SUMMARY OF PRODUCT CHARACTERISTICS

Radiopharmaceutical

1 NAME OF THE MEDICINAL PRODUCT

Pertector 2.3 - 57.1 GBq radionuclide generator

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Sodium pertechnetate (^{99m}Tc) injection is produced by means of a (^{99}Mo/^{99m}Tc) generator. Technetium (^{99m}Tc) decays with the emission of gamma radiation with an energy of 140 keV and a half-life of 6.02 hours to technetium (^{99}Tc) which, in view of its long half-life of 2.13 x 10^5 years, can be regarded as quasi stable.

The radionuclide generator containing the parent isotope ^{99}Mo, adsorbed on a chromatographic column delivers sodium pertechnetate (^{99m}Tc) injection in sterile solution.

The ^{99}Mo on the column is in equilibrium with the formed daughter isotope ^{99m}Tc. The generators are supplied with the following ^{99}Mo activity amounts at activity reference time which deliver the following technetium (^{99m}Tc) amounts, assuming a 100% theoretical yield and 24 hours time from previous elution and taking into account that branching ratio of ^{99}Mo is about 87 %:

^{99m}Tc activity (Maximal theoretical eluable activity at calibration date, 12:00 CET) in GBq

2.00	4.00	5.00	6.00	7.50	8.00	10.00	12.00	13.00	15.00

^{99}Mo activity (at calibration date, 12:00 CET) in GBq

2.3	4.6	5.7	6.9	8.5	9.1	11.4	13.7	14.9	17.1

^{99m}Tc activity (Maximal theoretical eluable activity at calibration date, 12:00 CET) in GBq

17.00	18.50	20.00	23.00	25.00	30.00	35.00	40.00	50.00

^{99}Mo activity (at calibration date, 12:00 CET) in GBq

19.4	21.1	22.9	26.3	28.6	34.3	40.0	45.7	57.1

The technetium (^{99m}Tc) radioactivity available by a single elution contained in the sodium pertechnetate (^{99m}Tc) injection depends on the sodium molybdate (^{99}Mo) amount on the column. the volume of the elution solution and the time period from the previous elution.

Excipient(s) with known effect:
Each mL of sodium pertechnetate (^{99m}Tc) solution contains 3.6 mg of sodium.

For the full list of excipients. see section 6.1.

3 PHARMACEUTICAL FORM

Radionuclide generator

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

The eluate from the radionuclide generator (sodium pertechnetate (^{99m}Tc) injection) is indicated for:

- labelling of various kits for radiopharmaceutical preparation developed and approved for radiolabelling with such solution
- Thyroid scintigraphy: direct imaging and measurement of thyroid uptake to give information on the size. position. nodularity and function of the gland in case of thyroid disease.
- Salivary gland scintigraphy: diagnosis of chronic sialadenitis (e.g. Sjögren's Syndrom) as well as assessment of salivary gland function and duct patency in salivary glands disorders and monitoring of the response to therapeutic interventions (in particular radio iodine therapy).
- Location of ectopic gastric mucosa (Meckel's diverticulum).
- Lacrimal duct scintigraphy: to assess functional disorders of lacrimation and monitoring of the response to therapeutic interventions.
- Shunt scintigraphy: after injection of the sterilesodium(^{99m}Tc)pertechnetate solution into a Rickham reservoir to test the patency of ventricular shunts in hydrocephalus.

4.2 Posology and method of administration

Posology

This medicinal product is for use in designated nuclear medicine facilities only, and should only be handled by authorised personnel.

If sodium pertechnetate (^{99m}Tc) is administered intravenously, activities may vary widely according to the clinical information required and the equipment employed. The injection of activities greater than local DRLs (Diagnostic Reference Levels) should be justified for certain indications. Recommended activities are as follows:

Adults (70 kg) and elderly population

- Thyroid scintigraphy: 20-80 MBq
- Salivary gland scintigraphy: 30 to 150 MBq for static images
  up to 370 MBq for dynamic images
- Meckel's diverticulum scintigraphy: 300-400 MBq
- Lacrimal duct scintigraphy: 2-4 MBq per drop per eye
- Shunt scintigraphy: 3-4 MBq

Renal impairment
Careful consideration of the activity to be administered is required since an increased radiation exposure is possible in these patients.

Paediatric population
The use in children and adolescents has to be considered carefully, based upon clinical needs and assessing the risk/benefit ratio in this patient group.

The activity to be administered to children and adolescents must be adapted and may be calculated according to the recommendations of the European Association of Nuclear Medicine (EANM) paediatric dosage card; the activity administered to children and to adolescents may be calculated by multiplying a baseline activity (for calculation purposes) by the weight-dependent correction factor given in the table below (see Table 1).

$$A[MBq]_{Administered} = \text{Baseline Activity} \times \text{Multiple}$$

Thyroid scintigraphy:
Activity administered [MBq] = 5.6 MBq x correction factor (Table 1).

A minimal activity of 10 MBq is necessary for obtaining images of sufficient quality.

Identification/location of ectopic gastric mucosa:
Activity administered [MBq] = 10.5 MBq x correction factor (Table 1).

A minimal activity of 20 MBq is necessary in order to obtain images of sufficient quality.

Table 1:
Thyroid scintigraphy and Identification/location of ectopic gastric mucosa:

Weight-dependent correction factors in the paediatric population according to the EANM-May 2008 guidelines

Weight [kg]	Multiple	Weight [kg]	Multiple	Weight [kg]	Multiple
3	1	**22**	5.29	**42**	9.14
4	1.14	**24**	5.71	**44**	9.57
6	1.71	**26**	6.14	**46**	10.00
8	2.14	**28**	6.43	**48**	10.29

10	2.71	**30**	6.86	**50**	10.71
12	3.14	**32**	7.29	**52-54**	11.29
14	3.57	**34**	7.72	**56-58**	12.00
16	4.00	**36**	8.00	**60-62**	12.71
18	4.43	**38**	8.43	**64-66**	13.43
20	4.86	**40**	8.86	**68**	14.00

Salivary gland scintigraphy:

The Paediatric Task Group of EANM (1990) recommends that the activity to be administered to a child should be calculated from the body weight according to the table below (see Table 2) with a minimum dose of 10 MBq in order to obtain images of sufficient quality.

Table 2: *Salivary gland scintigraphy:*

Weight-dependent correction factor in the paediatric population according to EANM 1990 recommendations

Weight [kg]	Multiple	Weight [kg]	Multiple	Weight [kg]	Multiple
3	0.1	**22**	0.50	**42**	0.78
4	0.14	**24**	0.53	**44**	0.80
6	0.19	**26**	0.56	**46**	0.82
8	0.23	**28**	0.58	**48**	0.85
10	0.27	**30**	0.62	**50**	0.88
12	0.32	**32**	0.65	**52-54**	0.90
14	0.36	**34**	0.68	**56-58**	0.92
16	0.40	**36**	0.71	**60-62**	0.96
18	0.44	**38**	0.73	**64-66**	0.98
20	0.46	**40**	0.76	**68**	0.99

Lacrimal duct scintigraphy and shunt scintigraphy:

Recommended activities apply as well for adults as for children.

Method of administration

For multidose use.

For intravenous or ocular use.

For instructions on extemporary preparation of the medicinal product before administration, see section 12.

For patient preparation, see section 4.4.

In thyroid scintigraphy, salivary gland scintigraphy and identification/location of ectopic gastric mucosa, the sodium pertechnetate (^{99m}Tc) solution is administered by intravenous injection.

In lacrimal duct scintigraphy, drops are instilled in each eye (ocular use).

In shunt scintigraphy sterile sodium(^{99m}Tc)pertechnetate solution is injected into a Rickham reservoir.

Image acquisition

Thyroid scintigraphy: 20 minutes after intravenous injection.

Salivary gland scintigraphy: immediately after intravenous injection and at regular intervals for 15 minutes.
Dynamic images performed immediately after injection and at regular intervals up to 30 minutes.
The dynamic acquisition is recommended.

Identification/location of ectopic gastric mucosa: immediately after intravenous injection and at regular intervals for 30 minutes.

Lacrimal duct scintigraphy: dynamic acquisition within 2 minutes after instillation, followed by static images acquired at regular intervals within 20 minutes.

4.3 Contraindications

Hypersensitivity to the active substance or to any of the excipients listed in section 6.1.

Information on the contraindications to the use of a kit for a radiopharmaceutical for radiolabelling can be found in the summary of product characteristics and the package leaflet for the kit.

4.4 Special warnings and precautions for use

Potential for hypersensitivity or anaphylactic reactions
If hypersensitivity or anaphylactic reactions occur, the administration of the medicinal product must be discontinued immediately and intravenous treatment initiated, if necessary. To enable immediate action in emergencies, the necessary medicinal products and equipment such as endotracheal tube and ventilator must be immediately available.

Individual benefit/risk justification
For each patient, the radiation exposure must be justifiable by the likely benefit. The activity administered should in every case be as low as reasonably achievable to obtain the required diagnostic information.

Renal impairment
Careful consideration of the benefit/risk ratio in these patients is required since an increased radiation exposure is possible.

Paediatric population
For information on the use in paediatric population, see section 4.2 and 5.1.
Careful consideration of the indication is required since the effective dose per MBq is higher than in adults (see section 11).

Thyroid blocking is of special importance in the paediatric patient population except for thyroid scintigraphy.

Patient preparation
Pre-treatment of patients with thyroid-blocking medicinal products may be necessary for certain indications.
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 examination in order to reduce radiation.

To avoid false positive results or to minimise irradiation by reduction of pertechnetate[^{99m}Tc] accumulation in the thyroid and salivary glands, a thyroid blocking agent should be given prior to lacrimal duct scintigraphy or Meckel's diverticulum scintigraphy.
Conversely a thyroid blocking agent must NOT be used before thyroid, parathyroid or salivary glands scintigraphy.
Before the application of sodium pertechnetate (^{99m}Tc) solution for scintigraphy of Meckel's diverticulum the patient should be fasted for 3 to 4 hours to reduce intestinal peristalsis.

After in vivo labelling of erythrocytes using stannous ions for reduction sodium pertechnetate (^{99m}Tc) is primarily built into erythrocytes, therefore Meckel's scintigraphy should be performed before or some days after in vivo labelling of erythrocytes.

After previous nuclear medicine studies using a stannous (II)-containing kit for a radiopharmaceutical product a waiting period of at least 8 days is indicated, as otherwise it may cause an undesirable labelling of red blood cells.

After the procedure
Close contact with infants and pregnant women should be restricted for the following 12 hours.

Specific warnings
Sodium pertechnetate (^{99m}Tc) solution for injection contains 3.6 mg/mL of sodium.
Depending on the time when the injection is administered, the content of sodium given to the patient may in some cases be greater than 1 mmol (23 mg). This should be taken into account in patient on low sodium diet.

In salivary gland scintigraphy a lower specificity of the method should be expected compared to MR sialography.

When sodium pertechnetate (^{99m}Tc) solution is used for labelling of a kit, the determination of the overall sodium content must take into account the sodium derived from the eluate and the kit. Please refer to the SmPC and the package leaflet of the kit.

For precautions with respect to environmental hazard, see section 6.6.

4.5 Interaction with other medicinal products and other forms of interaction

Atropine, isoprenaline and analgesics may cause a delay of gastric emptying and thereby cause a redistribution of (^{99m}Tc) pertechnetate in abdominal imaging.

Administration of laxatives should be withheld since they irritate the gas-

trointestinal tract. Contrast-enhanced studies (e.g. barium) and upper gastro-intestinal examination should be avoided within 48 h prior to administration of pertechnetate (^{99m}Tc) for Meckel's diverticulum scintigraphy.

Many pharmacological medicinal products are known to modify the thyroid uptake.

- antithyroid medicinal products (e.g. carbimazole or other imidazole derivatives such as propylthiouracil), salicylates, steroids, sodium nitroprusside, sodium sulfobromophtalein, perchlorate should be withheld for 1 week prior thyroid scintigraphy;
- phenylbutazone and expectorants should be withheld for 2 weeks;
- natural or synthetic thyroid preparations (e.g. sodium thyroxine, sodium liothyronine, thyroid extract) should be withheld for 2-3 weeks
- amiodarone, benzodiazepines, lithium should be withheld for 4 weeks
- intravenous contrast agents should not have been administered within 1-2 months.

Stannous (II) ions and sulfonamides may increase the concentration of sodium [^{99m}Tc] pertechnetate in red blood cells, and there may be decreased accumulation in plasma and cerebral lesions. Such medicines should be discontinued at least 8 days before the procedure.

Increased uptake of (^{99m}Tc) pertechnetate in the walls of the cerebral ventricles has been reported as a result of methotrexate-induced ventriculitis in cerebral shunt scintigraphy.

Incompatibilities: Radiopharmaceutical preparations labelled with sodium pertechnetate (^{99m}Tc) may not be mixed with other medicinal products. After a nuclear medicine examination using a radiopharmaceutical kit containing stannous ions a waiting time of at least 8 days before administration of sodium pertechnetate (^{99m}Tc) is recommended. Information on interactions when using a kit for a radiopharmaceutical for radiolabelling can be found in the manufacturer's product information for the relevant kit.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential

When an administration of radiopharmaceuticals to a woman of childbearing potential is intended, it is important to determine whether or not she is pregnant. Any woman who has missed a period should be assumed to be pregnant until proven otherwise. If in doubt about her potential pregnancy (if the woman has missed a period, if the period is very irregular, etc.), alternative techniques not using ionising radiation (if there are any) should be offered to the patient.

Pregnancy

Technetium-99m (as free pertechnetate) has been shown to cross the placental barrier.
Administration of pertechnetate (^{99m}Tc) to a woman who is known to be pregnant should be justified by medical need and a positive individual benefit risk assessment for the mother and the foetus. Alternative non-irradiating diagnostic modalities should be taken into account.

Direct administration of 400 MBq sodium pertechnetate (^{99m}Tc) to a patient results in an absorbed dose to the uterus of 3.2 mGy.
Following pretreatment of patients with a blocking agent, administration of 400 MBq sodium pertechnetate (^{99m}Tc) results in an absorbed dose to the uterus of 2.4 mGy.

Breastfeeding

Before administering radiopharmaceuticals to a mother who is breastfeeding, consideration should be given to the possibility of delaying the administration of radionuclide until the mother has ceased breastfeeding and to what is the most appropriate choice of radiopharmaceuticals, bearing in mind the secretion of activity in breast milk. If the administration is considered necessary, breastfeeding should be interrupted for 12 hours post administration and the expressed feeds discarded.
Close contact with infants should be restricted during this period.

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

Summary of the safety profile
Information on adverse reactions is available from spontaneous reporting. The reported reaction types are anaphylactoid reactions, vegetative reactions, as well as different kinds of injection site reactions. Sodium pertechnetate (^{99m}Tc) from the Pertector radionuclide generator is used for radioactive labelling of a variety of compounds. These medicinal products generally have a higher potential for adverse reactions than compounds than ^{99m}Tc, and therefore the reported adverse reactions are rather related to the labelled compounds than to ^{99m}Tc. The possible types of adverse reactions following intravenous administration of a ^{99m}Tc-labelled pharmaceutical preparation will be dependent on the specific compound being used. Such information can be found in the SmPC of the kit used for radiopharmaceutical preparation.

Tabulated list of adverse reactions
The frequencies of undesirable effects are defined as follows:
Very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000) and not known (cannot be estimated from the available data).

Immune system disorders
Frequency unknown*: Anaphylactoid reactions (e.g. dyspnoea, coma, urticaria, erythema, rash, pruritus, oedema at various location e.g. face oedema)

Nervous system disorders
Frequency unknown*: Vasovagal reactions (e.g. syncope, tachycardia, bradycardia, dizziness, headache, vision blurred, flushing)

Gastrointestinal disorders
Frequency unknown*: Vomiting, nausea, diarrhoea

General disorders and administration site conditions
Frequency unknown*: Injection site reactions due to extravasation (e.g. cellulitis, pain, erythema, swelling)

* Adverse reactions derived from spontaneous reporting

Exposure to ionising radiation is linked with cancer induction and a potential for development of hereditary defects. As the effective dose is 5.2 mSv when the maximal recommended activity of 400 MBq is administered these adverse reactions are expected to occur with a low probability.

Description of selected adverse reactions

Anaphylactic reactions (e.g. dyspnoea, coma, urticaria, erythema, rash, pruritus, oedema at various locations [e.g. face oedema])
Anaphylactic reactions have been reported following intravenous injection of sodium perchtechnetate (^{99m}Tc) and include various skin or respiratory symptoms like skin irritations, oedema, or dyspnoea.

Vegetative reactions (nervous system and gastrointestinal disorders)
Single cases of severe vegetative reactions have been reported, however, most of the reported vegetative reactions include gastrointestinal reactions like nausea or vomiting. Other reports include vasovagal reactions like headache or dizziness. Vegetative reactions are rather considered to be related to the examinational setting than to technetium (^{99m}Tc), especially in anxious patients.

General disorders and administration site conditions
Other reports describe local injection site reactions. Such reactions are related to extravasation of the radioactive material during the injection, and the reported reactions rank from local swelling up to cellulitis. Depending on the administered radioactivity and the labelled compound, extended extravasation may necessitate surgical treatment.

Reporting of suspected adverse reactions
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard. By reporting side effects you can help provide more information on the safety of this medicine.

4.9 Overdose

In the event of administration of a radiation overdose with sodium pertechnetate (^{99m}Tc), the absorbed dose should be reduced where

possible by increasing the elimination of the radionuclide from the body by defaecation, forced diuresis and frequent bladder voiding.

The uptake in the thyroid, salivary glands and the gastric mucosa can be significantly reduced when sodium perchlorate is given immediately after an accidentally high dose of sodium pertechnetate (^{99m}Tc) was administered.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Diagnostic radiopharmaceuticals, various thyroid diagnostic radiopharmaceuticals, ATC code: V09FX01.

No pharmacological activity has been observed in the range of doses administered for diagnostic purposes.

Paediatric population

The European Medicines Agency has waived the obligation to submit the results of studies with the reference medicinal product containing sodium pertechnetate (^{99m}Tc) in all subsets of the paediatric population in the granted indication (see section 4.2 for information on paediatric use).

5.2 Pharmacokinetic properties

Distribution

The pertechnetate ion has similar biological distribution to iodide and perchlorate ions, concentrating temporarily in salivary glands, choroid plexus, stomach (gastric mucosa) and in the thyroid gland, from which it is eliminated, unchanged. The pertechnetate ion also tends to concentrate in areas with increased vascularisation or with abnormal vascular permeability, particularly when pre-treatment with blocking agents inhibits uptake in glandular structures. With intact blood brain barrier, sodium pertechnetate (^{99m}Tc) does not penetrate into the brain tissue.

Organ uptake

In the blood 70-80% of the intravenously injected sodium pertechnetate (^{99m}Tc) is bound to proteins, primarily in an unspecific way to albumin. The unbound fraction (20-30%) accumulates temporarily in thyroid and salivary glands, stomach and nasal mucous membranes as well as in the plexus chorioideus.

Sodium pertechnetate (^{99m}Tc) in contrast to iodine, nevertheless, is neither used for the thyroid hormone synthesis (organification), nor absorbed in the small intestine. In the thyroid the maximum accumulation, depending on functional status and iodine saturation (in euthyroidism approx. 0.3-3%, in hyperthyroidism and iodine depletion up to 25%) is reached about 20 min after injection and then decreases quickly. This also applies for the stomach mucous membrane parietal cells and the salivary glands acinar cells.

In contrast to the thyroid which releases sodium pertechnetate (^{99m}Tc) in the bloodstream the salivary glands and the stomach secrete sodium pertechnetate (^{99m}Tc) in the saliva and gastric juice, respectively. The accumulation by the salivary gland lies in the magnitude of 0.5% of the applied activity with the maximum reached after about 20 minutes. One hour after injection, the concentration in the saliva is about 10-30 fold higher than in the plasma. The excretion can be accelerated by lemon juice or by stimulation of the parasympathetic nerve system, the absorption is reduced by perchlorate.

Elimination

Half life in plasma is approximately 3 hours. Sodium pertechnetate (^{99m}Tc) is not metabolised in the organism. One fraction is eliminated very quickly renally, the rest more slowly via faeces, salivary and tear liquid. Excretion during the first 24 hours following administration is mainly urinary (approximately 25 %) with faecal excretion occurring over the next 48 hours. Approximately 50 % of the administered activity is excreted within the first 50 hours. When selective uptake of pertechnetate (^{99m}Tc) in glandular structures is inhibited by the preadministration of blocking agents, excretion follows the same pathways but there is a higher renal clearance.

The above data are not valid when sodium pertechnetate (^{99m}Tc) is used for labelling of another radiopharmaceutical.

5.3 Preclinical safety data

There is no information on acute, subacute and chronic toxicity from single or repeated dose administration. The quantity of sodium pertechnetate (^{99m}Tc) administered during clinical diagnostic procedures is very small and, apart from allergic reactions, no other adverse reactions have been reported.
This medicinal product is not intended for regular or continuous administration.
Mutagenicity studies and long-term carcinogenicity studies have not been carried out.

Reproductive toxicity

Placental transfer of ^{99m}Tc from intravenously administered sodium pertechnetate (^{99m}Tc) has been studied in mice. The pregnant uterus was found to contain as much as 60% of the injected ^{99m}Tc when administered without perchlorate pre-administration. Studies performed on pregnant mice during gestation, gestation and lactation, and lactation alone showed changes in progeny which included weight reduction, hairlessness and sterility.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

The technetium-99m is generated from sodium [^{99}Mo]molybdate adsorbed onto an aluminium oxide column. The generator column is eluted with sterile sodium chloride solution to produce the eluate, Sodium Pertechnetate (^{99m}Tc) Injection, which contains the following excipients:

Sodium chloride
Water for injections

Benzododecinium bromide (bacteriostatic solution)

Nitric acid (pH adjustment)
Sodium hydroxide (pH adjustment)

6.2 Incompatibilities

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

6.3 Shelf life

Generator: 14 days from date of calibration. The calibration date and the expiry date are stated on the label.

Sodium pertechnetate (^{99m}Tc) eluate: After elution, use within 12 hours.

Elution vials with 0.9% NaCl solution and evacuated injection vials: 12 months.

6.4 Special precautions for storage

Generator:
Do not freeze.
Do not store above 30°C.

Sodium pertechnetate (^{99m}Tc) eluate:
Do not freeze.
Do not store above 25°C

For storage conditions after elution 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

Pertector is composed of (see figure):

- Sterile glass column filled with aluminium oxide (1), on which the primary radionuclide ^{99}Mo is adsorbed. The upper end and floor of the column are sealed with a rubber stopper that is secured by a metal cap.

- Stainless steel needle set (2) that provide the connection for the generator column with the eluent injection vials and the evacuated injection vials. During transport and intervals between elutions, these needles are protected by two injection vials containing a bacteriostatic solution (0.02% aqueous benzododecinium bromide solution).
- Lead shield (3) that is 50 mm thick, in which the generator column and needles are housed.
- Sterile filters (4 and 9) for the eluate and the air that is drawn into the eluate injection vial.
- Eluate volume control (5) that can be used to set the desired eluate volume (4 to 8 ± 0.5 ml) and, thus, the desired radioactive concentration of the eluate. This is set by turning the upper sleeve according to the scale that is illustrated.

The following material is supplied with the generator:
- 16 injection vials of elution solution (0.9% NaCl solution) and 16 evacuated injection vials (receptacles for the eluate).
- Shielding canister (8) that acts as a holder for the elution injection vial.

The injection vials (sodium chloride solution and vacuum) are 10 ml glass vials with rubber stoppers and a cap.
Elution solution (0.9% NaCl solution) and evacuated injection vials (vials for the eluate) can be ordered separately as accessories.

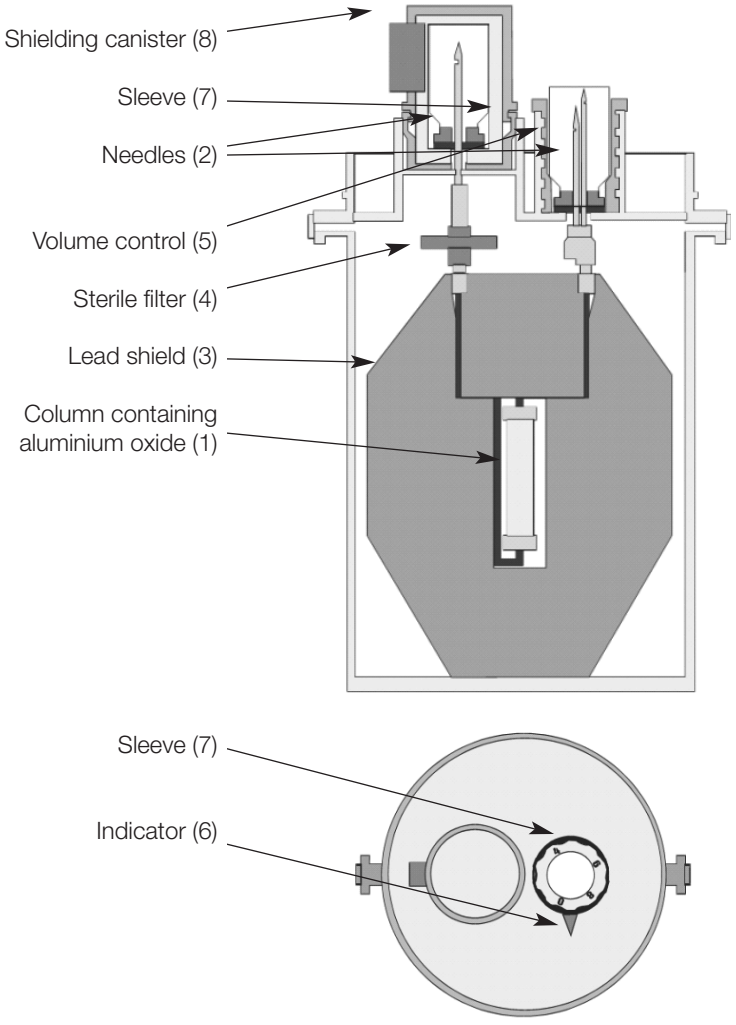

Figure: Generator construction

Pack sizes
Radionuclide generator with activities of 2.3, 4.6, 5.7, 6.9, 8.5, 9.1, 11.4, 13.7, 14.9, 17.1, 19.4, 21.1, 22.9, 26.3, 28.6, 34.3, 40.0, 45.7 or 57.1 GBq molybdenum-99 and corresponding variable technetium-99m activities at calibration time. The activity of the generator at the point of calibration is indicated on each pack.

6.6. Special precautions for disposal

General warnings
Radiopharmaceuticals should be received, used and administered only by authorised persons in designated clinical settings. Their receipt, storage, use, transfer and disposal are subject to the regulations and/or appropriate licences of the competent official organisation.
Radiopharmaceuticals should be prepared in a manner which satisfies both radiation safety and pharmaceutical quality requirements. Appropriate aseptic precautions should be taken.

For instructions on preparation of the medicinal product before administration, see sections 12.

If at any time the integrity of the generator or the vial with the eluted solution is compromised, it should not be used.

Administration procedures should be carried out in a way to minimise risk of contamination of the medicinal product and irradiation of the operators. Adequate shielding is mandatory.

The administration of radiopharmaceuticals creates risks for other persons from external radiation or contamination from spills of urine, vomitting, etc. Radiation protection precautions in accordance with national regulations must therefore be taken.
The residual activity of the generator must be estimated before disposal.

Safe handling
The weight of a generator is about 16 kg. When lifting and carrying the generator attention has to be payed to safety. To limit the risk of injuries, the regulations for safe handling currently in force, must be observed.

Disposal of generators after the expiry date
Any unused medicinal product or waste material should be disposed of in accordance with local requirements.
Full instructions describing how the return of generators to the manufacturer should be carried out are included with each generator. Users are reminded that all packaging, documentation and methods of transportation used must be in compliance with international transport regulations and all local regulations and codes of practice that relate to such matters.

7 MARKETING AUTHORISATION HOLDER

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9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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11 DOSIMETRY

Radiation exposure

Radiation exposure is dependent on premedication with blocking agents and on the extent of physical activity.
Estimates of the radiation doses absorbed by individual organs after direct application of sodium (^{99m}Tc) pertechnetate in healthy volunteers are given in the tables below. The values refer to applications without/with previously administered blocking agents. These data were taken from the publication "Radiation Dose to Patients from Radiopharmaceuticals" ICRP Publication 80 (Addendum 2 to ICRP Publication 53).

Table 3: Pertechnetate without pre-treatment with a blocking agent

Absorbed dose per unit activity administered (mGy/MBq)					
Organ	**Adults**	**15 years**	**10 years**	**5 years**	**1 year**
Adrenals	0.0037	0.0047	0.0072	0.011	0.019
Bladder	0.018	0.023	0.030	0.033	0.060
Bone surfaces	0.0054	0.0066	0.0097	0.014	0.026
Brain	0.0020	0.0025	0.0041	0.0066	0.012
Breast	0.0018	0.0023	0.0034	0.0056	0.011
Gall bladder	0.0074	0.0099	0.016	0.023	0.035
Gastrointestinal tract					
Stomach	0.026	0.034	0.048	0.078	0.16
Small intestine	0.016	0.020	0.031	0.047	0.082
Colon	0.042	0.054	0.088	0.14	0.27
Upper large intestine	0.057	0.073	0.12	0.20	0.38
Lower large intestine	0.021	0.028	0.045	0.072	0.13
Heart	0.0031	0.0040	0.0061	0.0092	0.017
Kidneys	0.0050	0.0060	0.0087	0.013	0.021
Liver	0.0038	0.0048	0.0081	0.013	0.022
Lungs	0.0026	0.0034	0.0051	0.0079	0.014
Muscles	0.0032	0.0040	0.0060	0.0090	0.016
Oesophagus	0.0024	0.0032	0.0047	0.0075	0.014
Ovaries	0.010	0.013	0.018	0.026	0.045
Pancreas	0.0056	0.0073	0.011	0.016	0.027
Red marrow	0.0036	0.0045	0.0066	0.0090	0.015
Salivary glands	0.0093	0.012	0.017	0.024	0.039
Skin	0.0018	0.0022	0.0035	0.0056	0.010
Spleen	0.0043	0.0054	0.0081	0.012	0.021
Testes	0.0028	0.0037	0.0058	0.0087	0.016
Thymus	0.0024	0.0032	0.0047	0.0075	0.014
Thyroid	0.022	0.036	0.055	0.12	0.22
Uterus	0.0081	0.010	0.015	0.022	0.037
Remaining organs	0.0035	0.0043	0.0064	0.0096	0.017
Effective dose (mSv/MBq)	**0.013**	**0.017**	**0.026**	**0.042**	**0.079**

The effective dose resulting from the intravenous administration of 400 MBq of sodium pertechnetate (^{99m}Tc) to an adult weighing 70 kg is about 5.2 mSv.

Table 4: Pertechnetate after pre-treatment with a blocking agent

Dose absorbed per activity administered (mGy/MBq)					
Organ	**Adults**	**15 years**	**10 years**	**5 years**	**1 year**
Adrenals	0.0037	0.0047	0.0072	0.011	0.019
Adrenals	0.0029	0.0037	0.0056	0.0086	0.016
Bladder	0.030	0.038	0.048	0.050	0.091
Bone surfaces	0.0044	0.0054	0.0081	0.012	0.022
Brain	0.0020	0.0026	0.0042	0.0071	0.012
Breast	0.0017	0.0022	0.0032	0.0052	0.010
Gall bladder	0.0030	0.0042	0.0070	0.010	0.013
Gastrointestinal tract					
Stomach	0.0027	0.0036	0.0059	0.0086	0.015
Small intestine	0.0035	0.0044	0.0067	0.010	0.018
Colon	0.0036	0.0048	0.0071	0.010	0.018
Upper large intestine	0.0032	0.0043	0.0064	0.010	0.017
Lower large intestine	0.0042	0.0054	0.0081	0.011	0.019
Heart	0.0027	0.0034	0.0052	0.0081	0.014
Kidneys	0.0044	0.0054	0.0077	0.011	0.019
Liver	0.0026	0.0034	0.0053	0.0082	0.015
Lungs	0.0023	0.0031	0.0046	0.0074	0.013
Muscles	0.0025	0.0031	0.0047	0.0072	0.013
Oesophagus	0.0024	0.0031	0.0046	0.0075	0.014
Ovaries	0.0043	0.0054	0.0078	0.011	0.019
Pancreas	0.0030	0.0039	0.0059	0.0093	0.016
Red marrow	0.0025	0.0032	0.0049	0.0072	0.013
Skin	0.0016	0.0020	0.0032	0.0052	0.0097
Spleen	0.0026	0.0034	0.0054	0.0083	0.015
Testes	0.0030	0.0040	0.0060	0.0087	0.016
Thymus	0.0024	0.0031	0.0046	0.0075	0.014
Thyroid	0.0024	0.0031	0.0050	0.0084	0.015
Uterus	0.0060	0.0073	0.011	0.014	0.023
Remaining organs	0.0025	0.0031	0.0048	0.0073	0.013
Effective dose (mSv/MBq)	**0.0042**	**0.0054**	**0.0077**	**0.011**	**0.019**

Following pre-treatment of patients with a blocking agent, the effective dose resulting from the administration of 800 MBq of sodium pertechnetate (^{99m}Tc) is about 3.36 mSv.

The radiation dose absorbed by the lens of the eye following administration of sodium pertechnetate (^{99m}Tc) for lacrimal duct scintigraphy is estimated to be 0.038 mGy/MBq. This results in an effective dose equivalent of less than 0.01 mSv for an administered activity of 4 MBq.

The specified radiation exposure is only applicable if all organs accumulating sodium (^{99m}Tc) pertechnetate will function normally. Hyper/hypofunction (e.g. of the thyroid, gastric mucosa or kidney) and extended processes with impairment to the blood-brain-barrier or renal elimination disorders, may result in changes to the radiation exposure, locally even in strong increases of it.

External radiation exposure

	Shielding with 50 mm lead
^{99}Mo-^{99m}Tc dose rate on the surface of generator (µSv/h x GBq)	31
^{99}Mo-^{99m}Tc dose rate at 1 m distance from the generator (µSv/h x GBq)	0.3

Measurements on the location and during work are critical and should be practised for more precise and instructive determination of overall radiation dose to the staff.

The finger dose rates on the surface of the shielding for an injection vial for elution that contains a typical eluate are:

Point of measurement	^{99m}Tc surface dose rate (µSv/h x GBq)
Lead shielding	< 0.1
Lead glass shielding	< 0.6

12 INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS

Instructions for elution

Elution of the generator must be performed in premises complying with the national regulations concerning the safety of use of radioactive products.

It is recommended that the elution of the generator and all other steps involving the sodium (^{99m}Tc) pertechnetate solution are carried out behind adequate additional shielding (e.g., 50 mm lead barrier). The syringes used for the production of the radiopharmaceutical must also be equipped with a protective lead lining (code OS-2, OS-5, OS-10 and OS-P-10).
Strict aseptic conditions must be applied during elution of the generator to preserve the sterility of the generator eluate. To guarantee optimum performance and safe handling of the generator, the sequence of steps described below must be adhered to.

Attention:

Do not rinse the needles and bottle stoppers with ethanol, ethyl ether or detergents.

Only the elution solution (0.9% sodium chloride solution) and the vacuum injection vials associated with this radionuclide generator are to be used for the elution of the radionuclide generator (see 6.5 "Nature and contents of container").

Preparation

- Open the transport container.
- Remove the eluate shielding canister that is in the upper floor of the container (at first delivery).
- Remove the upper floor of the container.
- Take out the packs containing the elution kits.

- Take out the generator and place it on the workbench.

Elution

- Unscrew the generator cap.
- Position the generator such that both vials containing bacteriostatic agent on the generator connectors are, in a parallel line to the user, and the control to adjust the eluate volume is clearly visible.
- Remove the vials containing the bacteriostatic agent from the generator needles.
- Set the eluate volume control as required.
  Warning: Make sure you do not screw the connector off the generator holder!
- Place the vial containing the eluent on the needle in the volume control holder. Pierce it such that the vial touches the base of the volume control holder.
- Place the evacuated vial in the shielding canister. Carefully press this on to the needle in the elution holder until the shielding canister is touching the floor of the elution holder.
- Wait until the elution is completed. The time required depends on the eluate volume and varies between 2, 3 and 4 minutes to obtain 4, 6 and 8 ml of eluate volume, respectively.
- Remove the shielding canister, take out the injection vial containing the eluate and determine the eluted activity using a suitable device.
- Remove the injection vial containing the elution solution. This is easy to grasp hold of if you turn the volume control to "0".
- Cover the generator needles again with the injection vials containing the bacteriostatic agent.
- Seal the generator with the cap.

Calculation of generator activity

The nominal activity of the generator is given as the activity of sodium (^{99m}Tc) pertechnetate at 12:00 CET on the day of calibration (Day 0, Table 5).

The activity that can be eluted between 08:00 and 12:00 ranges almost constantly between values of 96 to 100% of the nominal activity on the relevant day.

The highest activities are obtained when the break between elutions is not shorter than 23 to 24 hours.

Table 5: Theoretically elutable sodium (^{99m}Tc) pertechnetate activity for the relevant day

^{99}Mo generator activity [GBq]										
	2.3	**4.6**	**5.7**	**6.9**	**8.5**	**9.1**	**11.4**	**13.7**	**14.9**	**17.1**
^{99m}Tc generator activity [GBq]										
Day										
Day before day of calibration -5	7.1	14.1	17.6	21.2	26.4	28.2	35.3	42.3	45.8	52.9
-4	5.5	11.0	13.7	16.4	20.6	21.9	27.4	32.9	35.6	41.1
-3	4.3	8.5	10.7	12.8	16.0	17.0	21.3	25.6	27.7	32.0
-2	3.3	6.6	8.3	9.9	12.4	13.2	16.6	19.9	21.5	24.8
-1	2.6	5.1	6.4	7.7	9.6	10.3	12.9	15.4	16.7	19.3
Day of calibration	**2.00**	**4.00**	**5.00**	**6.00**	**7.50**	**8.00**	**10.00**	**12.00**	**13.00**	**15.00**
Day after day of calibration 1	1.55	3.11	3.89	4.66	5.83	6.22	7.77	9.33	10.10	11.66
2	1.21	2.42	3.02	3.62	4.53	4.83	6.04	7.25	7.85	9.06
3	0.94	1.88	2.35	2.82	3.52	3.76	4.69	5.63	6.10	7.04
4	0.73	1.46	1.82	2.19	2.74	2.92	3.65	4.38	4.74	5.47
5	0.57	1.13	1.42	1.70	2.13	2.27	2.84	3.40	3.69	4.25
6	0.44	0.88	1.10	1.32	1.65	1.76	2.20	2.64	2.87	3.31
7	0.34	0.69	0.86	1.03	1.28	1.37	1.71	2.06	2.23	2.57
8	0.27	0.53	0.67	0.80	1.00	1.07	1.33	1.60	1.73	2.00
9	0.21	0.41	0.52	0.62	0.78	0.83	1.03	1.24	1.35	1.55
10	0.16	0.32	0.40	0.48	0.60	0.64	0.80	0.96	1.05	1.21
11	0.13	0.25	0.31	0.38	0.47	0.50	0.63	0.75	0.81	0.94
12	0.10	0.19	0.24	0.29	0.36	0.39	0.49	0.58	0.63	0.73
13	0.08	0.15	0.19	0.23	0.28	0.30	0.38	0.45	0.49	0.57
14	0.06	0.12	0.15	0.18	0.22	0.23	0.29	0.35	0.38	0.44

^{99}Mo generator activity [GBq]									
	19.4	**21.1**	**22.9**	**26.3**	**28.6**	**34.3**	**40**	**45.7**	**57.1**
^{99m}Tc generator activity [GBq]									
Day									
Day before day of calibration -5	59.9	65.2	70.5	81.1	88.2	105.8	123.4	141.1	176.3
-4	46.6	50.7	54.8	63.0	68.5	82.2	95.9	109.6	137.0
-3	36.2	39.4	42.6	49.0	53.3	63.9	74.6	85.2	106.5
-2	28.1	30.6	33.1	38.1	41.4	49.7	57.9	66.2	82.8
-1	21.9	23.8	25.7	29.6	32.2	38.6	45.0	51.5	64.3

Day of calibration	**17.00**	**18.50**	**20.00**	**23.00**	**25.00**	**30.00**	**35.00**	**40.00**	**50.00**
Day after day of calibration 1	13.21	14.38	15.54	17.88	19.43	23.32	27.20	31.09	38.86
2	10.27	11.17	12.08	13.89	15.10	18.12	21.14	24.16	30.20
3	7.98	8.69	9.39	10.80	11.74	14.08	16.43	18.78	23.47
4	6.20	6.75	7.30	8.39	9.12	10.95	12.77	14.59	18.24
5	4.82	5.25	5.67	6.52	7.09	8.51	9.93	11.34	14.18
6	3.75	4.08	4.41	5.07	5.51	6.61	7.71	8.82	11.02
7	2.91	3.17	3.43	3.94	4.28	5.14	6.00	6.85	8.56
8	2.26	2.46	2.66	3.06	3.33	3.99	4.66	5.33	6.66
9	1.76	1.91	2.07	2.38	2.59	3.10	3.62	4.14	5.17
10	1.37	1.49	1.61	1.85	2.01	2.41	2.81	3.22	4.02
11	1.06	1.16	1.25	1.44	1.56	1.88	2.19	2.50	3.13
12	0.83	0.90	0.97	1.12	1.21	1.46	1.70	1.94	2.43
13	0.64	0.70	0.76	0.87	0.94	1.13	1.32	1.51	1.89
14	0.50	0.54	0.59	0.67	0.73	0.88	1.03	1.17	1.47

Table 6: Correction factors used to calculate the sodium (^{99m}Tc) pertechnetate activity as a function of the elution intervals

Time since last elution [h]												
0	2	4	6	8	10	12	14	16	18	20	23
Correction factor for ^{99}Mo decay												
1.0	0.979	0.960	0.940	0.919	0.900	0.881	0.863	0.845	0.828	0.811	0.785
Correction factor for increase in ^{99m}Tc												
0.0	0.21	0.39	0.51	0.62	0.71	0.79	0.85	0.89	0.93	0.96	1.0

Examples of the calculation

- A generator with a nominal activity of 15 GBq is eluted at 08:00 on Day "+2" and then again at 12:00 on the same day, which is 4 hours after the previous elution.
  The activity of the first elution is 9.06 GBq (see Table 5).
  The activity of the second elution is 9.06 x 0.960 x 0.39 = 3.39 GBq (Correction factors from Table 6).
- A generator with a nominal activity of 23 GBq is eluted at 08:00 on Day "+4" and then a second time at 14:00 on the same day, which is 6 hours after the previous elution.
  The activity of the first elution is 8.39 GBq (see Table 5).
  The activity of the second elution is 8.39 x 0.940 x 0.51 = 4.02 GBq (Correction factors from Table 6).

When sodium pertechnetate (^{99m}Tc) solution is used for kit labelling, please refer to the package leaflet of the concerned kit.

Quality control

Clarity of the solution, pH, radioactivity and the molybdenum (^{99}Mo) break-through must be checked before administration.

Properties of the eluate from the generator

The solution eluted is a clear and colourless sodium pertechnetate (^{99m}Tc) solution with following properties:

Elution yield	90 – 110%
Radiochemical purity of the eluate	> 98%
^{99}Mo content in the eluate	< 0.1%
Al^{3+} content in the eluate	< 5 µg/ml
Eluate pH	5.5 – 7.5

Quality control carried out by the user

The eluate complies with the European Pharmacopoeia specifications for sodium (^{99m}Tc) pertechnetate solutions for injection containing nuclear fission products.

Description of the analytical methods

Determination of molybdenum-99 breakthrough

Determine the radioactivity of molybdenum-99 using a calibrated meter.
Specification: ^{99}Mo content in the eluate < 0.1% (m/m)

The test for molybdenum (^{99}Mo) break-through can be performed either according to Ph. Eur. or to any other validated methods able to determine a molybdenum (^{99}Mo) content below 0.1 per cent of total radioactivity at the date and hour of administration.

Measurement of eluted activity

Measure the radioactivity using a suitable calibrated meter.

The first eluate obtained from this generator can be normally used, unless otherwise specified. The eluate can be used for kit labelling even eluted after 24 hours from the last elution, except if the use of fresh eluate is specified in the relevant kit SmPC.

Other information

Table 7: Molybdenum-99: Decay factors as a function of time from calibration point (^{99}Mo half-life, 66 hours)

GMT	Days before/after calibration point								
(h)	-10	-9	-8	-7	-6	-5	-4	-3	-2
2.00	13.8123	10.7349	8.3432	6.4844	5.0397	3.9169	3.0442	2.3660	1.8388
4.00	13.5252	10.5118	8.1698	6.3496	4.9349	3.8354	2.9809	2.3168	1.8006
6.00	13.2441	10.2933	8.0000	6.2176	4.8324	3.7557	2.9190	2.2686	1.7632
8.00	12.9688	10.0794	7.8337	6.0884	4.7319	3.6777	2.8583	2.2215	1.7265
10.00	12.6992	9.8699	7.6709	5.9618	4.6336	3.6012	2.7989	2.1753	1.6906
12.00	12.4353	9.6647	7.5114	5.8379	4.5373	3.5264	2.7407	2.1301	1.6555
14.00	12.1768	9.4638	7.3553	5.7166	4.4429	3.4531	2.6837	2.0858	1.6211
16.00	11.9237	9.2671	7.2024	5.5978	4.3506	3.3813	2.6280	2.0425	1.5874
18.00	11.6758	9.0745	7.0527	5.4814	4.2602	3.3110	2.5733	2.0000	1.5544
20.00	11.4332	8.8859	6.9061	5.3675	4.1716	3.2422	2.5198	1.9584	1.5221
22.00	11.1955	8.7012	6.7626	5.2559	4.0849	3.1748	2.4675	1.9177	1.4905
24.00	10.9628	8.5203	6.6220	5.1467	4.0000	3.1088	2.4162	1.8779	1.4595

GMT	Days before/after calibration point								
(h)	-1	0	1	2	3	4	5	6	7
2.00	1.4291	1.1107	0.8633	0.6709	0.5215	0.4053	0.3150	0.2448	0.1903
4.00	1.3994	1.0876	0.8453	0.6570	0.5106	0.3969	0.3084	0.2397	0.1863
6.00	1.3704	1.0650	0.8278	0.6433	0.5000	0.3886	0.3020	0.2347	0.1824
8.00	1.3419	1.0429	0.8105	0.6300	0.4896	0.3805	0.2957	0.2299	0.1786
10.00	1.3140	1.0212	0.7937	0.6169	0.4794	0.3726	0.2896	0.2251	0.1749
12.00	1.2867	1.0000	0.7772	0.6040	0.4695	0.3649	0.2836	0.2204	0.1713
14.00	1.2599	0.9792	0.7610	0.5915	0.4597	0.3573	0.2777	0.2158	0.1677
16.00	1.2337	0.9589	0.7452	0.5792	0.4502	0.3499	0.2719	0.2113	0.1642
18.00	1.2081	0.9389	0.7297	0.5672	0.4408	0.3426	0.2663	0.2069	0.1608
20.00	1.1830	0.9194	0.7146	0.5554	0.4316	0.3355	0.2607	0.2026	0.1575
22.00	1.1584	0.9003	0.6997	0.5438	0.4227	0.3285	0.2553	0.1984	0.1542
24.00	1.1343	0.8816	0.6852	0.5325	0.4139	0.3217	0.2500	0.1943	0.1510

GMT	Days before/after calibration point						
(h)	8	9	10	11	12	13	14
2.00	0.1479	0.1149	0.0893	0.0694	0.0540	0.0419	0.0326
4.00	0.1448	0.1125	0.0875	0.0680	0.0528	0.0411	0.0319
6.00	0.1418	0.1102	0.0856	0.0666	0.0517	0.0402	0.0313
8.00	0.1388	0.1079	0.0839	0.0652	0.0507	0.0394	0.0306
10.00	0.1360	0.1057	0.0821	0.0638	0.0496	0.0386	0.0300
12.00	0.1331	0.1035	0.0804	0.0625	0.0486	0.0378	0.0293
14.00	0.1304	0.1013	0.0787	0.0612	0.0476	0.0370	0.0287
16.00	0.1277	0.0992	0.0771	0.0599	0.0466	0.0362	0.0281
18.00	0.1250	0.0972	0.0755	0.0587	0.0456	0.0354	0.0275
20.00	0.1224	0.0951	0.0739	0.0575	0.0447	0.0347	0.0270
22.00	0.1199	0.0932	0.0724	0.0563	0.0437	0.0340	0.0264
24.00	0.1174	0.0912	0.0709	0.0551	0.0428	0.0333	0.0259

Table 8: Factors for the increase in technetium-99m at different points in time after the previous elution (^{99m}Tc half-life. 6.02 hours)

Hours	Factor	Hours	Factor	Hours	Factor	Hours	Factor
1	0.094	13	0.705	25	0.879	37	0.929
2	0.179	14	0.729	26	0.884	38	0.930
3	0.256	15	0.751	27	0.892	39	0.932
4	0.324	16	0.771	28	0.898	40	0.934
5	0.386	17	0.788	29	0.903	41	0.935
6	0.442	18	0.804	30	0.907	42	0.937
7	0.492	19	0.818	31	0.911	43	0.938
8	0.538	20	0.831	32	0.915	44	0.940
9	0.579	21	0.843	33	0.918	45	0.941
10	0.615	22	0.853	34	0.921	46	0.941
11	0.648	23	0.863	35	0.924	47	0.941
12	0.678	24	0.871	36	0.926	48	0.942