1. NAME OF THE MEDICINAL PRODUCT
Senti-Scint 1.0 mg powder for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Active substance:
Human Serum Albumin millimicroparticle aggregate 1.0 mg per vial
Excipients:
Contains 15.0 mg Glucose

For full list of excipients see 6.1

3. PHARMACEUTICAL FORM
The kit contains lyophilised, sterile, pyrogen free inactive preparation, sealed in nitrogen atmosphere. After reconstitution with the prescribed quantity of Technetium-99m sodium pertechnetate solution, the solution is clear, particle free and complies with the criteria of sterile injections.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
This medicinal product is for diagnostic use only. The product is a cold radiopharmaceutical. After reconstitution with sodium 99mTc-pertechnetate solution the agent may be used for Sentinel node lymphoscintigraphy in melanoma malignum and in breast cancer.

4.2 Posology and method of administration
Administration
For the labelling of one vial of lyophilised powder, use 1-5 ml of sterile 99mTc-99mTc sterile solution, the solution is clear, particle free and complies with the criteria of sterile injections.
The administration of 99mTc-Senti-Scint is intended for adults with a mean body weight of 70 kg is recommended. The activity for children may be calculated from the recommended range of adult administration. The Paediatric Task Group of EANM recommends calculating the administered activity based on the patient’s body weight.

4.3 Contraindications
Hypersensitivity to the active substance or to the excipients. The use of human albumin colloidal particles is contraindicated in persons with a history of hypersensitivity to products containing human albumin. Adequate medication and reanimation equipment must therefore always be kept available during the investigation.

4.4 Special warnings and precautions for use
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. The subcutaneous injection must be made without pressure into loose connective tissue. Prior to injection, an aspiration test should ascertain that no blood vessel was inadvertently punctured.

4.5 Interaction with other medicinal products and other forms of interaction
Not known.

4.6 Pregnancy and lactation
Women of childbearing potential
When it is necessary to inject radiopharmaceuticals to women of childbearing potential, the potential benefits of the investigation must be weighed against the potential risks of the radiation exposure to the mother and fetus.

Adequate medication and reanimation equipment must therefore always be kept available during the investigation. It cannot be administered to pregnant or lactating mothers or patients less than 18 years of age except when the value of the desired clinical information exceeds the risk of the radiation burden incurred by the patient.

4.7 Effects on ability to drive and use machines
Effects on ability to drive and use machines have not been described.

4.8 Undesirable effects
Rare: hypersensitivity
When a protein-containing radiopharmaceutical such as 99mTc-Senti-Scint is administered to a patient, hypersensitivity reactions may develop. Adequate medication and reanimation equipment must therefore always be kept available during the investigation.

For each patient, exposure to ionising radiation must be justifiable on the basis of the 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 (EDR) is less than 20 mSv.

4.9 Overdose
In the event of an overdose of radioactivity being administered when using 99mTc-Senti-Scint, no practical measure can be recommended to satisfactorily diminish tissue exposure as the label is poorly eliminated in urine and faeces. In the experiments with the Senti-Scint preparation in rats no signs indicative of toxicity were observed.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: diagnostic radiopharmacon, does not containing the labelling isotope. ATC code: V09DB03

At the chemical concentrations and activities used for diagnostic procedures 99mTc-Senti-Scint does not appear to exert any pharmacodynamic effects.

5.2 Pharmacokinetic properties
The Senti-Scint colloidal product produced from human serum albumin consists of particles between 100-600 nm in size. After subcutaneous injection into connective tissue the 99mTc-albumin colloidal particles are filtered into lymphatic capillaries. The 99mTc-albumin colloidal particles are then transported along the lymphatic vessels to regional lymph nodes and main lymphatic vessels, and are finally trapped into the reticular cells of functionary lymph nodes. 99mTc radioactivity passes through kidneys and is eliminated in urine.

5.3 Preclinical safety data
Pathological investigations during preclinical studies did not reveal pathological lesions in the organs of the laboratory animals. Mutagenicity, teratogenicity or carcinogenicity of the product has not been reported in the relevant literature.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Stannous(II) Chloride Dihydrate, Sodium Phosphate Monobasic, Sodium Phosphate Dibasic, Glucose, Nitrogen gas

6.2 Incompatibilities
Not known.

Method of Administration
Three-five subcutaneous injections are administered near to the lesion. Volume of 0.2 - 0.5 ml and 20 - 20 MBq per injection site is used. Imaging is carried out 20 minutes after injection and repeated 1.5 hours later until the appearance of the first lymph node.
Dose calculations were made with the standard MIRD method (MIRD Pamphlet No.1, Society of Nuclear Medicine, 1976). The Effective Dose Equivalence (EDE) was determined as specified in ICRP 53 (Ann. ICRP 18 (1-4), 1988). This value varied as follows: 5.74x10^-6 mSv/MBq for women and 5.74x10^-6 mSv/MBq, 5.76x10^-6 mSv/MBq and 5.76x10^-6 mSv/MBq respectively, for pregnant women in 3, 6 or 9-months.

12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Method of Preparation
Usual precaution regarding sterility and radioprotection should be respected. Place the vial containing the lyophilised substance in a lead shield having 3 mm wall thickness.

Ingest sterile 99mTc-sodium pertechnetate solution Ph. Eur. (max. 5.5 GBq) aspirically into the vial in a volume of 1-5 ml. Before removing the syringe, withdraw an equal volume (1-5 cm^3) of the nitrogen gas to normalise the pressure in the vial. (Do not use a breecher needle.)

Dissolve the lyophilised material by gently swirling, incubate at room temperature (20-25°C) for 20 min., and then shake gently before injection.

Fill out the enclosed label and place onto the vial.

Quality Control

Materials, reagents:
1. 2.0x20 cm silica gel coated plate (Kieselgel 60 DC-Alufolien)
2. Eluent: Acetone
3. Chromatographic tank
4. Syringe, needle, scissors, tweezers, radiation detector
Test:
1. Fill eluent to the chromatographic tank (2cm deep)
2. Apply the (5-10 µl) of sample solution and 99mTc sodium pertechnetate solution as reference at a distance of 3 cm from the lower edge and from the sides of the plate. Place the plate vertically into the chromatographic tank. The spots should be above the eluent level. Close the tank lid.
3. After development dry the plate and cut into 1 cm stripes. Use tweezers during the operation.
4. Measure the activity by NK-350 automatic or other suitable radiation detector.
5. After development in acetone the labelled product remains at the start point (Rf=0.0), and the unbound 99mTcO4^- is at the solvent front (Rf=0.9-1.0).
6. After measuring the activity , calculate the percentage of total activity bound to the carrier molecule, and the percentage of unbound 99mTcO4^- and other radiochemical impurity.

Calculation of labelling efficacy:
Activity value (cpm) at Rf = 0
99mTc-SENTI-SCINT (%) = \frac{Total activity of thin layer plate (cpm)}{Total activity of thin layer plate (cpm)} x100

Calculation of radiochemical impurities:
Activity value (cpm) at Rf = 1
Radiochemical impurities (%) = \frac{Total activity of thin layer plate (cpm)}{Total activity of thin layer plate (cpm)} x100

Labelling efficacy should be not less than 90%, and the radiochemical impurities should be not more than 10%.