Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

PENTACIS
Kit for the preparation of technetium (^{99m}Tc) pentetate injection

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Calcium trisodium pentetate 9.10 mg / vial

The product contains no antimicrobial preservative

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Powder for solution for injection.

Kit for radiopharmaceutical preparation.

White freeze-dried product.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

This medicinal product is for diagnostic use only.

a) After reconstitution with sodium pertechnetate (^{99m}Tc) solution the agent may be used for:

Dynamic renal scintigraphy for perfusion, function and urinary tract studies.

Measurement of glomerular filtration rate.

Cerebral angiography and brain scanning. As an alternative method, when computed tomography and/or magnetic resonance imaging are not available.

b) After inhalation of the nebulized technetium (^{99m}Tc) labelled substance:

Lung ventilation imaging.

c) After oral administration of the technetium (^{99m}Tc) labelled substance:

Studies of gastro-oesophageal reflux and gastric emptying.

4.2 Posology and method of administration

In adults, the following administered doses are recommended (other doses may be justifiable):

For intravenous use:

Measurement of glomerular filtration rate from plasma: 1.8-3.7 MBq.
Measurement of glomerular filtration rate using gamma camera combined with sequential dynamic renal scanning: 37-370 MBq.
Sequential scanning should begin immediately after injection. Optimal static imaging time is 1 hour post injection.

Brain scanning: 185-740 MBq.
For cerebral examinations, static images are obtained 1 hour and, if necessary, several hours after injection. Sequential dynamic scanning should begin immediately after injection.

For inhalation:

Lung ventilation imaging: 500-1000 MBq in nebuliser.
50-100 MBq in lung.

For oral use:
Study of gastro-oesophageal reflux and gastric emptying: 10-20 MBq.
Dynamic recording should be performed during the first minutes (up to 120 minutes for gastroduodenal transit).

Pediatric dose. The dose for children is adjusted according to body weight:

$$\text{Pediatric dose (MBq)} = \frac{\text{Adult dosage (MBq) X Child weight (Kg)}}{70}$$

In some circumstances, dose adjustment according to surface area may be appropriate.

$$\text{Pediatric dosage (MBq)} = \frac{\text{Adult dosage (MBq) X Child body surface } (m^2)}{1.73}$$

In very young children (up to 1 year) a minimum dose of 20 MBq is necessary in order to obtain images of sufficient quality, when technetium (^{99m}Tc) pentetate (DTPA) is used for kidney studies.

4.3 Contraindications

None known.

4.4 Special warnings and precautions for use

4.4.1. Special warnings

This radiopharmaceutical may be received, used and administered only by authorised persons in designated clinical settings. Its receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the local competent official organisations.

Radiopharmaceuticals should be prepared by the user in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken, complying with the requirements of Good Manufacturing Practice for pharmaceuticals.

4.4.2. Special precautions for use

In case of reduced renal function the radiation exposure can be increased, this should be considered in the assessment of the activity to be administered.

To reduce the radiation dose to the bladder, good hydration and frequent voiding of urine is recommended.

4.5 Interaction with other medicinal products and other forms of interaction

Many drugs may affect the function of tested organ and modify the uptake of technetium (^{99m}Tc) pentetate (DTPA) i.e.

Diagnostic use of captopril: dynamic renal scanning performed under controlled conditions and again one hour after oral administration of captopril (25-50 mg) may reveal haemodynamic changes in a kidney affected by renal artery stenosis. The blood pressure should be carefully monitored as patients with vascular disease are at risk of significant hypotension and renal impairment.

Diagnostic use of furosemide: the administration of intravenous furosemide during dynamic renal scanning increases elimination of technetium (^{99m}Tc) pentetate (DTPA) which may help to distinguish whether true obstruction exists in a dilated renal tract.

Cerebral angiography: psychotropic drugs increase blood flow in the territory of the external carotid artery. This may lead to the rapid uptake of tracer in the nasopharyngeal area during the arterial and capillary phases (hot nose phenomenon).

4.6 Fertility, pregnancy and lactation

Women of childbearing potential: when it is necessary to administer radioactive medicinal products to women of childbearing potential, information should always be sought about pregnancy. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. Where uncertainty exists it is important that radiation exposure should be the minimum consistent with achieving the desired clinical information. Alternative techniques which do not involve ionising radiation should be considered.

Pregnancy: radionuclide procedures carried out on pregnant women also involve radiation doses to the foetus. Only imperative investigations should be carried out during pregnancy, when the likely benefit exceeds the risk incurred by mother and foetus.

Lactation: before administering a radioactive medicinal product to a mother who is breast feeding consideration should be given as to whether the investigation could be reasonably delayed until the mother has ceased breast feeding and as to whether the most appropriate choice of radiopharmaceutical has been made, bearing in mind the secretion of radioactivity in breast milk. If the administration is considered necessary the breast feeding should be interrupted for 12 hours and the expressed feeds discarded. Breast feeding can be restarted when the level in the milk will not result in a radiation dose to the child greater than 1 mSv.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed.

4.8 Undesirable effects

In isolated cases the following adverse reactions have been reported: flushing, dizziness, dyspnoea, pruritus, urticaria and hypotension.

For each patient, exposure to ionising radiation must be justifiable on the basis of likely benefit. The activity administered must be such that the resulting radiation dose is as low as reasonably achievable bearing in mind the need to obtain the intended diagnostic or therapeutic result.

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. For diagnostic nuclear medicine investigations the current evidence suggests that these adverse effects will occur with low frequency because of the low radiation doses incurred.

For most diagnostic investigations using a nuclear medicine procedure the radiation dose delivered (E) is less than 20 mSv. Higher doses may be justified in some clinical circumstances.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via
HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

4.9 Overdose

In the event of the administration of a radiation overdose with technetium (^{99m}Tc) pentetate (DTPA) the absorbed dose to the patient should be reduced where possible by increasing the elimination of the radionuclide from the body by forced diuresis and frequent bladder voiding.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Radiopharmaceutical preparation for diagnostic use.
ATC codes: V09CA01 and V09EA01

At the chemical concentrations and activities used for diagnostic procedures technetium (^{99m}Tc) pentetate (DTPA) does not appear to exert any pharmacodynamic effects.

5.2 Pharmacokinetic properties

Following intravenous injection, technetium (^{99m}Tc) pentetate (DTPA) rapidly distributes throughout the extracellular fluid. Less than 5 % of the injected dose is bound to the plasma proteins. There is also a negligible binding of technetium (^{99m}Tc) pentetate (DTPA) to red blood cells. Technetium (^{99m}Tc) pentetate (DTPA) does not cross the normal blood-brain barrier but diffuses weakly in breast milk.
Plasma clearance is multiexponential with an extremely fast component.

The complex remains stable in vivo, more than 98 % of urine radioactivity is in the form of a chelate.
Approximately 90 % of the injected dose is eliminated in the urine within the first 24 hours mainly by glomerular filtration.
No retention of the compound has been demonstrated in the kidneys.
Plasma clearance may be delayed in patients with renal disease.

In subjects exhibiting oedema or ascites, distribution of the radionuclide in the extracellular space may be modified.

In lung ventilation studies, after inhalation, technetium (^{99m}Tc) pentetate (DTPA) diffuses rapidly from the pulmonary alveoles towards the vascular space where it is diluted. The half-life of technetium (^{99m}Tc) pentetate (DTPA) in the lungs is slightly less than 1 hour.
Many factors are likely to modify the permeability of the pulmonary epithelium like cigarette smoking.

Following oral administration, technetium (^{99m}Tc) pentetate (DTPA) does not pass through the digestive barrier.

5.3 Preclinical safety data

This agent is not intended for regular or continuous administration.

Repeated intravenous administration of $CaNa_3DTPA$ to rabbits and dogs for 14 days of doses that were 100 and 1000 times (respectively) the normal dose for humans produced no evidence of toxicity.

The minimum dose of CaDTPA causing abortion and fetal death in mice was approximately 3600 times the dose of $CaNa_3DTPA$ that is proposed for diagnosis in women.

Mutagenicity studies and long-term carcinogenicity studies have not been carried out.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Stannous chloride dihydrate
Sodium chloride
Under a nitrogen atmosphere

6.2 Incompatibilities

This medicinal product must not be mixed with other medicinal products except those mentioned in section 12.

6.3 Shelf life

1 year

After labelling, store at 2 ^{o}C-8^{o}C (in a refrigerator) and use within 4 hours with a maximum of 5 withdrawals per vial.

6.4 Special precautions for storage

Store at 2 ^{o}C-8^{o}C (in a refrigerator)

For storage conditions of the reconstituted medicinal product, see section 6.3

Storage of radiopharmaceuticals should be in accordance with national regulation on radioactive materials.

6.5 Nature and contents of container

15 ml, colourless, European Pharmacopoeia type I, drawn glass vials, closed with chlorobutyl rubber stoppers and aluminium caps.

Pack size: Kit of 5 multidose vials

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spills of urine, vomiting, etc. Radiation protection precautions in accordance with national regulations must therefore be taken.

Any unused product or waste material should be disposed of in accordance with local requirements.

7 MARKETING AUTHORISATION HOLDER

CIS Bio International
Route National 306
BP 32
91192 Gif-Sur-Yvette Cedex
France

8 MARKETING AUTHORISATION NUMBER

PA 0677/002/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 04 March 1999

Date of last renewal: 04 March 2009

10 DATE OF REVISION OF THE TEXT

July 2016

11 DOSIMETRY

(^{99m}Tc) technetium decays with the emission of gamma radiation with a mean energy of 140 keV and a half-life of 6 hours, to (^{99}Tc) technetium which can be regarded as quasi stable.

For this product the effective dose equivalent resulting from:

- an intravenous administered activity of 740 MBq to a patient with normal renal function is 3.6 mSv (per 70 kg individual).
- an inhalation (nebuliser) of 100 MBq is 0.6 mSv (per 70 kg individual).
- an oral administration of 20 MBq is 0.5 mSv (per 70 kg individual).

According to ICRP 53, 60, 80 (International Commission of Radiological Protection) the radiation doses absorbed by the patients are the following:

Normal renal function

ORGAN	ABSORBED DOSE PER UNIT OF ADMINISTERED ACTIVITY (mGy/MBq)				
	Adult	15 years	10 years	5 years	1 year
Adrenals	1.3E-03	1.7E-03	2.6E-03	3.8E-03	7.0E-03
Bladder wall	6.2E-02	7.8E-02	9.7E-02	9.5E-02	1.7E-01
Bone surfaces	2.3E-03	2.8E-03	4.0E-03	5.5E-03	9.9E-03
Brain	8.4E-04	1.0E-03	1.7E-03	2.7E-03	4.8E-03
Breast	7.1E-04	9.0E-04	1.3E-03	2.1E-03	4.0E-03
Gall bladder	1.5E-03	2.0E-03	3.6E-03	4.6E-03	6.0E-03
Gastrointestinal tract					
Stomach	1.3E-03	1.6E-03	2.7E-03	3.7E-03	6.7E-03
Small intestine	2.5E-03	3.1E-03	4.5E-03	5.7E-03	9.8E-03
Colon	3.0E-03	3.8E-03	5.4E-03	6.4E-03	1.1E-02
Upper large intestine	2.1E-03	2.7E-03	4.0E-03	5.4E-03	9.0E-03
wall	4.3E-03	5.3E-03	7.3E-03	7.7E-03	1.3E-02
Lower large intestine					
wall	1.1E-03	1.4E-03	2.1E-03	3.2E-03	5.8E-03
	3.9E-03	4.7E-03	6.7E-03	9.6E-03	1.7E-02
Heart	1.2E-03	1.5E-03	2.4E-03	3.5E-03	6.3E-03
Kidneys	9.9E-04	1.3E-03	1.9E-03	2.9E-03	5.3E-03
Liver	1.6E-03	2.0E-03	2.8E-03	3.7E-03	6.7E-03
Lungs	1.0E-03	1.3E-03	1.9E-03	2.9E-03	5.3E-03
Muscles	4.2E-03	5.3E-03	6.9E-03	7.8E-03	1.3E-02
Oesophagus	1.4E-03	1.8E-03	2.7E-03	4.0E-03	7.2E-03
Ovaries	1.4E-03	1.8E-03	2.6E-03	3.3E-03	5.6E-03
Pancreas	8.5E-04	1.0E-03	1.6E-03	2.3E-03	4.3E-03
Red marrow					
Skin	1.2E-03	1.6E-03	2.4E-03	3.6E-03	6.6E-03
	2.9E-03	4.0E-03	6.0E-03	6.9E-03	1.3E-02
Spleen	1.0E-03	1.3E-03	1.9E-03	2.9E-03	5.3E-03
Testes	1.0E-03	1.3E-03	2.0E-03	3.2E-03	5.8E-03
Thymus	7.9E-03	9.5E-03	1.3E-02	1.3E-02	2.2E-02
Thyroid					
Uterus	1.7E-03	2.0E-03	2.8E-03	3.7E-03	6.4E-03
Other tissue	4.9E-03	6.2E-03	8.2E-03	9.0E-03	1.6E-02
Effective dose (mSv/MBq)					

Abnormal renal function

ORGAN	ABSORBED DOSE PER UNIT OF ADMINISTERED ACTIVITY (mGy/MBq)				
	Adult	15 years	10 years	5 years	1 year
Adrenals	4.1E-03	5.1E-03	7.8E-03	1.2E-02	2.1E-02
Bladder wall	2.2E-02	2.7E-02	4.0E-02	5.8E-02	1.1E-01
Bone surfaces	4.4E-03	5.3E-03	7.9E-03	1.2E-02	2.1E-02
Breast	3.0E-03	3.0E-03	4.3E-03	6.9E-03	1.3E-02
Gastrointestinal tract					
Stomach wall	3.8E-03	5.0E-03	7.9E-03	1.1E-02	2.0E-02
Small intestine	4.7E-03	5.6E-03	8.6E-03	1.3E-02	2.3E-02
Upper large intestine wall	4.4E-03	5.6E-03	8.1E-03	1.3E-02	2.2E-02
Lower large intestine wall	4.7E-03	6.2E-03	9.6E-03	1.4E-02	2.5E-02
	7.9E-03	9.6E-03	1.4E-02	2.0E-02	3.4E-02
Kidneys	3.8E-03	4.6E-03	7.1E-03	1.1E-02	1.9E-02
Liver	3.3E-03	4.2E-03	6.2E-03	9.5E-03	1.7E-02
Lungs	4.9E-03	6.3E-03	9.4E-03	1.4E-02	2.4E-02
Ovaries	4.3E-03	5.4E-03	8.1E-03	1.2E-02	2.2E-02
Pancreas	5.2E-03	6.3E-03	9.0E-03	1.3E-02	2.2E-02
	4.0E-03	4.8E-03	7.2E-03	1.1E-02	2.0E-02
Red marrow	3.3E-03	4.5E-03	6.9E-03	1.1E-02	2.0E-02
Spleen	2.5E-03	4.3E-03	6.8E-03	1.1E-02	1.9E-02
Testes	6.3E-03	7.5E-03	1.1E-02	1.7E-02	2.9E-02
Thyroid	3.3E-03	4.0E-03	6.1E-03	9.4E-03	1.7E-02
Uterus	4.9E-03	6.2E-03	9.3E-03	1.4E-02	2.5E-02
Other tissue					
Effective dose (mSv/MBq)					

The radiation doses given to man on administration by aerosol of (^{99m}Tc) DTPA are the following:

ORGAN	**ABSORBED DOSE PER UNIT OF ADMINISTERED ACTIVITY (mGy/MBq)**				
	Adult	15 years	10 years	5 years	1 year
Adrenals	2.1E-03	2.9E-03	4.4E-03	6.7E-03	1.2E-02
Bladder wall	4.7E-02	5.8E-02	8.4E-02	1.2E-01	2.3E-01
Bone surfaces	1.9E-03	2.4E-03	3.5E-03	5.3E-03	9.8E-03
Breast	1.9E-03	1.9E-03	3.3E-03	4.8E-03	7.8E-03
Gastrointestinal tract					
Stomach wall	1.7E-03	2.2E-03	3.5E-03	5.1E-03	8.9E-03
Small intestine	2.1E-03	2.6E-03	4.1E-03	6.3E-03	1.1E-02
Upper large intestine	1.9E-03	2.4E-03	3.8E-03	6.1E-03	1.0E-02
wall	3.2E-03	4.2E-03	6.3E-03	8.8E-03	1.5E-02
Lower large intestine					
wall	4.1E-03	5.1E-03	7.2E-03	1.1E-02	1.9E-02
	1.9E-03	2.5E-03	3.7E-03	5.5E-03	9.7E-03
Kidneys	1.7E-02	2.6E-02	3.6E-02	5.4E-02	1.0E-01
Liver	3.3E-03	4.1E-03	6.1E-03	8.9E-03	1.5E-02
Lungs	2.1E-03	2.6E-03	4.0E-03	6.1E-03	1.1E-02
Ovaries					
Pancreas	2.7E-03	3.4E-03	4.7E-03	6.2E-03	9.6E-03
	1.9E-03	2.4E-03	3.6E-03	5.6E-03	9.9E-03
Red marrow	2.1E-03	3.1E-03	5.2E-03	7.9E-03	1.5E-02
Spleen	9.9E-04	1.7E-03	2.7E-03	4.4E-03	7.8E-03
Testes	5.9E-03	7.2E-03	1.1E-02	1.6E-02	2.7E-02
Thyroid					
Uterus	1.8E-03	2.2E-03	3.2E-03	4.9E-03	8.6E-03
Other tissue	6.3E-03	8.5E-03	1.2E-02	1.8E-02	3.3E-02
Effective dose (mSv/MBq					

The radiation doses given to man on administration per os of (^{99m}Tc) DTPA are the following (D.J. GAMBINI, R. GRANIER : Manuel pratique de Médecine Nucléaire)

ORGAN	**ABSORBED DOSE PER UNIT OF ADMINISTERED ACTIVITY (mGy/MBq)**
Stomach	8.6E-02
Small intestine	7.0E-02
Red marrow	1.2E-03
Ovaries	3.5E-03
Testes	1.7E-03
Effective dose equivalent (mSv/MBq)	2.5E-02

After calculation according to ICRP 60, the effective dose is 2.6E-02 mSv/MBq.

12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

PENTACIS is a kit for the preparation of technetium (^{99m}Tc) pentetate injection, containing a sterile, pyrogen-free, freeze-dried product under nitrogen.

The product is to be used after reconstitution by the addition of sterile, pyrogen-free, isotonic sodium pertechnetate (^{99m}Tc), allowing the preparation of technetium (^{99m}Tc) pentetate injection (technetium (^{99m}Tc) diethylenetriamine pentaacetate, i.e. technetium (^{99m}Tc) DTPA).

Radiopharmaceuticals should be prepared by the user in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken, complying with the requirements of Good Manufacturing Practice for pharmaceuticals

Method of preparation
Take a vial from the kit and put it in an appropriate lead shielding. Using a hypodermic syringe, introduce through the rubber stopper 5 ml of sterile pyrogen-free sodium pertechnetate (^{99m}Tc) injection, activity varying from 3.7 MBq to maximum 2000 MBq.

Sodium pertechnetate (^{99m}Tc) injection should comply with European Pharmacopoeia specifications. Do not use a breather needle as the contents are under nitrogen: after introduction of the volume of sodium pertechnetate (^{99m}Tc) injection, without removing the needle, withdraw an equivalent volume of nitrogen in order to avoid excess pressure in the vial.

Shake for about 2 minutes.

The obtained preparation is a clear and colourless solution, with a pH ranging between 4.0 and 7.5.
Before use, limpidity of the solution after preparation, pH, radioactivity and gamma spectrum will be checked.

The vial should never be opened and must be kept inside its lead shielding. The solution should be removed aseptically through the stopper with a sterile lead protected syringe.

A maximum of 5 withdrawals per vial is recommended.

Quality control
The quality of labelling (radiochemical purity) could be checked according to the following procedure.

Methods
Thin-layer chromatography or ascending paper chromatography

Thin-layer chromatography

Materials and reagents

1 Chromatographic sheets
2 fiber-glass sheet strips (2.5 x 20 cm) A and B coated with silica gel and previously heated at 110 °C for 10 minutes.

On each strip trace two fine lines parallel to the ends of the strips, the one being called "deposit line" at 2 cm, the other one being called "solvent line" at 10 cm from the "deposit line".

2 Mobile phases
Solvent A : 0.9 % sodium chloride solution
Solvent B : methyl ethyl ketone

3 Chromatographic tanks

2 glass tanks A and B of suitable size for the chromatographic sheets used and provided with a tightly fitting lid.

4 Miscellaneous
Forceps, syringes, needles, appropriate counting assembly.

Procedure

1 Respectively place into the chromatographic tanks A and B a sufficient volume of the mobile phases A and B and let equilibrate at room temperature for a few minutes

2 Apply 5 to 10 µL of the preparation to the "deposit line" of strips A and B using a syringe and needle.

3 Using forceps, introduce each strip vertically into the corresponding chromatographic tank for development with the "deposit line" downward. Close the chromatographic tanks and allow the solvent to migrate to the "solvent line".

4 Remove the strips with forceps and dry in the air.

5 Determine distribution of radioactivity with an appropriate detector.

6 Calculations
With the mobile phase A, impurities in colloidal form (hydrolysed technetium (^{99m}Tc)) remain at the "deposit line" (Rf 0). Technetium (^{99m}Tc) pentetate complex and pertechnetate ion (free technetium (^{99m}Tc)) migrate near to the "solvent line".

Calculate the percentage of hydrolysed (^{99m}Tc) technetium

$$\% \text{ hydrolysed technetium } (^{99m}\text{Tc}) = \frac{\text{Radioactivity at Rf 0}}{\text{Total radioactivity of strip A}} \times 100$$

With mobile phase B, pertechnetate ion (free technetium (^{99m}Tc)) migrates near to the "solvent line" (Rf 1). Technetium (^{99m}Tc) pentetate complex and impurities in colloidal form remain at the "deposit line".

Calculate the percentage of free technetium(^{99m}Tc)

$$\% \text{ free technetium } (^{99m}\text{Tc}) = \frac{\text{Radioactivity at Rf 1}}{\text{Total radioactivity of strip B}} \times 100$$

7 The sum of the percentages of radioactivity corresponding to hydrolysed (^{99m}Tc) technetium and free technetium (^{99m}Tc) should not be greater than 5.0 %.

Paper chromatography (alternative method)

Materials and reagents

1- Paper chromatography
2 “Whatman 1” type sheets (2.5 x 20 cm) A and B

On each paper strip, trace two thin lines parallel to the ends of the strip: one is called “deposit line” at 2 cm from the bottom, the other one is called “solvent line” at 10 cm above from the deposit line.

2- Mobile phases

A : 0.9 % sodium chloride solution
B : methyl ethyl ketone

3- 2 glass tanks A and B (as a chromatographic chamber) provided with a device allowing to suspend the chromatographic paper and also to lower it without opening the chamber.

4- Forceps, scissors, syringes, needles, appropriate counting assembly

Procedure

1- Respectively place a sufficient volume of the mobile phases A and B into the glass tanks A and B and let equilibrate for about 5-10 minutes.

2- Apply 5 to 10 µL of the radiolabelled preparation to the deposit line of each of the paper strip A and B using a syringe and needle. **Do not let dry the spot.**

3- Using forceps, suspend a paper strip into each of the tanks and close the lids. In both cases, lower the paper into the mobile phase (the deposit line should be above the solvent surface) and allow the solvent to migrate to the solvent line.

4- Remove the paper strips and dry in the air.

5- Determine distribution of radioactivity with an appropriate detector. Identify each radioactive spot by calculating the Rf.

6- Calculations
In system A, impurities in colloidal form (hydrolised technetium (^{99m}Tc)) remain at the starting point, whereas pertechnetate ion (free technetium (^{99m}Tc)) and technetium (^{99m}Tc) pentetate complex migrate around Rf 0.7 and 1.0 respectively.

In system B, impurities in colloidal form and technetium (^{99m}Tc) pentetate complex remain at the starting point, whereas pertechnetate ion (free technetium (^{99m}Tc)) migrates around Rf 1.0.

Measure the radioactivity of each considered impurity spot by integration of the peaks.

Calculate the percentage of hydrolysed technetium (^{99m}Tc):

$$\% \text{ hydrolysed technetium } (^{99m}\text{Tc}) = \frac{\text{Radioactivity at Rf 0}}{\text{Total radioactivity of strip A}} \times 100$$

Calculate the percentage of free technetium (^{99m}Tc):

$$\% \text{ free technetium } (^{99m}\text{Tc}) = \frac{\text{Radioactivity at Rf 1}}{\text{Total radioactivity of strip B}} \times 100$$

Calculate the sum of the percentages of radioactivity corresponding to impurities in the chromatograms obtained in systems A and B (% hydrolysed technetium (^{99m}Tc) + % free technetium (^{99m}Tc)).

7- The sum of the percentages of radioactivity corresponding to impurities in the chromatograms obtained in systems A and B should not exceed 5.0 %

Any unused product or waste material should be disposed of in accordance with local requirements.