TECEOS

Kit for the preparation of Technetium (\(^{99m}\text{Tc}\)) 3,3-diphosphono-1,2-propanedicarboxylic acid (DPD) injection.

SUMMARY OF PRODUCT CHARACTERISTICS
1. NAME OF THE MEDICINAL PRODUCT

TECEOS
Kit for the preparation of Technetium \(^{99m}\text{Tc}\) 3.3-diphosphono-1.2-propanedicarboxylic acid (DPD) injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

1 vial contains 13.0 mg 3.3-diphosphono-1.2-propanedicarboxylic acid, tetrasodium salt (DPD)

Teceos is to be used after reconstitution by the addition of sterile, pyrogen-free, isotonic sodium pertechnetate \(^{99m}\text{Tc}\) injection, not included in this kit, allowing the preparation of technetium \(^{99m}\text{Tc}\)-DPD injection.

Excipients: Sodium

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Kit for radiopharmaceutical preparation
White, lyophilised powder for injection

4. CLINICAL PARTICULARS

4.1. Therapeutic indications

This medicinal product is for diagnostic use only.

After reconstitution with sodium pertechnetate \(^{99m}\text{Tc}\) solution the agent may be used for bone scintigraphy, where it delineates areas of altered osteogenesis.

4.2. Posology and method of administration

Adults
The average activity administered by a single intravenous injection is 500 MBq (300 -700 MBq). Other activities may be justifiable.
Images obtained shortly after injection (e.g. in the so-called "3-phase bone scan" procedure) will only partly reflect metabolic bone activity. Late phase static scintigraphy should be performed not earlier than 2 hours after injection.
The patient should void before scanning.
Children
The dose to be administered to a child should be a fraction of the adult dose calculated from the body weight according to the following table.

<table>
<thead>
<tr>
<th>Fraction of adult dose</th>
<th>3 kg = 0.1</th>
<th>22 kg = 0.50</th>
<th>42 kg = 0.78</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 kg</td>
<td>0.14</td>
<td>24 kg = 0.53</td>
<td>44 kg = 0.80</td>
</tr>
<tr>
<td>6 kg</td>
<td>0.19</td>
<td>26 kg = 0.56</td>
<td>46 kg = 0.82</td>
</tr>
<tr>
<td>8 kg</td>
<td>0.23</td>
<td>28 kg = 0.58</td>
<td>48 kg = 0.85</td>
</tr>
<tr>
<td>10 kg</td>
<td>0.27</td>
<td>30 kg = 0.62</td>
<td>50 kg = 0.88</td>
</tr>
<tr>
<td>12 kg</td>
<td>0.32</td>
<td>32 kg = 0.65</td>
<td>52-54 kg = 0.90</td>
</tr>
<tr>
<td>14 kg</td>
<td>0.36</td>
<td>34 kg = 0.68</td>
<td>56-58 kg = 0.92</td>
</tr>
<tr>
<td>16 kg</td>
<td>0.40</td>
<td>36 kg = 0.71</td>
<td>60-62 kg = 0.96</td>
</tr>
<tr>
<td>18 kg</td>
<td>0.44</td>
<td>38 kg = 0.73</td>
<td>64-66 kg = 0.98</td>
</tr>
<tr>
<td>20 kg</td>
<td>0.46</td>
<td>40 kg = 0.76</td>
<td>68 kg = 0.99</td>
</tr>
</tbody>
</table>

In very young children (up to 1 year) a minimum dose of 40 MBq is necessary in order to obtain images of sufficient quality.

4.3. Contraindications

Hypersensitivity to the active substance or to any of the excipients.

4.4. Special warnings and precautions for use

In infants and children particular attention should be paid to the relatively higher radiation exposure to the epiphyses in growing bone.

Appropriate precautions should be taken concerning the activity which is eliminated by the patients, to avoid any contamination. To reduce the radiation exposure to the bladder wall, sufficient hydration of the patient and frequent voiding is recommended.

To avoid accumulation of tracer in the musculature it is advised that strenuous exercise be discouraged immediately after injection until satisfactory bone imaging has been affected.

Inadvertent or accidental subcutaneous administration of technetium ($^{99m}$Tc) 3.3-diphosphono-1.2-propanedicarboxylic acid should be avoided as perivascular inflammation has been described for ($^{99m}$Tc) diphosphonates.

Radiopharmaceuticals intended for administration to patients 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 Pharmaceutical Manufacturing Practice for pharmaceuticals.

4.5. Interactions with other medicinal products and other forms of interaction

As for all other diphosphonates the following potential interactions have to be taken into account.

An increased extrasosseous accumulation of the radiotracer is reported for iron containing compounds, acute administration of diphosphonates, several cytostatic and immunosuppressive drugs, aluminium-containing antacids, X-ray contrast media, antibiotics, anti-inflammatory substances, injections of calcium gluconate, heparin calcium and γ-amino caproic acid.
4.6. Pregnancy and lactation

**Pregnancy**
Only imperative investigations should be carried out during pregnancy, when the likely benefit exceeds the risk incurred by the mother and the foetus.

Radionuclide procedures carried out on pregnant women also involve radiation doses to the foetus.

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.

Administration of 700 MBq technetium (\(^{99m}\)Tc) 3.3-diphosphono-1,2-propanedicarboxylic acid to a patient with normal bone uptake results in an absorbed dose to the uterus of 4.27 mGy. The dose decreases to 2.03 mGy in patients with high bone uptake and/or severely impaired kidney function. Doses above 0.5 mGy would be regarded as a potential risk for the foetus.

**Lactation**
If the administration is considered necessary, one breast feed should be banked prior to injection and the subsequent one discarded after injection. Breast feeding can be restarted 4 hours post injection.

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 activity to breast milk.

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

Literature reports for similar diphosphonates list skin rashes, pruritus, hot flushes during the injection and nausea. For Teceos such reactions have been observed extremely rare.

<table>
<thead>
<tr>
<th>Congenital and familial/genetic disorders</th>
<th>Hereditary defects¹.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not known (cannot be estimated from the available data)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Gastro-intestinal disorders</th>
<th>Nausea².</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very rare (&lt;1/10.000)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Skin and subcutaneous disorders</th>
<th>Rash², pruritus².</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very rare (&lt;1/10.000)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Neoplasms benign and malignant (including cysts and polyps)</th>
<th>Cancer induction¹.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not known (cannot be estimated from the available data)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Vascular disorders</th>
<th>Hot flushes².</th>
</tr>
</thead>
<tbody>
<tr>
<td>Very rare (&lt;1/10.000)</td>
<td></td>
</tr>
</tbody>
</table>

¹ Linked with ionising radiation.
² Onset of the reaction is commonly 4-24 hours post-injection.

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 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 is less than 20 mSv. Higher doses may be justified in some clinical circumstances.

4.9. Overdose

In the event of the administration of a radiation overdose with technetium (⁹⁹ᵐTc) 3,3-di-phosphono-1,2-propanedicarboxylic acid 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 bladder voiding.
5. PHARMACOLOGICAL PROPERTIES

5.1. Pharmacodynamic properties

V 09 BA 04 – Diagnostic radiopharmaceuticals for skeleton, technetium ($^{99m}$Tc) compounds.

At the chemical concentrations of radiopharmaceutical and excipients used for diagnostic procedures technetium ($^{99m}$Tc) 3.3-diphosphono-1.2-propanedicarboxylic acid does not appear to exert any pharmacodynamic effect.

5.2. Pharmacokinetic properties

In the first few minutes after injection the activity is distributed among abdomen and kidneys. The proceeding clearance from these compartments is demonstrated by an accumulation of activity in the skeletal system. The clearance from blood can be described by a two-phase curve with a half-life of $T_1 = 15$ min and $T_2 = 100$ min. In comparison to other diphosphonates technetium ($^{99m}$Tc) 3.3-diphosphono-1.2-propanedicarboxylic acid shows the lowest protein binding in plasma. Initially after injection a relatively high level of activity in the plasma is observed which is followed by the rapid clearance from blood. This behaviour could be explained by a reabsorption process in the kidneys. Compared with other diphosphonates a smaller amount of activity is excreted in the urine and therefore a high level of technetium ($^{99m}$Tc) 3.3-diphosphono-1.2-propanedicarboxylic acid is deposited in the skeleton with a maximum 1 hour after injection. Afterwards this level remains constant for several hours. The unchanged complex is eliminated by the kidneys. Around 1 hour after injection 30 % of the administered activity is excreted in the urine. The amount of unlabeled DPD within the recommended dosage has no influence on the elimination process. The elimination by liver and bowel is negligible. Bone scintigraphy is a sensitive but unspecific diagnostic method. The accumulation in the bone depends on the level of blood supply and the extent of the osteogenesis. For healthy persons whole body retention of $40 \pm 4 \%$ of technetium ($^{99m}$Tc) 3.3-diphosphono-1.2-propanedicarboxylic acid was measured. This value increases in the case of widespread metastases, primary hyperparathyroidism and osteoporosis.

5.3. Preclinical safety data

This agent is not intended for regular or continuous administration. Mutagenicity studies and long-term carcinogenicity studies have not been carried out. Animals suffered no harm from the human dosage in repeated dose toxicity studies in rats and Beagle dogs.

6. PHARMACEUTICAL PARTICULARS

6.1. List of excipients

N-(4-aminobenzyl)-L-glutamic acid, monosodium salt
Stannous oxide
Nitrogen
6.2. **Incompatibilities**

Provided the "Instructions for use, handling and disposal" are carefully followed, no incompatibilities are to be expected.

On no account must a solution containing carbohydrate be used for dilution (e.g. glucose, laevulose) and the injection must not be given by means of a slow infusion which contains such solutions. As with other diphosphonates, in such cases the diagnostic value of the test may be seriously impaired as the bone uptake falls dramatically in favour of massive renal visualisation.

6.3. **Shelf life**

13 months. The expiry date is indicated on the outer packaging and on each vial.

The labelled product should be used within 8 hours after the labelling.

6.4. **Special precautions for storage**

Do not store the kit and the labelled product above 25°C.

Storage should be in accordance with national regulations for radioactive materials.

6.5. **Nature and contents of container**

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

Pack size: 5 multidose vials.

6.6. **Special precautions for disposal and other handling**

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

7. **MARKETING AUTHORISATION HOLDER**

CIS bio international
Route Nationale 306
BP 32
F-91192, GIF-SUR-YVETTE Cedex
France

8. **MARKETING AUTHORISATION NUMBER**

Denmark: DK R 1171
Finland: 11229
9. **DATE OF FIRST AUTHORISATION**

Finland: 29.11.1993

10. **DATE OF REVISION OF THE TEXT**

Friday, 29 June 2012

11. **DOSIMETRY**

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

The dosimetry data were quoted from ICRP publication 53 for phosphonates.

**Normal bone uptake**

**Radiation exposure**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Absorbed dose per unit activity administered (mGy/MBq)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adult</td>
</tr>
<tr>
<td>Adrenals</td>
<td>0.0019</td>
</tr>
<tr>
<td>Bladder wall</td>
<td>0.050</td>
</tr>
<tr>
<td>Bone surfaces</td>
<td>0.063</td>
</tr>
<tr>
<td>Breast</td>
<td>0.00088</td>
</tr>
<tr>
<td>GI-tract</td>
<td></td>
</tr>
<tr>
<td>Stomach wall</td>
<td>0.0012</td>
</tr>
<tr>
<td>Small intest</td>
<td>0.0023</td>
</tr>
<tr>
<td>ULI wall</td>
<td>0.0020</td>
</tr>
<tr>
<td>LLI wall</td>
<td>0.0038</td>
</tr>
<tr>
<td>Kidneys</td>
<td>0.0073</td>
</tr>
<tr>
<td>Liver</td>
<td>0.0013</td>
</tr>
<tr>
<td>Lungs</td>
<td>0.0013</td>
</tr>
<tr>
<td>Ovaries</td>
<td>0.0035</td>
</tr>
<tr>
<td>Pancreas</td>
<td>0.0016</td>
</tr>
<tr>
<td>Red marrow</td>
<td>0.0096</td>
</tr>
<tr>
<td>Spleen</td>
<td>0.0014</td>
</tr>
<tr>
<td>Testes</td>
<td>0.0024</td>
</tr>
<tr>
<td>Thyroid</td>
<td>0.0010</td>
</tr>
<tr>
<td>Uterus</td>
<td>0.0061</td>
</tr>
<tr>
<td>Other tissue</td>
<td>0.0019</td>
</tr>
<tr>
<td>Effective dose equivalent (mSv/MBq)</td>
<td>0.0080</td>
</tr>
</tbody>
</table>
High bone uptake and/or severely impaired kidney function

Radiation exposure

<table>
<thead>
<tr>
<th>Organ</th>
<th>Absorbed dose per unit activity administered (mGy/MBq)</th>
<th>Adult</th>
<th>15 years</th>
<th>10 years</th>
<th>5 years</th>
<th>1 year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adrenals</td>
<td></td>
<td>0.0035</td>
<td>0.0050</td>
<td>0.0072</td>
<td>0.011</td>
<td>0.021</td>
</tr>
<tr>
<td>Bladder wall</td>
<td></td>
<td>0.0025</td>
<td>0.0035</td>
<td>0.0054</td>
<td>0.0074</td>
<td>0.015</td>
</tr>
<tr>
<td>Bone surfaces</td>
<td></td>
<td>0.12</td>
<td>0.16</td>
<td>0.26</td>
<td>0.43</td>
<td>1.0</td>
</tr>
<tr>
<td>Breast</td>
<td></td>
<td>0.0021</td>
<td>0.0021</td>
<td>0.0032</td>
<td>0.0051</td>
<td>0.0096</td>
</tr>
<tr>
<td>GI-tract</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach wall</td>
<td></td>
<td>0.0026</td>
<td>0.0032</td>
<td>0.0051</td>
<td>0.0073</td>
<td>0.014</td>
</tr>
<tr>
<td>Small intest</td>
<td></td>
<td>0.0031</td>
<td>0.0038</td>
<td>0.0057</td>
<td>0.0085</td>
<td>0.016</td>
</tr>
<tr>
<td>ULI wall</td>
<td></td>
<td>0.0029</td>
<td>0.0036</td>
<td>0.0053</td>
<td>0.0086</td>
<td>0.015</td>
</tr>
<tr>
<td>LLI wall</td>
<td></td>
<td>0.0034</td>
<td>0.0042</td>
<td>0.0065</td>
<td>0.0096</td>
<td>0.018</td>
</tr>
<tr>
<td>Kidneys</td>
<td></td>
<td>0.0030</td>
<td>0.0037</td>
<td>0.0056</td>
<td>0.0087</td>
<td>0.016</td>
</tr>
<tr>
<td>Liver</td>
<td></td>
<td>0.0027</td>
<td>0.0033</td>
<td>0.0049</td>
<td>0.0075</td>
<td>0.014</td>
</tr>
<tr>
<td>Lungs</td>
<td></td>
<td>0.0030</td>
<td>0.0037</td>
<td>0.0053</td>
<td>0.0081</td>
<td>0.015</td>
</tr>
<tr>
<td>Ovaries</td>
<td></td>
<td>0.0029</td>
<td>0.0041</td>
<td>0.0059</td>
<td>0.0089</td>
<td>0.016</td>
</tr>
<tr>
<td>Pancreas</td>
<td></td>
<td>0.0032</td>
<td>0.0040</td>
<td>0.0059</td>
<td>0.0089</td>
<td>0.016</td>
</tr>
<tr>
<td>Red marrow</td>
<td></td>
<td>0.018</td>
<td>0.023</td>
<td>0.037</td>
<td>0.072</td>
<td>0.14</td>
</tr>
<tr>
<td>Spleen</td>
<td></td>
<td>0.0026</td>
<td>0.0034</td>
<td>0.0051</td>
<td>0.0078</td>
<td>0.015</td>
</tr>
<tr>
<td>Testes</td>
<td></td>
<td>0.0023</td>
<td>0.0027</td>
<td>0.0039</td>
<td>0.0060</td>
<td>0.011</td>
</tr>
<tr>
<td>Thyroid</td>
<td></td>
<td>0.0024</td>
<td>0.0037</td>
<td>0.0054</td>
<td>0.0083</td>
<td>0.014</td>
</tr>
<tr>
<td>Uterus</td>
<td></td>
<td>0.0029</td>
<td>0.0037</td>
<td>0.0054</td>
<td>0.0082</td>
<td>0.015</td>
</tr>
<tr>
<td>Other tissue</td>
<td></td>
<td>0.0030</td>
<td>0.0036</td>
<td>0.0053</td>
<td>0.0081</td>
<td>0.015</td>
</tr>
<tr>
<td>Effective dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>equivalent (mSv/MBq)</td>
<td></td>
<td>0.0082</td>
<td>0.011</td>
<td>0.017</td>
<td>0.028</td>
<td>0.061</td>
</tr>
</tbody>
</table>

For this product the effective dose equivalent resulting from an administered activity of 700 MBq is typically 5.6 mSv (per 70 kg individual).

For an administered activity of 700 MBq the typical radiation dose to the target organ (bone) is 44.1 mGy and the typical radiation dose to the critical organ (bladder wall) is 35 mGy.

In cases of high bone uptake and/or severely impaired kidney function, the effective dose equivalent resulting form an administered activity of 700 MBq of technetium($^{99m}$Tc)$_3$3-diphosphono-1,2-propanedicarboxylic acid is 5.7 mSv. The typical radiation dose to the target organ is 84 mGy and the typical radiation dose to the critical organ (red marrow) is 12.6 mGy.
TECEOS is a kit for the preparation of technetium ($^{99m}$Tc) DPD Injection, containing a sterile, progen-free, freeze-dried product under vacuum.

**Method of preparation**
Normal safety precautions for the handling of radioactive materials should be observed in addition to the use of aseptic technique to maintain sterility of the vial contents.

Take a vial from the kit and put it in an appropriate lead shielding.

Using a hypodermic syringe, introduce through the rubber stopper 2 to 10 ml of sterile and pyrogen-free sodium pertechnetate ($^{99m}$Tc) injection, radioactivity varying as a function of the volume from 370 to maximum 11100 MBq sodium pertechnetate ($^{99m}$Tc) injection should comply with European Pharmacopoeia specifications.

Do not use a breather needle as the content is under vacuum.

Shake for about 5 minutes.

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.

**Quality control**
The radiochemical purity of the final radiolabelled preparation can be tested according to one of the following procedures:

**Methods**
Thin Layer Chromatography (TLC) or ascending paper chromatography

**Thin Layer Chromatography**

**Materials and reagents**

1. Chromatography support: two fiberglass plates A and B coated with silica gel (ITLC-SG, 2.5 × 20 cm), previously heated at 110 °C for 10 min and cooled to room temperature before use. Trace a thin line called “deposit line” 2 cm from the bottom of each support. Draw a thin line called "solvent frontline” 15 cm from the “deposit line”.

2. Mobile phases:
   - A: 1M sodium acetate solution
   - B: Methyl ethyl ketone

3. Chromatography tanks
   Two glass tanks A and B of appropriate size fitted with a lid ensuring a tight seal.

4. Miscellaneous
   Forceps, syringes, needles, appropriate counter unit.
**Procedure**

1. Introduce a sufficient volume of the corresponding mobile phase (approx. 1.5 cm deep) into tanks A and B. Allow to equilibrate for approx. 30 min.

2. By using a syringe equipped with a needle, apply a drop of the solution to be tested (approx. 1 to 5 µl) on the “deposit line” of each plate. Proceed quickly to avoid any degradation of the solution. Do not allow the spot to dry.

3. By using forceps, introduce each plate in the tank containing the corresponding mobile phase, then close the lid. Lower the support into the mobile phase by letting the “deposit line” above the surface of solvent. Allow the solvent to migrate up to the “solvent frontline” (approx. 10 min. development time).

4. Remove the plates with forceps and allow to air dry.

5. Determine the distribution of radioactivity by using an appropriate detector. Measure the radioactivity of each spot by peak integration. With mobile phase A, Rf of hydrolysed ($^{99m}$Tc) is 0, whereas Rf of (free ($^{99m}$Tc) + $^{99m}$Tc-DPD) is around 0.8 - 1.0. With mobile phase B, Rf of free ($^{99m}$Tc) is around 1.0, whereas Rf of (hydrolysed ($^{99m}$Tc) + $^{99m}$Tc-DPD) is 0.

6. Calculations

   \[
   \% \text{ free (~}^{99m}\text{Tc)} = \frac{\text{Radioactivity of the spot at Rf 1}}{\text{Total radioactivity of the plate B}} \times 100
   \]

   \[
   \% \text{ hydrolysed (~}^{99m}\text{Tc)} = \frac{\text{Radioactivity of the spot at Rf 0}}{\text{Total radioactivity of the plate A}} \times 100
   \]

   \[
   \% \text{ (~}^{99m}\text{Tc)-DPD = 100} \% - [\% \text{ free (~}^{99m}\text{Tc)} + \% \text{ hydrolysed (~}^{99m}\text{Tc)}]
   \]

7. The percentage of (~$^{99m}$Tc)-DPD must be equal to at least 95 %, the percentage of free ($^{99m}$Tc) should not exceed 2.0 % and the percentage of hydrolysed ($^{99m}$Tc) should not exceed 2.0 %.

**Ascending paper chromatography**

**Materials and reagents**

1. Chromatographic systems
   - Chromatographic system A:
     - Support A: Whatman 31ET type (2.5 × 20 cm)
     - Mobile phase A: 1M sodium chloride solution
   - Chromatographic system B:
     - Support B: Whatman 1 type (2.5 × 20 cm)
     - Mobile phase B: methyl ethyl ketone

   Trace a thin line called “deposit line” 2 cm from the bottom of each support. Draw a thin line called “solvent frontline” 10 cm from the “deposit line”.

2. Chromatography tanks
   - Two glass tanks A and B of appropriate size fitted with a lid ensuring a tight seal.
3. Miscellaneous
   Forceps, syringes, needles, appropriate counter unit

Procedure
1. Introduce a sufficient volume of the corresponding mobile phase (approx. 1.5 cm deep) into tanks A and B. Allow to equilibrate for approx. 30 min.

2. By using a syringe equipped with a needle, apply a drop of the solution to be tested (approx. 1 to 5 µl) on the "deposit line" of each support. Proceed quickly to avoid any degradation of the solution. Do not allow the spot to dry.

3. By using forceps, introduce each support in the tank containing the corresponding mobile phase, and then close the lid. Lower the support into the mobile phase by letting the "deposit line" above the surface of solvent. Allow the solvent to migrate up to the "solvent frontline" (approx. 20 min. development time).

4. Remove the supports with forceps and allow to air dry.

5. Determine the distribution of radioactivity by using an appropriate detector. Measure the radioactivity of each spot by peak integration.
   With the chromatographic system B, Rf of free ($^{99m}$Tc) is around 1.0, whereas Rf of (hydrolysed ($^{99m}$Tc) + $^{99m}$Tc-DPD) is 0 and with the chromatographic system A, Rf of hydrolysed ($^{99m}$Tc) is 0, whereas Rf of (free ($^{99m}$Tc) + $^{99m}$Tc-DPD) is around 0.7 - 1.0.

6. Calculations

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

   \[
   \text{% hydrolysed ($^{99m}$Tc)} = \frac{\text{Radioactivity of the spot at Rf 0}}{\text{Total radioactivity of the support A}} \times 100
   \]

   \[
   \text{% ($^{99m}$Tc)-DPD} = 100 \% - [\text{% free ($^{99m}$Tc)} + \text{% hydrolysed ($^{99m}$Tc)}]
   \]

7. The percentage of technetium ($^{99m}$Tc)-DPD must be equal to at least 95 %, the percentage of free ($^{99m}$Tc) should not exceed 2.0 % and the percentage of hydrolysed ($^{99m}$Tc) should not exceed 2.0 %.