

<b>DRAX</b>  <b>IMAGE</b> <sup>®</sup>
<b>MAA</b>
Kit for the Preparation of Technetium Tc 99m Albumin Aggregated Injection
<b>DIAGNOSTIC</b>
For Intravenous Use
<b>DESCRIPTION</b>

The kit consists of reaction vials which contain the sterile, non-pyrogenic, non-radioactive ingredients necessary to produce Technetium Tc 99m Albumin Aggregated Injection for diagnos-tic use by intravenous injection.

Each 10 mL reaction vial contains 2.5 mg of albumin aggre-gated, 5.0 mg of albumin human, 0.1 mg of stannous chloride dihydrate and 1.2 mg of sodium chloride; the contents are in a lyophilized form under an atmosphere of nitrogen. Sodium hydroxide and/or hydrochloric acid is used for pH adjustment prior to lyophilization so that the pH of the reconstituted radiopharmaceutical is 5.4 to 6.0. No bacteriostatic preserva-tive is present.


The human serum albumin was non-reactive when tested for Hepatitis B Surface Antigen (HBsAg), antibodies to Human Immunodeficiency Virus (HIV-1/HIV-2), antibody to Hepatitis C Virus (anti-HCV) and antigen to Human Immunodeficiency Virus (HIV-1). The aggregated particles are formed by denaturation of human albumin 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 micrometres, while the typical average size is 20 to 40 micrometres; none is greater than 150 micrometres.

Technetium Tc 99m Albumin Aggregated Injection for intra-venous use is in its final dosage form when sterile isotonic sodium pertechnetate solution is added to each vial. Not less than 90% of the pertechnetate Tc 99m added to a reaction vial is bound to aggregates at preparation time and remains bound throughout the 8-hour lifetime of the preparation.

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The recommended intravenous dose range for the average (70 kg) adult patient is 37 to 148 MBq (1 to 4 mCi) of Technetium Tc 99m Albumin Aggregated Injection after reconstitution with oxidant-free Sodium Pertechnetate Tc 99m Injection. The suggested range of particle numbers for a single injection is 200,000 to 700,000 with the recommended 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.

In paediatric patients, the suggested intravenous dose to be employed for perfusion lung imaging is in the range of 0.925 MBq 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 MBq 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 paediatric patient as indicated in Table 5.

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**Table 5**  
**Paediatric Radiation Dose from Tc 99m MAA for Lung Imaging\***

Age	Newborn		1 year		5 years		10 years		15 years	
Weight (kg)	3.5		12.1		20.3		33.5		55.0	
Maximum recommended dose in megabecquerels and millicuries	MBq	mCi	MBq	mCi	MBq	mCi	MBq	mCi	MBq	mCi
	18.5	0.5	22.2	0.6	37	1.0	62.9	1.7	103.6	2.8
Range of particles administered	10,000 to 50,000		50,000 to 150,000		200,000 to 300,000		200,000 to 300,000		200,000 to 700,000	
Absorbed radiation dose in milligray and rads for the maximum dose	mGy	rads	mGy	rads	mGy	rads	mGy	rads	mGy	rads
<b>Organ</b>										
Total body	0.60	0.06	0.30	0.03	0.31	0.031	0.48	0.048	0.41	0.041
Lungs	19.00	1.9	6.60	0.66	5.80	0.58	8.70	0.87	7.70	0.77
Liver	1.40	0.14	0.60	0.06	0.62	0.062	1.80	0.18	1.20	0.12
Bladder wall	2.10	0.21 <sup>(1)</sup>	1.50	0.15 <sup>(1)</sup>	3.10	0.31 <sup>(2)</sup>	3.90	0.39 <sup>(2)</sup>	4.10	0.41
Ovaries	0.38	0.038	0.20	0.02	0.19	0.019	0.44	0.044	0.41	0.041
Testes	0.31	0.031	0.13	0.013	0.19	0.019	0.20	0.02	0.36	0.036

<sup>[1)</sup> 2.0 hour voiding interval

<sup>[2)</sup> 4.8 hour voiding interval

**\*Assumptions:**

- Used biologic data from Kaul *et al.*, Berlin, 1973. (3)
- For the newborn, 1-year old, and 5-year old, the “S” values calculated from the preliminary phantoms of ORNL were used. The 10-year old, 15-year old and adult “S” values were taken from Henrichs *et al.*, Berlin, 1980. (4)

**ACTION**

Immediately following intravenous injection, more than 80 % of the aggregated albumin 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 to 10 micrometres, the material is taken up by the reticulo-endothelial system. Above 10 micrometres, 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 aggregated albumin is sufficiently fragile for 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 indicate an average of 20% elimination of the injected technetium Tc 99m dose within 24 hours after administration.

#### 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 paediatric patients.

Technetium Tc 99m Albumin Aggregated Injection may be used in adults as an imaging agent to aid in the evaluation of peritoneovenous 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.

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The number of particles available per millicurie dose of tech-netium Tc 99m will vary depending on the physical decay of the technetium that has occurred. The number of particles available in any dose and volume to be administered may be calculated by means of the following formulas:

V<sub>a</sub> = 






D
C
×

F

r




 and P = 






V

a


N
V

Tc

Where:

V<sub>a</sub> = Volume to be administered in mL

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

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

F<sub>r</sub> = Fraction of technetium Tc 99m remaining after the time of calibration (see Table 3)

P = Number of particles in dose to be administered

N = The number of particles per vial which is assumed to be 6 x 10<sup>6</sup>

V<sub>Tc</sub> = The volume of solution added to the reaction vial

#### WARNINGS

The literature contains reports of deaths occurring after the administration of albumin aggregated to patients with pre-existing severe pulmonary hypertension. Instances of hemo-dynamic or idiosyncratic reactions to preparations of tech-netium Tc 99m albumin aggregated have also 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 main-tained.

In patients with right-to-left heart shunts, additional risk may exist due to the rapid entry of aggregated albumin 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 aggre-gated albumin are used in man. Epinephrine, antihistamines, and corticosteroids should be available for immediate use.

The intravenous administration of any particulate materials such as aggregated albumin imposes a small temporary mechanical impediment to blood flow. While this effect is probably physiologically insignificant in most patients, the administration of aggregated albumin 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 prepara-tion of Technetium Tc 99m Albumin Aggregated Injection and are **NOT** to be administered directly to the patient.

The technetium Tc 99m labelling 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 °C to 8 °C and discarded 8 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.

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Using proper shielding, parenteral drug products should be visually inspected for particulate matter and discoloration prior to administration.

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

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

#### DIRECTIONS FOR PREPARATION

The preparation of Technetium Tc 99m Albumin Aggregated Injection may be accomplished by the following procedure. Use aseptic procedure throughout and take precautions to minimize radiation exposure by the use of suitable shielding. Waterproof gloves should be worn during the preparation procedure.

Before reconstituting a vial it should be inspected for cracks and/or a melted plug or any other indication that the integrity of the vacuum seal has been lost.

It is anticipated that any Tc 99m generator approved in Canada would be suitable as a source of sodium pertechnetate Tc 99m, however, complete data is not available to confirm this. DRAXIMAGE should be contacted for any available information.

The Tc 99m pertechnetate eluate should be less than 2 hours old and should be obtained from a generator which has been eluted within the last 24 hours.

To prepare Technetium Tc 99m Albumin Aggregated Injection:

- Remove the protective disc from the reaction vial and swab the closure with an alcohol swab.
- Place the vial in a suitable lead vial shield which has a minimum wall thickness of 3 mm (1/8 inch) and a fitted lead cap. Obtain 2 to 8 mL of sterile, non-pyrogenic sodium pertechnetate Tc 99m using a shielded syringe. The recommended maximum amount of technetium Tc 99m (at the time of elution) to be added to a reaction vial is 5.18 gigabecquerels (140 mCi). Sodium pertechnetate Tc 99m solutions containing an oxidizing agent are not suitable for use.

If blood is drawn into the syringe, any 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 and Teratogenicity

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.

##### Paediatric Use


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

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- Using a shielded syringe, aseptically add the sodium pertechnetate Tc 99m solution to the reaction vial, while avoiding the build up of excessive pressure in the vial. Pressure build up may be avoided by injecting several millilitres of pertechnetate solution into the reaction vial, then withdrawing several millilitres of nitrogen gas (present to prevent oxidation of the complex) into the syringe. The procedure is repeated as necessary until the entire amount of pertechnetate is added to the vial and normal pressure is established within the vial.

- Place the lead cap on the vial shield and mix the contents of the shielded vial by repeated gentle inversion until all the material is suspended. Avoid the formation of foam. Using proper shielding, the vial should be visually inspected to ensure that the suspension is free of foreign matter before proceeding; if it is not, the radiopharmaceutical should not be used. To ensure maximum radiolabelling, allow the preparation to stand for 15 minutes after mixing at 2 °C to 8 °C.

- Assay the product in a suitable calibrator, record the radioassay information on the label which has a radiation warning symbol. Also note the time and date of preparation. Apply the label to the vial shield.


- The radiochemical purity of the finished preparation should be determined prior to patient administration. The radio-chemical purity should not be less than 90 %.

- Withdrawals for administration must be made aseptically using a sterile needle (18 to 21 gauge) and syringe. Since the vials contain nitrogen, the vials should not be vented. If repeated withdrawals are made, the replacement of the contents of the vial with air should be minimized.

- The finished preparation should be discarded after 8 hours. It should also be retained during its life in a lead vial shield with the lead cap in place.

#### ADVERSE REACTIONS


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
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**Table 1**  
**Principal Radiation Emission Data**

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

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