SUMMARY OF PRODUCT CHARACTERISTICS
(MAG3)

1 NAME OF THE MEDICINAL PRODUCT
Technemag kit for radiopharmaceutical preparation (MAG3)

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
One vial contains S-benzoyl-mercapto-acetyl-triglycin (Betiatide), 1 mg

To be used with sodium (^{99m}Tc) pertechnetate (not included in this kit) for the preparation of the diagnostic agent: Technetium (^{99m}Tc) tiatide.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Kit for radiopharmaceutical preparation
Powder for solution for injection.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
This medicinal product is for diagnostic use only.

After reconstitution and labelling with sodium (^{99m}Tc) pertechnetate solution, the diagnostic agent technetium (^{99m}Tc) tiatide may be used for the evaluation of nephrological and urological disorders in particular for the study of morphology, perfusion, and function of the kidney and characterisation of urinary outflow.

4.2 Posology and method of administration
Adults and the elderly:
37-185 MBq (1-5 mCi), depending on the pathology to be studied and the method to be used. Studies of renal blood flow or transport through the ureters generally require a larger dose than studies of intra-renal transport, whereas renography requires smaller activities than sequential scintigraphy.

Children:
Although Technemag may be used in paediatric patients, formal studies have not been performed. Clinical experience indicates that for paediatric use the activity should be reduced. Because of the variable relationship between the size and body weight of patients it is sometimes more satisfactory to adjust activities to body surface area. A practical approach is to adopt the recommendations of the Paediatric Task Group of the European Association of Nuclear Medicine (EANM). See table below.

Activities in children. Fraction of adult activity (Paediatric Task Group EANM, 1990).		
3 kg = 0.1	22 kg = 0.50	42 kg = 0.78
4 kg = 0.14	24 kg = 0.53	44 kg = 0.80
6 kg = 0.19	26 kg = 0.56	46 kg = 0.82

Activities in children. Fraction of adult activity (Paediatric Task Group EANM, 1990).		
3 kg = 0.1	22 kg = 0.50	42 kg = 0.78
8 kg = 0.23	28 kg = 0.58	48 kg = 0.85
10 kg = 0.27	30 kg = 0.62	50 kg = 0.88
12 kg = 0.32	32 kg = 0.65	52-54 kg = 0.90
14 kg = 0.36	34 kg = 0.68	56-58 kg = 0.92
16 kg = 0.40	36 kg = 0.71	60-62 kg = 0.96
18 kg = 0.44	38 kg = 0.73	64-66 kg = 0.98
20 kg = 0.46	40 kg = 0.76	68 kg = 0.99

Reductions of the amount of radioactivity to less than 10 % of the dose for adults will generally result in technically unsatisfactory procedures. In general, the risks are likely to relate to the level of radiation, as the chemical doses are quite small (about 0.2 mg for 185 MBq).
The administration of a diuretic or an ACE inhibitor during the diagnostic procedure is sometimes used for differential diagnosis of nephrological and urological disorders. The scintigraphic investigation is usually performed immediately after administration

4.3 Contraindications

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

4.4 Special warnings and special precautions for use

The patient should be well hydrated before the start of the examination and urged to void as often as possible during the first hours after the study in order to reduce radiation.

The agent is not suited for exact monitoring of effective renal plasma flow respectively blood flow in patients with seriously impaired renal function.

Small amounts of ^{99m}Tc-labelled impurities may be present and/or are formed during the labelling process. As some of these impurities are distributed to the liver and excreted via the gall bladder they may influence the late phase (after 30 minutes) of a dynamic renal study due to the overlap of kidney and liver in the region of interest.

Radiopharmaceutical agents should only be used by qualified personnel with the appropriate government authorization for the use and manipulation of radionuclides.

Excipients:
The injection contains sodium, 3.54 mg/ml. This needs to be taken into consideration for patients on a controlled sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

Technetium (^{99m}Tc) tiatide has not been described to interfere with agents commonly prescribed to or given to patients requiring investigations with Technetium (^{99m}Tc) tiatide (e.g. antihypertensives and medicinal products used to treat or prevent organ transplant rejection).

However, the single administration of a diuretic or ACE inhibitor is sometimes used in the differential diagnosis of nephrological and urological disorders.

Administered contrast media may impair tubular renal excretion and thereby influence the technetium (^{99m}Tc) tiatide clearance.

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.

Lactation

Interruption of breast-feeding depends on the dosage. Breast-feeding can take place when the level in the milk will not result in a radiation dose to a child greater than 1 mSv.

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 in breast milk.

Above 100 MBq

If administration above 100 MBq is considered necessary, the mother should be advised to interrupt breastfeeding until measurements on the expressed milk samples indicate that the effective dose to the infant will be less than 1 mSv.

Below 100 MBq

Interruption of breastfeeding is not necessary if activities below 100 MBq are administered.

4.7 Effects on the 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

A few mild anaphylactoid reactions have been reported, characterised by urticarial rash, swelling of eyelids and coughing.

Congenital and familial/genetic disorders Not known (cannot be estimated from the available data)	Hereditary defects [1].
Nervous system disorder Not known (cannot be estimated from the available data)	Cerebral convulsion[2].
Neoplasms benign and malignant (including cysts and polyps) Not known (cannot be estimated from the available data)	Cancer induction[1].
Immune system disorders Rare to very rare (<1/1.000)	Anaphylactoid reactions such as urticarial rash, swelling of eyelids and coughing.

[1] Linked with ionising radiation.
[2] Seen in a 15 days old child. Causal relationship not established.

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.

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 nuclear medicine procedures the radiation dose delivered (Effective Dose Equivalent, EDE) is less than 20 mSv. Higher doses might be justified in some clinical circumstances

4.9 Overdose

The risk of an excessive technetium (^{99m}Tc) tiatide dose is largely theoretical and most likely to be due to excessive radiation exposure. In such circumstances the radiation to the body (kidney, bladder and gall bladder) can be reduced by forced diuresis and frequent bladder voiding.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Diagnostic radiopharmaceuticals, renal system, technetium (^{99m}Tc) compounds.

At the chemical doses envisaged technetium (^{99m}Tc) tiatide Injection has no known pharmacodynamic action.
Measuring the activity over the kidneys allows renal blood flow, intrarenal tubular transit times and excretion via the outflow tracts to be recorded separately for both kidneys.

5.2 Pharmacokinetic properties

After intravenous injection technetium (^{99m}Tc) tiatide is rapidly cleared from the blood by the kidneys.
Technetium (^{99m}Tc) tiatide has a relatively high binding to plasma proteins. In normal renal function 70 % of the administered dose has been excreted after 30 minutes and more than 95 % after 3 hours. These latter percentages are dependent on the pathology of the kidneys and the urogenital system. The mechanism of excretion is predominantly based on tubular secretion. Glomerular filtration accounts for 11 % of total clearance.

5.3 Preclinical safety data

Acute, subacute (8 days) and chronic (13 weeks) toxicity studies as well as mutagenicity studies were performed. At the studied dose levels, up to 1000 times the maximal human dose, no toxicological effects were observed. Similarly, mutagenic effects have not been observed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

- Disodium tartrate
- Stannous (II) chloride, 0.04 mg

After reconstitution of the vial contents and after labelling with the eluate of a ^{99m}Tc-generator (usually 0.9 % sodium chloride) the aqueous injection solution will in addition to sodium chloride also contain disodium tartrate and tin (II) chloride.
The vial does not contain a preservative agent.

Properties of the medicinal product after labelling:

- Clear to slightly opalescent, colourless, aqueous solution.
- pH 5.0-6.0
- Osmolality: slightly hypertonic.

6.2 Incompatibilities

Major incompatibilities are not known. However, in order not to compromise the stability of ^{99m}Tc-tiatide, preparations should not be administered together with other drugs.

6.3 Shelf life

12 month

After radiolabeling: 5 hours. Do not store above 25°C after radiolabeling. Do not refrigerate or freeze.

6.4 Special precautions for storage

Store in a refrigerator (2°C-8°C). Keep the vials in the outer carton in order to protect from light.
For storage conditions after radiolabeling of the 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

The labelled 10 ml injection vials are closed with rubber stopper and aluminum cap. One box contains six (6) vials, one Instruction Manual and one Quality Certificate.

6.6 Special precautions for disposal and other handling

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.

The contents of the vial are to be labelled with Sodium Pertechnetate (^{99m}Tc) Injection. After reconstitution with the sodium (^{99m}Tc) pertechnetate solution, the diagnostic agent technetium (^{99m}Tc) tiatide is obtained upon boiling.

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.

The formation of labelled impurities is minimal, when using an eluate with the smallest possible volume. Therefore, labelling should be done using an eluate with the highest possible radioactive concentration. Only eluates obtained from a ^{99m}Tc-generator, which has been eluted once in the preceding 24 hours, should be used. Moreover, only eluates obtained from a ^{99m}Tc-generator, which has not been in use for more than one week, have to be used.
Dilution of the preparation should be done with saline.
After reconstitution and labelling the solution may be used for one or more administrations.

7. DOSIMETRY

The following assumptions have been made in this model:

- In the normal case following intravenous administration of MAG3, the substance is rapidly distributed in the extracellular fluid and excreted entirely by the renal system according to the kidney-bladder model. Total body retention is described by a three-exponential function. The renal transit time is assumed to be 4 minutes as for Hippuran.
- When renal function is bilaterally impaired, it is assumed that the clearance rate of the substance is one tenth of that of the normal case, that the renal transit time is increased to 20 minutes, and that a fraction of 0.04 is taken up in the liver.
- As an example of acute unilateral renal blockage, it is assumed that a fraction of 0.5 of the administered radiopharmaceutical is taken up by one kidney and slowly released to the blood with a half-time of 5 days and subsequently excreted by the other kidney, which is assumed to function normally.

Normal renal function:

Absorbed doses ^{99m}Tc MAG3, ^{99m}Tc 6.02 h

	Absorbed dose per unit activity administered (mGy/MBq)				
Organ	Adult	15 years	10 years	5 years	1 year
Adrenals	3.9E-04	5.1E-04	8.2E-04	1.2E-03	2.5E-03
Bladder	1.1E-01	1.4E-01	1.7E-01	1.8E-01	3.2E-01
Bone surfaces	1.3E-03	1.6E-03	2.1E-03	2.4E-03	4.3E-03
Brain	1.0E-04	1.3E-04	2.2E-04	3.5E-04	6.1E-04
Breast	1.0E-04	1.4E-04	2.4E-04	3.9E-04	8.2E-04
Gall bladder	5.7E-04	8.7E-04	2.0E-03	1.7E-03	2.8E-03
GI-tract					
Stomach	3.9E-04	4.9E-04	9.7E-04	1.3E-03	2.5E-03
SI	2.3E-03	3.0E-03	4.2E-03	4.6E-03	7.8E-03
Colon	3.4E-03	4.3E-03	5.9E-03	6.0E-03	9.8E-03
ULI	1.7E-03	2.3E-03	3.4E-03	4.0E-03	6.7E-03)
LLI	5.7E-03	7.0E-03	9.2E-03	8.7E-03	1.4E-02)
Heart	1.8E-04	2.4E-04	3.7E-04	5.7E-04	1.2E-03
Kidneys	3.4E-03	4.2E-03	5.9E-03	8.4E-03	1.5E-02
Liver	3.1E-04	4.3E-04	7.5E-04	1.1E-03	2.1E-03
Lungs	1.5E-04	2.1E-04	3.3E-04	5.0E-04	1.0E-03
Muscles	1.4E-03	1.7E-03	2.2E-03	2.4E-03	4.1E-03
Oesophagus	1.3E-04	1.8E-04	2.8E-04	4.4E-04	8.2E-04
Ovaries	5.4E-03	6.9E-03	8.7E-03	8.7E-03	1.4E-02
Pancreas	4.0E-04	5.0E-04	9.3E-04	1.3E-03	2.5E-03
Red marrow	9.3E-04	1.2E-03	1.6E-03	1.5E-03	2.1E-03
Skin	4.6E-04	5.7E-04	8.3E-04	9.7E-04	1.8E-03
Spleen	3.6E-04	4.9E-04	7.9E-04	1.2E-03	2.3E-03
Testes	3.7E-03	5.3E-03	8.1E-03	8.7E-03	1.6E-02
Thymus	1.3E-04	1.8E-04	2.8E-04	4.4E-04	8.2E-04
Thyroid	1.3E-04	1.6E-04	2.7E-04	4.4E-04	8.2E-04
Uterus	1.2E-02	1.4E-02	1.9E-02	1.9E-02	3.1E-02
Remaining Organs	1.3E-03	1.6E-03	2.1E-03	2.2E-03	3.6E-03
Effective dose (mSv/MBq)	**7.0E-03**	**9.0E-03**	**1.2E-02**	**1.2E-02**	**2.2E-02**
The bladder wall contributes up to 80 % of the effective dose. Effective dose if bladder is emptied 1 or 0,5 hours after administration:					
1 hour 30 min.	2.5E-03 1.7E-03	3.1E-03 2.1E-03	4.5E-03 2.9E-03	6.4E-03 3.9E-03	6.4E-03 6.8E-03
For an administered activity of 185 MBq (Maximal dose) the effective dose is 1.3 mSv. The absorbed dose in the target organ (kidney) is 0.63 mGy and the typical radiation dose to the critical organ (bladder wall) is 20 mGy.					

Abnormal renal function:

Absorbed doses ^{99m}Tc MAG3, ^{99m}Tc 6.02 h

	Absorbed dose per unit activity administered (mGy/MBq)				
Organ	Adult	15 years	10 years	5 years	1 year
Adrenals	1.6E-03	2.1E-03	3.2E-03	4.8E-03	8.6E-03
Bladder	8.3E-02	1.1E-01	1.3E-01	1.3E-01	2.3E-01
Bone surfaces	2.2E-03	2.7E-03	3.8E-03	5.0E-03	9.1E-03
Brain	6.1E-04	7.7E-04	1.3E-03	2.0E-03	3.6E-03
Breast	5.4E-04	7.0E-04	1.1E-03	1.7E-03	3.2E-03
Gall bladder	1.6E-03	2.2E-03	3.8E-03	4.6E-03	6.4E-03
GI-tract					
Stomach	1.2E-03	1.5E-03	2.6E-03	3.5E-03	6.1E-03
SI	2.7E-03	3.5E-03	5.0E-03	6.0E-03	1.0E-02
Colon	3.5E-03	4.4E-03	6.1E-03	6.9E-03	1.1E-02
ULI	2.2E-03	3.0E-03	4.3E-03	5.6E-03	9.3E-03)
LLI	5.1E-03	6.3E-03	8.5E-03	8.6E-03	1.4E-02)
Heart	9.1E-04	1.2E-03	1.8E-03	2.7E-03	4.8E-03
Kidneys	1.4E-02	1.7E-02	2.4E-02	3.4E-02	5.9E-02
Liver	1.4E-03	1.8E-03	2.7E-03	3.8E-03	6.6E-03
Lungs	7.9E-04	1.1E-03	1.6E-03	2.4E-03	4.5E-03
Muscles	1.7E-03	2.1E-03	2.9E-03	3.6E-03	6.4E-03
Oesophagus	7.4E-04	9.7E-04	1.5E-03	2.3E-03	4.1E-03
Ovaries	4.9E-03	6.3E-03	8.1E-03	8.7E-03	1.4E-02
Pancreas	1.5E-03	1.9E-03	2.9E-03	4.3E-03	7.4E-03
Red marrow	1.5E-03	1.9E-03	2.6E-03	3.1E-03	5.0E-03
Skin	7.8E-04	9.6E-04	1.5E-03	2.0E-03	3.8E-03
Spleen	1.5E-03	1.9E-03	2.9E-03	4.3E-03	7.4E-03
Testes	3.4E-03	4.7E-03	7.1E-03	7.8E-03	1.4E-02
Thymus	7.4E-04	9.7E-04	1.5E-03	2.3E-03	4.1E-03
Thyroid	7.3E-04	9.5E-04	1.5E-03	2.4E-03	4.4E-03
Uterus	1.0E-02	1.2E-02	1.6E-02	1.6E-02	2.7E-02
Remaining Organs	1.7E-03	2.1E-03	2.8E-03	3.4E-03	6.0E-03
Effective dose (mSv/MBq)	**6.1E-03**	**7.8E-03**	**1.0E-02**	**1.1E-02**	**1.9E-02**
For an administered activity of 185 MBq (Maximal dose) the effective dose is 1.1 mSv. The absorbed dose in the target organ (kidney) is 2.6 mGy and the typical radiation dose to the critical organ (bladder wall) is 15 mGy.					

Acute unilateral renal function:
Absorbed doses ^{99m}Tc MAG3, ^{99m}Tc 6.02 h

	Absorbed dose per unit activity administered (mGy/MBq)				
Organ	Adult	15 years	10 years	5 years	1 year
Adrenals	1.1E-02	1.4E-02	2.2E-02	3.2E-02	5.5E-02
Bladder	5.6E-02	7.1E-02	9.1E-02	9.3E-02	1.7E-01
Bone surfaces	3.1E-03	4.0E-03	5.8E-03	8.4E-03	1.7E-02
Brain	1.1E-04	1.4E-04	2.3E-04	3.9E-04	7.5E-04
Breast	3.8E-04	5.1E-04	1.0E-03	1.6E-03	3.0E-03
Gall bladder	6.2E-03	7.3E-03	1.0E-02	1.6E-02	2.3E-02
GI-tract					
Stomach	3.9E-03	4.4E-03	7.0E-03	9.3E-03	1.2E-02
SI	4.3E-03	5.5E-03	8.5E-03	1.2E-02	1.9E-02
Colon	3.9E-03	5.0E-03	7.2E-03	9.2E-03	1.5E-03
ULI	4.0E-03	5.1E-03	7.6E-03	1.0E-02	1.6E-02)
LLI	3.8E-03	4.8E-03	6.7E-03	8.2E-03	1.3E-02)
Heart	1.3E-03	1.6E-03	2.7E-03	4.0E-03	6.1E-03
Kidneys	2.0E-01	2.4E-01	3.3E-01	4.7E-01	8.1E-01
Liver	4.4E-03	5.4E-03	8.1E-03	1.1E-02	1.7E-02
Lungs	1.1E-03	1.6E-03	2.5E-03	3.9E-03	7.2E-03
Muscles	2.2E-03	2.7E-03	3.7E-03	5.1E-03	8.9E-03
Oesophagus	3.8E-04	5.4E-04	8.5E-04	1.5E-03	2.3E-03
Ovaries	3.8E-03	5.1E-03	7.1E-03	9.2E-03	1.5E-02
Pancreas	7.4E-03	9.0E-03	1.3E-02	1.8E-02	2.9E-02
Red marrow	3.0E-03	3.6E-03	5.0E-03	6.0E-03	8.3E-03
Skin	8.2E-04	1.0E-03	1.5E-03	2.2E-03	4.2E-03
Spleen	9.8E-03	1.2E-02	1.8E-02	2.6E-02	4.0E-02
Testes	2.0E-03	2.9E-03	4.5E-03	5.0E-03	9.8E-03
Thymus	3.8E-04	5.4E-04	8.5E-04	1.5E-03	2.3E-03
Thyroid	1.7E-04	2.3E-04	4.5E-04	9.2E-04	1.6E-03
Uterus	7.2E-03	8.7E-03	1.2E-02	1.3E-02	2.2E-02
Remaining Organs	2.1E-03	2.6E-03	3.6E-03	4.7E-03	8.0E-03
Effective dose (mSv/MBq)	**1.0E-02**	**1.2E-02**	**1.7E-02**	**2.2E-02**	**3.8E-02**
For an administered activity of 185 MBq (Maximal dose) the effective dose is 1.85 mSv. The absorbed dose in the target organ (kidney) is 37 mGy and the typical radiation dose to the critical organ (bladder wall) is 10 mGy.					

8. INSTRUCTIONS FOR THE PREPARATION OF RADIOPHARMACEUTICALS

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.

Instructions for labelling

For labelling it is recommended to use an eluate with the highest possible radioactive concentration, as the formation of labelled impurities is the least when using an eluate with the smallest possible volume.

Elute a ^{99m}Tc generator in a 5 ml volume, according to the fractionated elution technique and follow the directions for use for the generator. Use 4 ml eluate. The desired amount of ^{99m}Tc, with a maximum of 1110 MBq (30 mCi). Add this volume to a vial of **Technemag**.

For this a thin needle must be used (G20 or higher) so that the puncture hole closes again. This prevents the water from entering the vial during the heating and cooling steps that follow.

Heat immediately during 15 minutes in boiling water. During heating the vial should be standing upright in order to prevent traces of metal coming off the rubber stopper, so influencing the labelling procedure unfavourably. Cool down the vial to room temperature in cold water. The preparation is ready for administration.

This ^{99m}Tc labelled preparation having a concentration of 1110 MBq per 4 ml can be used until four hours after completion of the heating step.

To obtain a more concentrated preparation, use no more than 1 ml eluate, with a maximum activity of 925 MBq (25 mCi) and dilute to 3 ml with saline solution (0.9 %). Follow the procedure as described above to complete the preparation.
This preparation is stable for one hour only. Preferably use eluates obtained by fractionated elution. Follow the pertinent directions for use of the generator.

Precaution during the labelling procedure
To indicate that during the heating and the cooling step no contamination of the contents of the vial has occurred, the user is advised to add a suitable dyestuff to the heating bath and to the cooling bath (e.g. methylene blue to make a concentration of 1 % or sodium fluorescein to make a concentration of 0.1 %). The radiolabelled product vial should be examined for contamination (taking appropriate radiological protective measures) prior to use.

Instructions for quality control
The following methods may be used:

1. HPLC method:
   The radiochemical purity of the labelled substance is examined by high performance liquid chromatography (HPLC) using a suitable detector of radioactivity, on a 25 cm RP18 column, flow rate 1.0 ml/min.

   Mobile phase A is a 19:1 mixture of phosphate solution (1000 parts 0.01 M NaH_2PO_4 and 114 parts 0.01 M Na_2HPO_4, adjusted to pH 6) and ethanol.
   Mobile phase B is a 1:9 mixture of water and methanol.
   Use a gradient elution program with the following parameters:

Time (min.):	Flow (ml/min.):	% A	% B
10	1	100	0
7	1	0	100
4	2	100	0

   The tiatide peak appears at the end of the passage of mobile phase A.
   The injection volume is 5 µl and the total count rate per channel must not exceed 30.000.

   Requirement:

	t = 0	after 4 hours
Tiatide	≥ 96.0 %	≥ 95.0 %
Total front fractions	≤ 3.0 %	≤ 3.0 %
Methanol fraction	≤ 4.0 %	≤ 4.0 %

2 Simplified rapid procedure.
   This method may be used as an alternative for the above mentioned methods. The purpose of this method is to check the labelling procedure, as performed by the user in the hospital.

The method is based on cartridges, which are widely used as sample pretreatment of aqueous solutions for chromatography. The cartridge (e.g. Sep-Pak C18, Waters) is washed with 10 ml absolute ethanol, followed by 10 ml 0.001M hydrochloric acid. Remaining residues of the solutions are removed by 5 ml of air.

The Technetium (^{99m}Tc) tiatide solution (e.g. 0.1 ml) is applied on the cartridge. Elute with 5 ml 0.001 M HCl and collect the eluate. Elute with 5 ml of a phosphate buffer (0.01 M, pH=6.0) containing 0.5 % ethanol.
Combine both eluates (together: sum of hydrophilic impurities). Further elute the cartridge with 10 ml phosphate buffer (pH=6.0) containing 7 % ethanol. This third eluate contains Technetium (^{99m}Tc) tiatide. Finally, elute the cartridge with 10 ml absolute ethanol. This final eluate contains lipophilic impurities.

Measure the radioactivity and calculate the respective percentages. Use the combined eluted radioactivity as 100 %.

Requirement:
Technetium (^{99m}Tc) tiatide: not less than 90 %.
Hydrophilic impurities: not more than 5 %.
Lipophilic impurities: not more than 5 %.

Other information/precautions
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.