Ultra-TechneKow® FM

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Ultra-TechneKow® FM (Technetium Tc 99m Generator)	100/107

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For the Production of
Sodium Pertechnetate Tc 99m Injection

Revised 7/95

DESCRIPTION:
The Ultra-TechneKow FM Generator is prepared with fission-produced molybdenum-99 adsorbed onto alumina in a lead shielded column. This generator provides a closed system for the production of sterile metastable technetium-99m, which is produced by the decay of molybdenum-99. Sterile, non-pyrogenic isotonic solutions of Sodium Pertechnetate Tc 99m can be obtained conveniently by periodic aseptic elution of the generator. These solutions should be crystal clear.

The carrier-free solution may be used as is, or diluted to the proper concentration. Over the life of the generator, an elution will contain a technetium 99m yield of 70% to 86% in terms of the amount of molybdenum-99 on the generator column.

Each eluate of the generator should not contain more than the U.S.P. limit of 0.15 kilobecquerel molybdenum-99 per megabecquerel technetium -99m (0.15 microcurie Mo-99 per millicurie Tc-99m) per administered dose at the time of administration and an aluminum ion concentration of not more than 10 micrograms per milliliter of the generator eluate, both of which must be determined by the user before administration.

Since the eluate does not contain an antimicrobial agent, it should not be used after 12 hours from the time of generator elution.

Physical Characteristics:
Technetium-99m decays by isomeric transition with a physical half-life of 6.02 hours.[1] The principal photon that is useful for detection and imaging studies is listed in Table 1.

Table 1. Principal Radiation Emission Data

Radiation	Mean %/ Distribution	Energy (keV)
Gamma-2	89.07	140.5

External Radiation:
The specific gamma ray constant for technetium-99m is 0.78 R/hr-mCi at 1 cm. The first half-value layer is 0.01 7 cm of lead (Pb). A range of values for the relative attenuation of the radiation emitted by this radionuclide that results from interposition of various thicknesses of Pb is shown in Table 2. For example, the use of 0.25 cm thickness of Pb will attenuate the radiation emitted by a factor of about 1000.

Table 2. Radiation Attenuation by Lead Shielding

Shield Thickness (Pb) cm	Coefficient of Attenuation
0.017	0.5
0.08	10^{-1}
0.16	10^{-2}
0.25	10^{-3}
0.33	10^{-4}

Molybdenum-99 decays to technetium-99m with a molybdenum-99 half-life of 2.75 days. The physical decay characteristics of molybdenum-99 are such that only 88.6% of the decaying molybdenum-99 atoms form technetium-99m. Generator elutions may be made at any time, but the amount of technetium-99m available will depend on the interval measured from the last elution. Approximately 47% of the maximum available technetium-99m is reached after 6 hours and 95% after 23 hours. To correct for physical decay of technetium-99m, the fractions that remain at selected intervals of time are shown in Table 3.

Table 3. Physical Decay Chart; Technetium-99m, Half-Life 6.02 Hours

Hours	Fraction Remaining	Hours	Fraction Remaining
0*	1.000	7	0.447
1	0.891	8	0.398
2	0.794	9	0.355
3	0.708	10	0.316
4	0.631	11	0.282
5	0.562	12	0.251
6	0.501		

*Calibration time.

Clinical Pharmacology:
The pertechnetate ion distributes in the body similarly to the iodide ion but is not organified when trapped in the thyroid gland. Pertechnetate tends to accumulate in intracranial lesions with excessive neovascularity or an altered blood-brain barrier. It also concentrates in the thyroid gland, salivary glands, stomach and choroid plexus. After intravenous administration it remains in the circulatory system for sufficient time to permit blood pool, organ perfusion, and major vessel studies. It gradually equilibrates with the extracellular space. A fraction is promptly excreted via the kidneys.

Following the administration of Sodium Pertechnetate Tc 99m as an eye drop, the drug mixes with tears within the conjunctival space. Within seconds to minutes it leaves the conjunctival space and escapes into the inferior meatus of the nose through the nasolacrimal drainage system. During this process the pertechnetate ion passes through the canaliculi, the lacrimal sac and the nasolacrimal duct. In the event of any anatomical or functional blockage of the drainage system there will be a backflow resulting in tearing (epiphora). Thus the pertechnetate escapes the conjunctival space in the tears.

While the major part of the pertechnetate escapes within a few minutes of normal drainage and tearing, it has been documented that there is some degree of transconjunctival absorption with turnover of 1.5% per minute in normal individuals, 2. 1% per minute in patients without any sac and 2.7% per minute in patients with inflammed conjunctiva due to chronic dacryocystitis. Individual values may vary but these rates are probably representative and indicate that the maximum possible pertechnetate absorbed will remain below one thousandth of that used in other routine diagnostic procedures.

Indications and Usage:
Sodium Pertechnetate Tc 99m is used IN ADULTS as an agent for:
- Brain Imaging (including cerebral radionuclide angiography)
- Thyroid Imaging
- Salivary Gland Imaging
- Placenta Localization
- Blood Pool Imaging (including radionuclide angiography)
- Urinary Bladder Imaging (direct isotopic cystography) for the detection of vesico-ureteral reflux
- Nasolacrimal Drainage System Imaging (dacryoscintigraphy)

Sodium Pertechnetate Tc 99m is used IN CHILDREN as an agent for:
- Brain Imaging (including cerebral radionuclide angiography)
- Thyroid Imaging
- Blood Pool Imaging (including radionuclide angiography)
- Urinary Bladder Imaging (direct isotopic cystography) for the detection of vesico-ureteral reflux.

Contraindications:
None known.

Warnings:
Radiation risks associated with the use of Sodium Pertechnetate Tc 99m are greater in children than in adults and, in general, the younger the patient the greater the risk owing to greater absorbed radiation doses and longer life expectancy. These greater risks should be taken firmly into account in all benefit-risk assessments involving children.

PRECAUTIONS:
As in the use of any radioactive material, care should be taken to minimize radiation exposure to the patient consistent with proper patient management and to insure minimum radiation exposure to occupational workers.

Radiopharmaceuticals should be used only by physicians who are qualified by training and experience in the safe use and handling of radionuclides and whose experience and training have been approved by the appropriate government agency authorized to license the use of radionuclides.

After the termination of the nasolacrimal imaging procedure, blowing the nose and washing the eyes with sterile distilled water or an isotonic sodium chloride solution will further minimize the radiation dose.

Since the eluate does not contain an antimicrobial agent, it should not be used after 12 hours from time of generator elution.

Carcinogenesis, Mutagenesis,
Impairment of Fertility:
No long-term animal studies have been performed to evaluate carcinogenic or mutagenic potential or whether Sodium Pertechnetate Tc 99m may affect fertility in males or females.

Pregnancy Category C:
Animal reproductive studies have not been conducted with Sodium Pertechnetate Tc 99m. It is also not known whether Sodium Pertechnetate Tc 99m can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Sodium Pertechnetate Tc 99m should be given to pregnant women only if the expected benefits to be gained clearly outweigh the potential hazards.

Ideally, examinations using radiopharmaceutical drug products - especially those elective in nature - of women of childbearing capability should be performed during the first ten days following the onset of menses.

Nursing Mothers:
Technetium-99m is excreted in human milk during lactation, therefore, formula-feedings should be substituted for breast-feedings.

Pediatric Use:
See Indications and Usage and Dosage and Administration sections. Also see the description of additional risk under Warnings.

ADVERSE REACTIONS:
Allergic reactions including anaphylaxis have been reported infrequently following the administration of Sodium Pertechnetate Tc 99m.

DOSAGE AND ADMINISTRATION:
Sodium Pertechnetate Tc 99m is usually administered by intravenous injection, but can be given orally. When imaging the nasolacrimal drainage system, instill the Sodium Pertechnetate Tc 99m by the use of a device such as a micropipette or similar method which will ensure the accuracy of the dose.

For imaging the urinary bladder and ureters (direct isotopic cystography), the Sodium Pertechnetate Tc 99m is administered by direct instillation aseptically into the bladder via a urethral catheter, following which the catheter is flushed with approximately 200 mL of sterile saline directly into the bladder.

The dosage employed varies with each diagnostic procedure. If the oral route is elected, the patient should fast for at least six (6) hours before and two (2) hours after administration.

The suggested dose ranges employed for various diagnostic indications in the average ADULT PATIENT (70 kg) are as follows:

Vesico-ureteral imaging:	18.5 to 37 MBq (0.5 to 1 mCi)
Brain imaging:	370 to 740 MBq (10 to 20 mCi)
Thyroid gland imaging:	37 to 370 MBq (1 to 10 mCi)
Salivary gland imaging:	37 to 185 MBq (1 to 5 mCi)
Placenta localization:	37 to 111 MBq (1 to 3 mCi)
Blood pool imaging:	370 to 1110 MBq (10 to 30 mCi)
Nasolacrimal drainage system:	Maximum dose of 3.7 MBq (100 μCi)

The recommended dosages in PEDIATRIC PATIENTS are:

Vesico-ureteral imaging:	18.5 to 37 MBq (0.5 to 1 mCi)
Brain imaging:	5.18 to 10.36 MBq (140 to 280 μCi) per kg body weight
Thyroid gland imaging:	2.22 to 2.96 MBq (60 to 80 μCi) per kg body weight
Blood pool imaging:	5.18 to 10.36 MBq (140 to 280 μCi) per kg body weight

Minimum dose of 111 to 185 MBq (3 to 5 mCi) should be employed if radionuclide angiography is performed as part of the brain imaging or blood pool imaging procedures.

NOTE: Up to 1 gram of pharmaceutical grade potassium perchlorate in a suitable base or capsule may be given orally prior to administration of Sodium Pertechnetate Tc 99m for brain imaging, placenta localization and blood pool imaging. When Sodium Pertechnetate Tc 99m is used in children for brain or blood pool imaging, administration of potassium perchlorate is especially important to minimize the absorbed radiation dose to the thyroid gland.

The patient dose should be measured by a suitable radioactivity calibration system immediately prior to administration.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration whenever solution and container permit. The solution to be administered as the patient dose should be crystal clear and contain no particulate matter.

Radiation Dosimetry:
The estimated absorbed radiation doses[2] to an average ADULT patient (70 kg) from an intravenous injection of a maximum dose of 1110 megabecquerels (30 millicuries) of Sodium Pertechnetate Tc 99m distributed uniformly in the total body of subjects not pretreated with blocking agents, such as pharmaceutical grade potassium perchlorate, are shown in Table 4. For placental localization studies, when a maximum dose of 111 megabecquerels (3 millicuries) is used, it is assumed to be uniformly equilibrated between maternal and fetal tissues.

The estimated absorbed radiation doses to an ADULT patient from the nasolacrimal imaging procedure using a maximum dose of 3.7 megabecquerels (100 microcuries) of Sodium Pertechnetate Tc 99m are shown in Table 5.

Table 4. Absorbed Radiation Doses From Intravenous Injection (ADULTS)

Tissue	1110MBq (30 mCi) Dose				111MBq (3mCi) Dose	
	Resting Population		Active Population			
	mGy	rads	mGy	rads	mGy	rads
Bladder Wall	15.9	1.59	25.5	2.55		
Gastrointestinal tract:						
Stomach Wall	75.0	7.50	15.3	1.53		
Upper large Intestine Wall	20.4	2.04	36.0	3.60		
Lower large Intestine Wall	18.3	1.83	33.0	3.30		
Red Marrow	5.7	0.57	5.1	0.51		
Testes	2.7	0.27	2.7	0.27		
Ovaries	6.6	0.66	9.0	0.90		
Thyroid	39.0	3.90	39.0	3.90		
Brain	4.2	0.42	3.6	0.36		
Total Body	4.2	0.42	3.3	0.33		
Placenta					0.5	0.05
Fetus					0.5	0.05

Table 5. Absorbed Radiation Doses from Dacryoscintigraphy

Tissue	3.7 MBq (100 µCi) Dose of Sodium Pertechnetate Tc 99m	
	mGys	rads
Eye Lens: If lacrimal fluid turnover is 16%/min	0.140	.014
If lacrimal fluid turnover is	0.022	.002
If drainage system is blocked	4.020	.402
Total Body*	0.011	.001
Ovaries*	0.030	.003
Testes*	0.009	.001
Thyroid*	0.130	.013

*Assuming no blockage of draining system. MIRD Dose Estimate Report No. 8, J Nucl. Med., 17: 74-77, 1976

In PEDIATRIC patients, the maximum radiation doses when a dose of 185 megabecquerels (5 millicuries) Sodium Pertechnetate Tc 99m is administered to a neonate (3.5 kg) for brain or blood pool imaging with radionuclide angiography are shown in Table 6.

In pediatric patients, an average 30 minute exposure to 37 megabecquerels (1millicurie) of Sodium Pertechnetate Tc 99m following instillation for direct cystography, results in an estimated absorbed radiation dose of approximately 300 micrograys (30 millirads) to the bladder wall and 40 to 50 micrograys (4 to 5 millirads) to the gonads.[3]

Table 6. Absorbed Radiation Doses From Intravenous Injection (PEDIATRIC)

	37 MBq (1 mCi) Dose		185 MBq (5mCi) Dose	
Tissue	mGy	rads	mGy	rads
Thyroid (without perchlorate)	46.0	4.60	230.0	23.0
Thyroid (with perchlorate)	9.7	0.97	48.5	4.85
Large Bowel (with perchlorate)	19.0	1.90	95.5	9.55
Testes	1.0	0.10	5.1	0.51
Ovaries	2.2	0.22	11.0	1.10
Total Body	1.5	0.15	7.6	0.76

HOW SUPPLIED:

The Ultra-TechneKow FM (Technetium Tc 99m) Generators contain the following amount of molybdenum-99 at the date and time of calibration stated on the label.

Catalog No.

101 18.5 gigabecquerels (0.50 curie)

106	27.75	gigabecquerels	(0.75 curie)
102	37	gigabecquerels	(1.0 curie)
103	55.5	gigabecquerels	(1.5 curies)
104	74	gigabecquerels	(2.0 curies)
105	92.5	gigabecquerels	(2.5 curies)
107	111	gigabecquerels	(3.0 curies)

Each generator is supplied with the following components for the elution of the generator

6 — Evacuated Collecting Vials, 10 mL, Sterile, Non-pyrogenic.

6 — Sterile Luer-Lok needles with plastic covers

6 — Pressure-sensitive "Caution - Radioactive Material" collecting vial labels

6 — Pressure-sensitive radioassay data labels for lead elution shield

The sterile, non-pyrogenic solution used to elute the generator column contains 0.9% sodium chloride. The eluant does not contain an antimicrobial agent.

EVACUATED COLLECTING VIALS. Collecting vials are available on request in 5, 10, 20 and 30 milliliter sizes.

Storage:
Store generator and Sodium Pertechnetate Tc 99m solution at room temperature (15°C to 30°C).

Expiration Date:
The generator should not be used after the expiration date stated on the label.

The expiration time of the Sodium Pertechnetate-Tc 99m solution is not later than 12 hours after time of elution. If the eluate is used to reconstitute a kit, the radiolabeled kit should not be used after 12 hours from the time of generator elution or after the expiration time stated on the labeling for the prepared drug, whichever is earlier.

Directions for Use of the Ultra-TechneKow FM Generator:
NOTE 1: Immediately upon delivery, the generator should be placed within a minimum of one inch of leadshielding in such a manner so as to minimize radiation exposure to attending personnel. The Mallinckrodt Medical, Inc. Auxiliary Shield, Catalog #024, effects such protection.

NOTE 2: Wear waterproof gloves during the elution procedure and during subsequent reconstitution of kits with the eluate.

NOTE 3: Use a shielded syringe to withdraw patient dose or transfer Sodium Pertechnetate Tc 99m into mixing vials during kit reconstitution.

Eluting the generator every 24 hours will provide optimal amounts of Sodium Pertechnetate Tc 99m. However, the generator may be eluted whenever sufficient amounts of technetium Tc 99m have accumulated within the column.

For Example:

Time After First Elution (hrs.)	Approximate Yield (% of First Elution)
1	10
2	19

3	27
4	35
5	41
6	47

First Elution:

1. Remove the protective cap from the bottom of the dispenser plunger and attach a sterile Luer-Lok needle. Remove plastic needle cover.

2. Place collecting vial in the elution shield. Remove white plastic dust cover and clean rubber closure of collecting vial with antiseptic swab.

Figure 1. Ultra-TechneKow FM Generator Assembly 3/4 Side View

3. Slide elution shield into the dispensing station as far as it will go. The dispensing station automatically centers the collecting vial under the needle.

4. Depress dispenser plunger completely and rotate clockwise one-quarter turn (Figure 2). The dispenser needle at this time will have pierced the rubber closure of the evacuated collecting vial and the elution procedure will be in progress. If the plunger is left in this position, the elution will continue until completion. The elution process may be stopped at any volume desired by releasing the plunger.

   Figure 2. Plunger Operation (Top View)

5. Rotate dispenser plunger counterclockwise one-quarter turn to release it and withdraw the needle from collecting vial. Remove elution shield from dispensing station.

6. Replace dispenser needle with sterile Luer-Lok needle with plastic needle cover in place. Do not remove this cover until the next elution of the Ultra TechneKow FM Generator.

7. Determine the technetium-99m concentration and molybdenum-99 content for dispensing purposes.

   NOTE: Molybdenum-99 Breakthrough Limit

   The acceptable limit is 0.15 kilobecquerel molybdenum-99 per megabecquerel technetium-99m (0.15 microcurie Mo-99 per millicurie Tc-99m) at the time of administration.

8. Determine the aluminum ion concentration of the eluate.

   NOTE: Aluminum Ion Breakthrough Limit

   The acceptable limit is not more than 10 micrograms per milliliter of eluate.

Subsequent Elutions:

1. Remove plastic needle cover from dispenser needle and discard.

2. Repeat steps 2 through 8 above.

Vacuum Loss:
If the vacuum in the collecting vial is lost, do not attempt to re-evacuate the vial, but discard and use a new collecting vial.

NOTE: Pumping the plunger will NOT produce elution if the vacuum is lost since the plunger is merely a valve mechanism.

DISPOSAL:
Following use, the intact generator assembly should be either returned to Mallinckrodt Medical, Inc. or allowed to decay for 20 half-lives of the molybdenum Mo 99. Monitor the unshielded generator column with a low-level survey meter. If no significant radiation level above background is indicated, the column may then be disposed of through the regular refuse system.

This generator is approved for use by persons licensed by the U.S. Nuclear Regulatory Commission to use byproduct material identified in Section 35.200 or under equivalent licenses of Agreement States.

[1] Kocher, David C., "Radioactive Decay Data Tables", DOE/TIC-11026, 108 (1981).

[2] Modified from: Summary of Current Radiation Dose Estimates to Normal Humans from Tc 99m as Sodium Pertechnetate. MIRD Dose Estimate Report No. 8. J. Nucl. Med., 17 (1):74-7, 1976.

[3] Conway, J.J., et al., Direct and indirect radionuclide cystography. J. Urol. 113:689-693, May 1975.

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