

MPI MAA KIT
Kit for the Preparation of Technetium Tc 99m
Albumin Aggregated Injection
DIAGNOSTIC — FOR INTRAVENOUS USE

DESCRIPTION: The kit consists of 10 multidose reaction vials which contain the sterile, non-pyrogenic, non-radioactive ingredients necessary to produce Technetium Tc99m Albumin Aggregated Injection for diagnostic use by intravenous injection. Each 10 mL reaction vial contains 2.5 mg of albumin aggregated, 5.0 mg of Albumin Human, 0.06 mg (minimum) stannous chloride (maximum stannous and stannic chloride 0.11 mg) and 1.2 mg of sodium chloride; the contents are in a lyophilized form under an atmosphere of nitrogen. Sodium hydroxide or hydrochloric acid has been used for pH adjustment. No bacteriostatic preservative is present.

The Albumin Human was non-reactive when tested for hepatitis B surface antigen (HB_s Ag) by radioimmunoassay. The aggregated particles are formed by denaturation of Albumin Human in a heating and aggregation process. Each vial contains 4 to 8 million particles. By light microscopy, more than 90% of the particles are between 10 and 70 micrometers, while the typical average size is 20 to 40 micrometers; none is greater than 150 micrometers.

Technetium Tc 99m Albumin Aggregated Injection for intravenous use is in its final dosage form when sterile isotonic sodium pertechnetate solution is added to each vial. No less than 90% of the pertechnetate Tc 99m added to a reaction vial is bound to aggregate at preparation time and remains bound throughout the 6 hour lifetime of the preparation.

Physical Characteristics: Technetium Tc 99m decays by isomeric transition with a physical half-life of 6.02 hours.¹

The principal photon that is useful for detection and imaging studies is listed in Table 1.

Table 1. Principal Radiation Emission Data¹

Radiation	Mean %/Disintegration	Mean Energy (keV)
Gamma-2	89.07	140.5

¹Kocher, David C., "Radioactive Decay Data Tables," DOE/ TIC-11026. 108(1981).

External Radiation: The specific gamma ray constant for Tc 99m is 0.78 R/hr-mCi at 1 cm. The first half-value layer is 0.017 cm of Pb. A range of values for the relative attenuation of the radiation emitted by this radionuclide that results from interposition of various thicknesses of Pb is shown in Table 2. For example, the use of a 0.25 cm thickness of Pb will attenuate the radiation emitted by a factor of 1,000.

Table 2. Radiation Attenuation of Lead (Pb) Shielding

Shield Thickness (Pb)cm	Coefficient of Attenuation
0.017	0.5
0.08	10 ⁻¹
0.15	10 ⁻²
0.25	10 ⁻³
0.33	10 ⁻⁴

To correct for physical decay of this radionuclide the fractions that remain at selected intervals after the time of calibration are shown in Table 3.

TABLE 3

Physical Decay Chart: Tc 99m half-life 6.02 hours			
Hours	Fraction Remaining	Hours	Fraction Remaining
0	1.000	5	0.562
1	0.891	6	0.501
2	0.794	8	0.398
3	0.708	10	0.316
4	0.631	12	0.251

CLINICAL PHARMACOLOGY: Immediately following intravenous injection, more than 80% of the albumin aggregated is trapped in the pulmonary alveolar capillary bed. The imaging procedure can thus be started as soon as the injection is complete. Assuming that a sufficient number of radioactive particles has been used, the distribution of radioactive aggregated particles in the normally

perfused lung is uniform throughout the vascular bed, and will produce a uniform image. Areas of reduced perfusion will be revealed by a corresponding decreased accumulation of the radioactive particles, and are imaged as areas of reduced photon density.

Organ selectivity is a direct result of particle size. Below 1-10 micrometers, the material is taken up by the reticuloendothelial system. Above 10 micrometers, the aggregates become lodged in the lung by a purely mechanical process. Distribution of particles in the lungs is a function of regional pulmonary blood flow.

The albumin aggregated is sufficiently fragile for the capillary micro-occlusion to be temporary. Erosion and fragmentation reduce the particle size, allowing passage of the aggregates through the pulmonary alveolar capillary bed. The fragments are then accumulated by the reticuloendothelial system.

Lung to liver ratios greater than 20:1 are obtained in the first few minutes post-injection. Elimination of the technetium Tc 99m aggregated albumin from the lungs occurs with a half-life of about 2 to 3 hours. Cumulative urinary excretion studies show an average of 20% elimination of the injected technetium Tc 99m dose 24 hours post-administration.

Following administration of technetium Tc 99m albumin aggregated by intraperitoneal injection, the radiopharmaceutical mixes with the peritoneal fluid. Clearance from the peritoneal cavity varies from insignificant, which may occur with complete shunt blockage, to very rapid clearance with subsequent transfer into the systemic circulation when the shunt is patent.

Serial images should be obtained of both the shunt and lung (target organ). However, an adequate evaluation of the difference between total blockage of the shunt and partial blockage may not be feasible in all cases.

INDICATIONS AND USAGE: Technetium Tc 99m Albumin Aggregated Injection is a lung imaging agent which may be used as an adjunct in the evaluation of pulmonary perfusion in adults and children.

Technetium Tc 99m Albumin Aggregated injection may be used in adults as an imaging agent to aid in the evaluation of peritoneo-venous (LeVeen) shunt patency.

CONTRAINDICATIONS: Technetium Tc 99m Albumin Aggregated Injection should not be administered to patients with severe pulmonary hypertension.

The use of Technetium Tc 99m Albumin Aggregated Injection is contraindicated in persons with a history of hypersensitivity reactions to products containing human serum albumin.

WARNINGS: Although adverse reactions specifically attributable to Technetium Tc 99m Albumin Aggregated Injection have not been noted, the literature contains reports of deaths occurring after the administration of albumin aggregated to patients with pre-existing severe pulmonary hypertension. Instances of hemodynamic or idiosyncratic reactions to preparations of Technetium Tc 99m albumin aggregated have been reported.

PRECAUTIONS:

General: The contents of the kit before preparation are not radioactive. However, after the sodium pertechnetate Tc 99m is added, adequate shielding of the final preparation must be maintained.

In patients with right to left heart shunts, additional risk may exist due to the rapid entry of albumin aggregated into the systemic circulation. The safety of this agent in such patients has not been established. Hypersensitivity reactions are possible whenever protein-containing materials such as pertechnetate labelled albumin aggregated are used in man. Epinephrine, antihistamines and corticosteroids should be available for immediate use.

The intravenous administration of any particulate materials such as albumin aggregated imposes a temporary small mechanical impediment to blood flow. While this effect is probably physiologically insignificant in most patients, the administration of albumin aggregated is possibly hazardous in acute cor pulmonale and other states of severely impaired pulmonary blood flow.

The components of the kit are sterile and non-pyrogenic. It is essential to follow directions carefully and to adhere to strict aseptic procedures during preparation.

Contents of the vials are intended only for use in the preparation of Technetium Tc 99m Albumin Aggregated Injection and are *NOT* to be administered directly to the patient.

The technetium Tc 99m labeling reactions involved depend on maintaining the stannous ion in the reduced state. Hence, sodium pertechnetate Tc 99m containing oxidants should not be employed.

The preparation contains no bacteriostatic preservative. Technetium Tc 99m Albumin Aggregated Injection should be stored at 2-6°C and discarded 6 hours after reconstitution.

Technetium Tc 99m Albumin Aggregated Injection is physically unstable and consequently the particles settle with time. Failure to agitate the vial adequately before use may result in non-uniform distribution of radioactive particles.

If blood is drawn into the syringe unnecessary delay prior to injection may result in clot formation *in situ*. Do not use if clumping of the contents is observed.

Technetium Tc 99m Albumin Aggregated Injection, as well as other radioactive drugs, must be handled with care. Once sodium pertechnetate Tc 99m is added to the vial, appropriate safety measures must be used to minimize radiation exposure to clinical personnel. Care must also be taken to minimize the radiation exposure to patients in a manner consistent with proper patient management.

Radiopharmaceuticals should be used only by physicians who are qualified by training and experience in the safe use and handling of radionuclides and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides.

Carcinogenesis, Mutagenesis, Impairment of Fertility: No long term animal studies have been performed to evaluate carcinogenic potential or whether Technetium Tc 99m Albumin Aggregated Injection affects fertility in males or females.

Pregnancy Category C: Animal reproduction and teratogenicity studies have not been conducted with Technetium Tc 99m Albumin Aggregated Injection. It is also not known whether Technetium Tc 99m Albumin Aggregated Injection can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. There have been no studies in pregnant women. Technetium Tc 99m Albumin Aggregated Injection should be given to a pregnant woman only if clearly needed.

Ideally, examinations using radiopharmaceuticals, especially those elective in nature, of a woman of childbearing capability, should be performed during the first few (approximately 10) days following the onset of menses.

Nursing Mothers: Technetium Tc 99m is excreted in human milk during lactation. Therefore formula feedings should be substituted for breast feedings.

Pediatric Use: The lowest possible number of particles should be used in right-to-left shunting in neonates, and in severe pulmonary disease.

ADVERSE REACTIONS: The literature contains reports of deaths occurring after the administration of albumin aggregated to patients with pre-existing severe pulmonary hypertension. Instances of hemodynamic or idiosyncratic reactions to preparations of technetium Tc 99m albumin aggregated have been reported (see Warnings).

DOSAGE AND ADMINISTRATION: The recommended intravenous dose range for the average (70kg) ADULT patient for lung imaging is 37 to 148 megabecquerels (1-4 millicuries) of Technetium Tc 99m Albumin Aggregated Injection after reconstitution with oxidant-free Sodium Pertechnetate Tc 99m Injection.

The suggested intraperitoneal dosage range used in the average patient (70 kg) for peritoneo venous (LeVeen) shunt patency evaluation is 37 to 111 megabecquerels (1 to 3 millicuries). Adequate measures should be taken to assure uniform mixing with peritoneal fluid. Serial images of both the shunt and target organ should be obtained and correlated with other clinical findings. Alternatively, the drug may be administered by percutaneous transtubal injection. The suggested percutaneous transtubal (efferent limb) dosage range for the average patient (70kg) is 12 to 37 megabecquerels (0.3 to 1.0 millicurie) in a volume not to exceed 0.5 mL.

The recommended number of particles per single injection is 200,000 to 700,000 with the suggested number being approximately 350,000. Depending on the activity added and volume of the final reconstituted product, the volume of the dose may vary from 0.2 to 1.4 mL.

The number of particles available per dose of Technetium Tc 99m Albumin Aggregated Injection will vary depending on the physical decay of the technetium Tc 99m that has occurred. The number of particles in any dose and volume to be administered may be calculated as follows:

Assume the average number of particles per via! = 6.0×10^6

If

V_{Tc} = volume of solution added to reaction vial

D = desired dose to be administered in MBq (mCi)

C = concentration at calibration time of sodium pertechnetate solution to be added to the reaction vial in MBq/mL (mCi/mL)

V_a = volume to be administered in mL

P = number of particles in dose to be administered

F_r = fraction of technetium Tc 99m remaining after the time of calibration (see Table 3)

Then:

$$V_a = \frac{D}{C \times F_r} \quad \text{and} \quad P = \frac{V_a}{V_{Tc}} \times 6.0 \times 10^6$$

In PEDIATRIC patients, the suggested intravenous dose to be employed for perfusion lung imaging is in the range of 0.925 to 1.85 MBq per kilogram (25 to 50 μ Ci/kg) of body weight, a usual dose is 1.11 MBq per kilogram [30 μ Ci/kg]. except in newborns, in whom the administered dose should be 7.4 to 18.5 MBq (200 to 500 μ Ci). Not less than the minimum dose of 7.4 MBq (200 μ Ci) should be employed for this procedure. The number of particles will vary with age and weight of the child as indicated in Table 5.

Parenteral drug products should be visually inspected for particulate matter and discoloration prior to administration whenever solution and container permit.

The patient dose should be measured by a suitable radioactivity calibration system immediately prior to administration. Mix the contents of the vial by gentle inversion just prior to withdrawing a patient dose.

Mix the contents of the syringe just before injection. If blood is drawn in to the syringe, any unnecessary delay prior to injection may lead to clot formation. For optimum results and because of rapid lung clearance of the radiopharmaceutical, it is suggested that the patient be positioned under the imaging apparatus before administration. Slow injection is recommended. Lung imaging may begin immediately after intravenous injection of the radiopharmaceutical. Due to high kidney uptake, imaging later than one-half hour after administration will yield poor results.

RADIATION DOSIMETRY: The estimated absorbed radiation doses² to an average ADULT patient (70 kg) from an intravenous injection of 148 MBq (4 mCi) of Technetium Tc 99m Albumin Aggregated Injection are shown in Table 4.

Table 4. Absorbed Radiation Doses

Organs	mGy/148MBq	rads/4 mCi
Total body	0.60	0.060
Lungs	8.8	0.88
Liver	0.72	0.072
Spleen	0.68	0.068
Kidneys	0.44	0.044
Bladder Wall		
2.0 hr. void	1.2	0.12
4.8 hr. void	2.2	0.22
Testes		
2.0 hr. void	0.24	0.024
4.8 hr. void	0.26	0.026
Ovaries		
2.0 hr. void	0.30	0.030
4.8 hr. void	0.34	0.034

²Method of calculation:

"S" Absorbed Dose per Unit Cumulated Activity for Selected Radionuclides and Organs, MIRD Pamphlet No. 11 (1975).

In PEDIATRIC patients, the radiation absorbed doses using the maximum recommended dose for lung imaging are based on 1.85 MBq (50 μ Ci) per kilogram of body weight [except in the newborn where the maximum recommended dose of 18.5 MBq (500 μ Ci) is used] and are shown in Table 5, which lists the maximum dose for children from newborn to adults. Note the recommendations regarding number of particles to be administered.

Table 6 represents the absorbed radiation dose resulting from the intraperitoneal administration of 111 megabecquerels (3 millicuries) of technetium Tc 99m albumin aggregated.

HOW SUPPLIED:

MPI MAA Kit

Kit for the Preparation of Technetium Tc 99m Albumin Aggregated Injection

Product No. 4432.

Each kit contains 10 reaction vials, each vial containing in lyophilized form, sterile and non-pyrogenic:

Albumin Aggregated	2.5 mg
Albumin Human	5.0 mg
Stannous Chloride (minimum)	0.06 mg
(Maximum stannous and stannic chloride)	0.11 mg)
Sodium Chloride	1.2 mg

HCl or NaOH has been used for pH adjustment. The vials are sealed under an atmosphere of nitrogen.

Twenty labels with radiation warning symbols and a package insert are supplied in each carton.