

## PRODUCTION OF LYOPHILIZED KITS FOR LABELLING WITH <sup>99m</sup>Tc

Centro de Radiofarmácia - IPEN/CNEN-SP

**Keywords:** radiopharmaceuticals production; kits lyophilized; nuclear medicine; radionuclide.

### Technetium-99m Diethylenetriaminepentaacetic Acid (<sup>99m</sup>Tc-DTPA)

The use of <sup>99m</sup>Tc-DTPA is for brain imaging renal flow study, and glomerular filtration rate measurement. Following intravenous injection, <sup>99m</sup>Tc-DTPA is rapidly cleared from the blood by glomerular filtration. Renal retention is 7% of the injected dose at 1 h and 95% is excreted within 24 h. It is neither secreted nor reabsorbed by the tubules and has negligible biliary excretion and elimination in feces. When the blood-brain barrier is compromised, <sup>99m</sup>Tc-DTPA accumulates in the brain lesions. To prepare <sup>99m</sup>Tc-DTPA injection, the recommended maximum amount of <sup>99m</sup>Tc to be added to a reaction vial is 3700 MBq (100 mCi). The dose range for intravenous injection to the average adult patient (70 Kg) is: brain imaging 555 to 740 MBq (15 to 20 mCi); kidney imaging and Glomerular Filtration Rate 74 to 185 MBq (2 to 5 mCi).

### Technetium-99m Methylene Diphosphonate (<sup>99m</sup>Tc-MDP)

The <sup>99m</sup>Tc-MDP is a skeletal imaging agent used to demonstrate areas of altered osteogenesis as seen, for example, in metastatic bone disease and osteomyelitis. When injected intravenously, <sup>99m</sup>Tc-MDP injection is rapidly cleared from the blood: about 50% of the dose is accumulated and retained by the skeleton, while the remaining 50% is excreted in the urine within 24 hours. About 10% of the injected dose remains in the blood at 1 hour post-injection, 5% at 2 hours, and less than 1% remains at 24 hours. To prepare <sup>99m</sup>Tc-MDP injection, the recommended maximum amount of <sup>99m</sup>Tc to be added to a reaction vial is 9250 MBq (250 mCi). The dose range for intravenous injection to average adult patient (70 Kg) is 370 to 740 MBq (10 to 20 mCi).

### Technetium-99m Dimercaptosuccinic (<sup>99m</sup>Tc-DMSA)

<sup>99m</sup>Tc-DMSA is used primarily for renal cortical imaging. Renal uptake of <sup>99m</sup>Tc-DMSA is 24% of the injected dose at 1 h. Using an autoradiographic technique in rats, it has been shown that at 1 h <sup>99m</sup>Tc-DMSA accumulates mostly in the proximal and distal tubular sites of the cortex and, to a lesser extent in the renal medulla, glomeruli, collecting tubules and blood vessels. Since <sup>99m</sup>Tc-DMSA is bound to plasma protein to a large extent (75-90%), glomerular filtration is insignificant compared with tubular secretion. <sup>99m</sup>Tc-DMSA has a slow renal clearance with 37% of the injected dose excreted within 24h. To prepare <sup>99m</sup>Tc-DMSA injection, the recommended maximum amount of <sup>99m</sup>Tc to be added to a reaction vial is 3700 MBq (100 mCi). The dose range for intravenous injection is 74 to 111 MBq (2 to 3 mCi), to average adult patient (70 Kg).

### Technetium-99m Diisopropyliminodiacetic Acid (<sup>99m</sup>Tc-DISIDA)

<sup>99m</sup>Tc-DISIDA is commonly used as hepatobiliary agent to evaluate hepatic function, biliary duct patency, also in cholescintigraphy. It is claimed to be the best hepatobiliary agent. Following the intravenous administration of <sup>99m</sup>Tc-DISIDA, it is cleared from the blood into the liver within five minutes. Prompt excretion through the biliary tree into the gallbladder and gut normally takes place within 15 to 30 minutes: The kidneys are imaged only transiently during the first 30 minutes post-injection. The gallbladder is visualized against a decreasing liver background and activity is subsequently observed in the intestinal tract. To prepare <sup>99m</sup>Tc-DISIDA injection, the recommended maximum amount of <sup>99m</sup>Tc to be added to a reaction vial is 3700 MBq (100 mCi). The dose range for intravenous injection is 111 to 185 MBq (3 to 5 mCi), to average adult patient (70 Kg).

### Technetium-99m Pyrophosphate (<sup>99m</sup>Tc-PYRO)

The <sup>99m</sup>Tc-PYRO is used for localization of primary bone tumors, metastatic tumors and metabolic bone diseases. It is used for localization of myocardial infarct. Following intravenous injection the <sup>99m</sup>Tc-PYRO is bound to bone surface probably as a result of adsorption on to the hydroxyapatite crystal. Radiopharmaceutical also accumulates in infarcted myocardium owing to adsorption onto amorphous calcium phosphate or by complexation with denatured native proteins and other macromolecules. The <sup>99m</sup>Tc-PYRO has been shown to have higher uptake in myocardial infarct than other products. To prepare <sup>99m</sup>Tc-PYRO injection, the recommended maximum amount of <sup>99m</sup>Tc to be added to a reaction vial is 3700 MBq (100 mCi). The dose range for intravenous injection to average adult patient (70 Kg) is: bone imaging: 185 to 555 MBq (5 to 15 mCi); myocardial studies: 555 to 740 MBq (15 to 20 mCi).

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### Technetium-99m I, I-Ethylcysteinate Dimer ( $^{99m}\text{Tc}$ -ECD)

$^{99m}\text{Tc}$ -ECD is used for diagnosis of acute cerebral infarction, and detection of intracerebral inflammatory conditions; localization of an abnormal focal area in the brain of patients with epilepsy and monitoring of therapy; detection of an abnormal focus in patients with head trauma and cerebrovascular accidents; differentiation of Alzheimer's disease from multi-infarct dementia.  $^{99m}\text{Tc}$ -ECD crosses the blood-brain barrier and accumulates in the brain in proportion to regional blood flow. The brain uptake at 5 min is 6.5% of the injected dose. The clearance of the activity from brain is biexponential with half-lives of 1.3 (40%) and 42.3 h (60%) in gray and white matter, respectively. Is rapidly cleared from blood with a half-life of approximately 0.8 min. At 5 min less than 10% of activity is found in the blood, while at 1 h 90% of the activity present in the blood is in non-lipophilic form. To prepare  $^{99m}\text{Tc}$ -ECD injection, the recommended maximum amount of  $^{99m}\text{Tc}$  to be added to a reaction vial is 3700 MBq (100 mCi). The dose range for intravenous injection to average adult patient (70 Kg) is 740 to 1110 MBq (20 to 30 mCi).

### Technetium-99m Tin Colloid ( $^{99m}\text{Tc}$ -Sn)

$^{99m}\text{Tc}$ -Sn injection is indicated for imaging areas of functional reticuloendothelial cells in the liver, and spleen. It is useful as an adjunct in the diagnosis, localization and evaluation of liver and spleen pathology. Following intravenous administration,  $^{99m}\text{Tc}$ -Sn injection is rapidly cleared by the reticuloendothelial system from the blood. Uptake of the radioactive colloid by organs of the reticuloendothelial system is dependent upon both their relative blood flow rates and the functional capacity of the phagocytic cells. To prepare  $^{99m}\text{Tc}$ -Sn injection, the recommended maximum amount of  $^{99m}\text{Tc}$  to be added to a reaction vial is 3700 MBq (100 mCi). The dose range for intravenous injection to average adult patient (70 Kg) is 37 to 148 MBq (1 to 4 mCi).

### Technetium-99m Dextran-70 ( $^{99m}\text{Tc}$ -DEX-70) and Technetium-99m Dextran-500 ( $^{99m}\text{Tc}$ -DEX-500)

$^{99m}\text{Tc}$ -DEX-70 and  $^{99m}\text{Tc}$ -DEX-500 are used as a lymphoscintigraphic agent. Lymphoscintigraphy is currently performed with radiolabelled colloids in the particle size range of 5-500 nm, commonly injected subcutaneously. Because of the slow outflow from the injection site of the colloid particles a high absorbed dose can be received. Also dynamic studies are difficult to perform. Dextran labeled with  $^{99m}\text{Tc}$  was reported to have a faster clearance from the injection site and perhaps also better reflects the lymph flow. To prepare  $^{99m}\text{Tc}$ -Dex-70 and  $^{99m}\text{Tc}$ -Dex-500 injections, the recommended maximum amount of  $^{99m}\text{Tc}$  to be added to a reaction vial is 3700 MBq (100 mCi). The dose range for intravenous injection of the  $^{99m}\text{Tc}$ -Dex-70 and  $^{99m}\text{Tc}$ -Dex-500 to average adult patient (70 Kg) is 111 to 185 MBq (3 to 5 mCi).

### Technetium-99m N,N'-Ethylene-L,L-dicysteine ( $^{99m}\text{Tc}$ -EC)

$^{99m}\text{Tc}$ -EC injection is indicated for isotope diagnostic kidney scintigraphy, dynamic imaging examinations of the kidneys. Application is especially recommended in case of the following diseases: pyelonephritis, nephrolythiasis, ureterolythiasis, hydronephrosis, other parenchyma affections, polycystic kidney and vesico renal reflux. After administered intravenously, Tc-99m-EC leaves the blood rapidly through the kidneys, where it is excreted in the tubular way. The normal washout route is kidneys - ureters - urinary bladder and this applies to the cases of deficient kidney functions, too. Consequently, none of the liver and the spleen is visualised on the pictures. Tc-99m-EC leaves the bloodstream very rapidly: maximum activity of the kidneys (Tmax) can be observed 3-3.5 minutes after administration in normal cases. Biological half life is < 11 minutes when the kidney function is intact. During 20-25 minutes of the dynamic kidney study, 75-80% of Tc-99m-EC is excreted with urine. Impaired kidney function increases both Tmax and T1/2 significantly. However, it is to be noticed that not even a tiny fraction of Tc-99m-EC remains in the bloodstream or passes out through another way, consequently, the liver does not appear on the picture even in case of impaired kidney function. The kidney image has the best resolution, the parenchyma is well confinable and the calyx is clearly visible within the kidney. To prepare  $^{99m}\text{Tc}$ -EC injection, the recommended maximum amount of  $^{99m}\text{Tc}$  to be added to a reaction vial is 1850 MBq (50 mCi).

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### Technetium-99m Sodium Phytate ( $^{99m}\text{Tc}$ -PHYTATE)

$^{99m}\text{Tc}$ -PHYTATE is indicated for imaging areas of functional reticuloendothelial cells in the liver, spleen and bone marrow. It is useful as an adjunct in the diagnosis, localization and evaluation of liver and spleen pathology. Following intravenous administration, is rapidly cleared by the reticuloendothelial system from the blood. Uptake of the radioactive colloid by organs of the reticuloendothelial system in dependent upon both the relative blood flow rates and the functional capacity of the phagocytic cells. To prepare  $^{99m}\text{Tc}$ -PHYTATE injection, the recommended maximum amount of  $^{99m}\text{Tc}$  to be added to a reaction vial is 3700 MBq (100 mCi). The dose range for intravenous injection to average adult patient (70 Kg) is 74 to 111 MBq (2 to 3 mCi).

### Technetium-99m Macroaggregated Albumin ( $^{99m}\text{Tc}$ -MAA)

$^{99m}\text{Tc}$ -MAA is used as a lung imaging agent for the detection of regional disturbances of pulmonary arterial blood flow in a variety of lung disorders. The major application lies in the diagnosis and management of pulmonary embolism. Following intravenous injection, greater than 80% of the aggregated albumin is immediately trapped in the pulmonary arteriolar-capillary bed. The imaging procedure can thus be started as soon as the injection is completed. Assuming that a sufficient number of radioactive particles have been used, uniform perfusion will produce a uniform image. Areas of reduced perfusion will show a corresponding lack of radioactivity which is seen as an area of reduced photon density. The trapped macroaggregates are broken down to form smaller particles, which are cleared by the reticuloendothelial system with an effective half-life of 4-5 h. Approximately 50-60% of the activity is excreted by kidneys in 48 h, and 1,5-3%, is secreted in human breast milk. To prepare  $^{99m}\text{Tc}$ -MAA injection, the recommended maximum amount of  $^{99m}\text{Tc}$  to be added to a reaction vial is 3700 MBq (100 mCi). The dose range for intravenous injection to average adult patient (70 Kg) is 37 to 148 MBq (1 to 4 mCi).

### Technetium-99m Human Serum Albumin ( $^{99m}\text{Tc}$ -HSA)

$^{99m}\text{Tc}$ -HSA is commonly used in cardiovascular studies in the diagnosis of pericardial effusion, intracardiac shunts, ventricular or major vessel aneurysm, major vascular pathway obstruction, congestive heart failure and midline mediastinal masses. It is also helpful in confirming suspected placenta previa. After intravenous injection  $^{99m}\text{Tc}$ -HSA is uniformly distributed throughout the vascular compartment. The blood clearance is slow with 46% of the administered dose remaining in circulation at 1 h. The urine and feces usually contain less than 0,5% of the injected dose at 24 hour. To prepare  $^{99m}\text{Tc}$ -HSA injection, the recommended maximum amount of  $^{99m}\text{Tc}$  to be added to a reaction vial is 3700 MBq (100 mCi). Administration:

: the dose range for intravenous injection to average adult patient (70 Kg) is 37 to 148 MBq (1 to 4 mCi).

### Technetium-99m Glucoheptonate ( $^{99m}\text{Tc}$ -GHA)

$^{99m}\text{Tc}$ -GHA is used for visualization of the kidneys, investigation of renal perfusion and morphology, evaluation of renal transplants, and imaging of brain tumors and other brain lesions. When injected intravenously,  $^{99m}\text{Tc}$ -GHA is rapidly cleared from the blood. In patients with normal renal function, less than 15% of the initial activity remains in the blood after one hour. About 40% of the injected dose is excreted in the urine in one hour while about 70% is excreted in 24 hours. In patients with renal disease, the blood clearance and urine excretion of the radiopharmaceutical are delayed. Up to 15% of the injected dose is retained in the kidneys with the remainder being excreted in the urine. The renal retention is greater in the cortex than in the medulla.  $^{99m}\text{Tc}$ -GHA tends to accumulate in intracranial lesions with excessive neo-vascularity or an altered blood-brain barrier. It does not accumulate in the choroid plexus or salivary glands. To prepare  $^{99m}\text{Tc}$ -GHA injection, the recommended maximum amount of  $^{99m}\text{Tc}$  to be added to a reaction vial is 3700 MBq (100 mCi). The dose range for intravenous injection to average adult patient (70 Kg) is: renal imaging studies: 185 to 370 MBq (5 to 10 mCi); brain imaging studies: 740 to 1110 MBq (20 to 30 mCi).