken by the formula:

$$2(A_U/A_S)$$

in which A_U and A_S are the absorbances of the solutions from the *Test preparation* and the *Standard preparation*, respectively. The protein concentration is not more than 1 mg, as aggregated albumin, per 37 MBq (1 mCi) of Tc 99m at the time of administration.

Biological distribution—Inject intravenously between 0.075 MBq and 0.75 MBq (2 µCi and 20 µCi) of Injection, in a volume not exceeding 0.2 mL, into the caudal vein of each of three 20- to 25-g mice. [NOTE—Other animal species, such as Sprague-Dawley rats (weighing 100 g to 175 g), may be used.] Five to 10 minutes after the injection, sacrifice the animals, and carefully remove the liver and lungs of each by dissection. Place each organ and the remaining carcass 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 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 80.0% of the radioactivity is found in the lungs, and not more than 5.0% of the radioactivity is found in the liver, in not less 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 the requirements under *Injections and Implanted Drug Products ⟨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 *Container Content*.

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

Auxiliary Information - Please check for your question in the FAQs before contacting USP.

Topic/Question	Contact	Expert Committee
TECHNETIUM TC 99M ALBUMIN AGGREGATED INJECTION	Documentary Standards Support	SM42020 Small Molecules 4
REFERENCE STANDARD SUPPORT	RS Technical Services RSTECH@usp.org	SM42020 Small Molecules 4

Chromatographic Database Information: Chromatographic Database

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