1836

DEPARTMENT OF THE ARMY
FITZSIMONS ARMY MEDICAL CENTER
DENVER, COLORADO 80240

MEDEO-X

15 April 1974

SUBJECT: Application for Amendment, Additional Information, Tc-99M Minitec Generator

Materials Branch
Directorate of Licensing
U. S. Atomic Energy Commission
Washington, D. C. 20545

1. Reference is made to your letter dated 26 March 1974 pertaining to our application dated 12 March 1974. (Fission Mo-99 generator.)

2. The following information is provided as requested.

a. Item 1: Confirmation is hereby given that the provisions contained in item 1 will be met by the Nuclear Medicine Service of this installation.

b. Item 2: The Minitec generator (contained in its own shield) will be stored within an area completely surrounded by 2 inches of lead. Elution occurs within the storage area and is accomplished using the manufacturers instruction, a copy of which is attached. The eluent and collecting vials are standard vials provided by Squibb with the generator. The collecting vial is enclosed in its own vial shield. Standard syringes are used to transfer eluent from collecting vial to patient. Syringe lead shields are routinely used. The entire process including injection occurs within the Nuclear Medicine laboratory.

c. Item 3: Whole body and extremity exposure is reduced by extensive training in handling generators and the elution process by the Chief, Nuclear Medicine, the Chief, Technician and the Radiation Protection Officer, in addition to placing the generator and performing the elution behind a lead shield. Eluates are handled in either the shielded collection vial or in a shield syringe. All personnel are monitored by the U. S. Army Film Badge Service wearing either the torso badge, wrist badge or both. Dose is monitored from time to time using TLD sources to support the film badge service. Emergency spills and accident instructions are posted throughout the laboratory. Review instructions in handling decontamination problems are provided periodically by the Radiation Protection Officer. All accidents

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and spills are reported directly to the RPO and the Assistant RPO who provide direct support with instrumentation, decontamination equipment, and labor. A copy of Annex R to the FAMC Health Physics SOP is attached as inclosure 2. It pertains to Contamination Control and Decontamination Procedures.

2 Incl
as

CHARLES E. WHITE
LTC, MSC
Radiation Protection Officer

CAUTION: NEW DRUG—Limited by United States law to ~~investigational use~~ approved Feb-74 for routine use

MINITEC™
Technetium 99m
GENERATOR

Minitec (Technetium 99m) Generator provides a means of obtaining a sterile, non-pyrogenic supply of Technetium 99m (^{99m}Tc), as sodium (^{99m}Tc) pertechnetate, a versatile scanning agent that can be administered intravenously or orally. ^{99m}Tc, the short-lived daughter ($T½=6$ hours) of Molybdenum 99 (^{99}Mo, $T½=67$ hours), is obtained from the generator by periodic elution. The amount (in millicuries) of ^{99m}Tc obtained in the initial elution will depend on the original potency of the generator, while the activity obtained from subsequent elutions will depend on the time interval between elutions.

Eluting the generator every 24 hours will provide optimal amounts of ^{99m}Tc. Most laboratories will therefore find it convenient to elute the generator each day at a specific time. However, the generator may be eluted whenever sufficient amounts of ^{99m}Tc have accumulated within the column.

DESCRIPTION

The fission product Molybdenum 99 used in the generator meets or exceeds the purity requirements of the Atomic Energy Commission with respect to allowable levels of contaminants. The aluminum concentration is not more than 10 mcg. per cc. of generator eluate. The eluate meets the A.E.C. limits for ^{99}Mo contamination, that is, not more than one microcurie ^{99}Mo per millicurie of ^{99m}Tc or five microcuries per dose of ^{99m}Tc administered. Each elution from the generator should be assayed before use for ^{99m}Tc activity and for the possible presence of ^{99}Mo. Directions for both assays are provided in this monograph. Material containing more than 5 microcuries of ^{99}Mo per dose of ^{99m}Tc pertechnetate exceeds Atomic Energy Commission limits and should not be administered. The generator consists of a specially designed lead shield containing an alumina-packed column which releases ^{99m}Tc upon elution. The lead shield has access ports at the top of the column, allowing aseptic elution and storage under conditions of constant shielding.

Supplied with the generator are vials of sterile, non-pyrogenic eluent, and suitable equipment for eluting, collecting, and assaying the Technetium 99m.

WARNINGS

Due to the high precalibration activities of technetium generators, the individual user should make certain that he takes proper precautions to insure that he is within his permitted possession limits (e.g. a 300 mCi generator calibrated for noon Friday will have an activity of approximately 845 mCi at 8 A.M. on the preceding Monday). In order to evaluate radiation hazards properly in the event of accidents or spills, it is essential that personnel be aware of the actual quantity of activity involved.

Maintain proper radiation safety precautions at all times. The column containing ^{99}Mo must not be removed from the lead shield at any time. The radiation field surrounding an unshielded column is quite high. Solutions of ^{99m}Tc withdrawn from the generator should always be adequately shielded. The early elutions from the generator are highly radioactive.

IMPORTANT

Since material obtained from the generator may be intended for intravenous administration, aseptic technique must be strictly observed in all handling. Only the eluent provided should be used to elute the generator. Do not administer material eluted from the generator if there is any evidence of foreign matter.

DIRECTIONS FOR ELUTING ^{99m}Tc

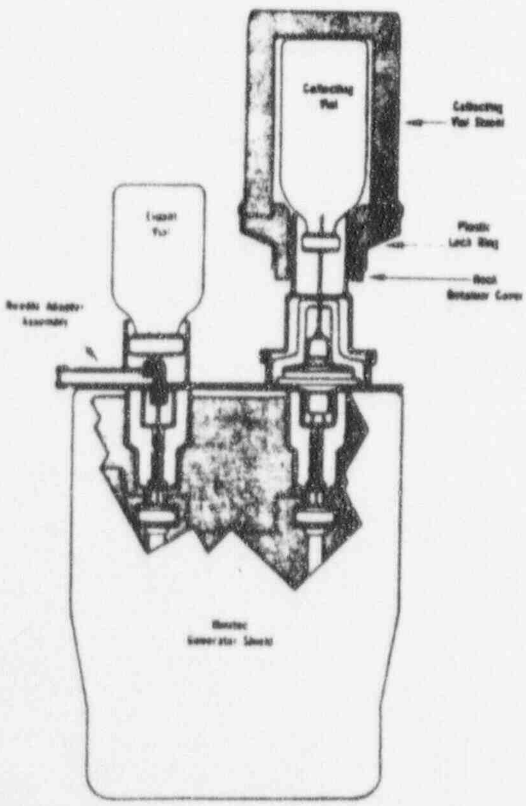
Read entire procedure before beginning elution. Carefully follow each step in the order described.

1. Attach sterile Needle Adapter Assembly to the lead generator shield:
   (a) Remove the two port plugs from top of the shield.
   (b) Using a sterile cotton-tipped applicator, swab the exposed rubber closures inside the port holes with a suitable germicide.
   (c) Position Assembly so that the guide pin on underside of Assembly will align with hole in shield; the needle ends will then align with port holes. (Assembly can only be mounted one way.)
   (d) Press Assembly into port holes so that it is firmly seated. The needles have now pierced the rubber closures. Be certain that Assembly is securely attached to the shield. Once seated, the Assembly should not be removed.
2. Attach Sterile Eluent vial:
   (Fits into the short compartment on Needle Adapter Assembly)
   (a) Swab rubber closure of eluent vial with germicide.
   (b) Remove cap from the short compartment on Assembly and firmly position eluent vial on the needles.

NOTE: THE ELUENT VIAL MUST BE ATTACHED TO THE NEEDLE ADAPTER ASSEMBLY BEFORE ATTACHING THE EVACUATED VIAL OR THE VACUUM IN THE EVACUATED VIAL WILL BE LOST.

3. Attach Sterile Evacuated Collecting Vial:
(Fits into the tall compartment on Needle Adapter Assembly)
   (a) Place collecting vial into the Collecting Vial lead shield, cover with the lead neck retainer cover and firmly secure cover to shield with the plastic lock ring.
   (b) Swab rubber closure of the lead-shielded collecting vial with germicide.
   (c) Remove cap from the tall compartment on Assembly and firmly position collecting vial on the needle. This will start the elution. Elution should be complete 3 minutes after eluent vial has emptied.
4. When elution is complete, replace collecting vial with the Minitec Needle Cover vial.
   (a) Swab rubber closure of needle cover vial with germicide.
   (b) Remove lead-shielded collecting vial (which now contains the radioactive eluate) from the needle and immediately position needle cover vial on the needle. Push needle cover vial on needle as far as it will go.
   (c) For added shielding of eluate, place lead cap over the lead-shielded collecting vial.
5. To maintain sterility of the system, after each milking, leave the empty Sterile Eluent vial (Step 2) in position and replace the collecting vial with the same needle cover vial (Step 4) until the generator is to be eluted again.

The following illustration shows generator assembled for elution.



DIRECTIONS FOR ASSAYING ^{99m}Tc ACTIVITY

The ^{99m}Tc activity of the Minitec Generator eluate may be assayed by the Whole Vial Assay Method described below. (Note: The Minitec Whole Vial Assay Kit is available upon request only.)

A ^{99m}Tc standard contained in a 5 cc. volume should be used to establish the ^{99m}Tc factor. A container having the same geometry as the collecting vial should be used to contain the 5 cc. ^{99m}Tc standard.

The Whole Vial Assay method can be performed with any scintillation detector used in conjunction with a pulse height analyzer (well-type scintillation spectrometer or an upright scintillation probe). The Whole Vial Assay components are: (A) top lid, (B) ring lid, (C) shield, (D) Cobalt 57 check source (from 5 to 15 μCi), (E) platform, and (F) lead absorbers.

1. Place the shield (C) on top of the well of a scintillation spectrometer; if the well aperture is too large for support, place the shield in the middle of the platform (E) and center over the well.
2. Set the discriminator to the 100 Kev to 200 Kev range. Record the background counting rate.
3. Insert a ^{99m}Tc standard* in the shield (C) and cover it with ring lid (B) and the top lid (A).
4. Count and record the ^{99m}Tc standard activity. (NOTE: If the count rate is too high, place lead absorbers (F) into the shield (C) until an acceptable count rate is obtained. To prevent errors, the lead absorbers should then be glued to the bottom of the shield.)
5. Replace the ^{99m}Tc standard with the ^{99m}Tc sample, cover as in step 3, and record the count rate of the ^{99m}Tc sample. (NOTE: The volume of the standard solution and the sample solution must be equal and in a container of the same geometry.)
6. Replace the shield (C) with the Cobalt 57 check source (D) and record count rate. [NOTE: Once the count rate of the Cobalt 57 check source has been determined, the continued use of the ^{99m}Tc standard is unnecessary provided the count rate of the check source does not vary more than $\pm 10\%$ from the expected count rate (after correction for radioactive decay).]
7. For subsequent assays only steps 5 and 6 need be followed.
8. Calculate the ^{99m}Tc factor as follows:

$$^{99m}\text{Tc factor} = \frac{\text{activity (mCi) of } ^{99m}\text{Tc standard}}{\text{net count rate (cpm) of } ^{99m}\text{Tc standard}}$$

Example:

activity of ^{99m}Tc standard = 10 mCi
count rate as determined in step 4 = 20,000 cpm

$$^{99m}\text{Tc factor} = \frac{10 \text{ mCi}}{20{,}000 \text{ cpm}} = 0.0005$$

9. The ^{99m}Tc factor (step 8) is used to determine the ^{99m}Tc activity in 5 cc. of eluate from the Sterile Generator provided the count rate of the Cobalt 57 check source is within $\pm$ 10% of the expected count rate. Calculate as follows:

$$^{99m}\text{Tc activity (mCi/5 cc.)} = {}^{99m}\text{Tc factor} \times \text{net count rate (cpm) of } ^{99m}\text{Tc sample}$$

*A ^{99m}Tc sample calibrated by existing methods, such as the dilution method, can be used as the initial standard.

Example:

^{99m}Tc factor = 0.0005
net count rate from unknown sample = 38,000 cpm

^{99m}Tc activity (mCi/5 cc) = 0.0005 × 38,000 = 19 mCi/5 cc

TEST FOR INSTRUMENT LINEARITY

The use of ^{99m}Tc generators has resulted in the assay of considerably larger quantities of activity (up to 1 Ci of ^{99m}Tc) than previously encountered. It would appear worthwhile, therefore, to check the accuracy of the assay methods for these larger quantities of activity. This is especially important since most instruments are calibrated with standards containing approximately 10 μCi of ^{99m}Tc while the initial eluates contain up to 900 mCi of ^{99m}Tc. It is not unlikely that spectrometers used in the whole vial assay procedure are not linear up to the count rates being encountered in initial assays, and that dose calibrators standardized on the lower scale are not accurate on the higher scales.

To check the assay procedures where yield problems are encountered with the high activity generators, the following is recommended:

1. Assay the entire ^{99m}Tc eluate on the first day of generator use by the procedure normally used. Record assay in millicuries/cc.

2. Withdraw 1 cc. of the eluate and transfer to an empty collecting vial. Add 4 cc. of water and mix thoroughly.

3. Assay the collecting vial containing the eluate-water solution. Record assay, corrected for decay, in total millicuries present in the vial.

4. If the calibration of the assay procedure is linear for the higher activities, the values obtained in Steps 1 and 3 should be identical. If the instrument is losing counts at the higher activities, the value obtained in Step 3 will be higher than that obtained in Step 1.

For example:

(a) The assay value in Step 1 is 660 mCi in 5 cc., therefore, the eluate contains 132 mCi/cc.
(b) The assay value in Step 3 is 169 mCi.
(c) Assuming that the 169 mCi value is correct, since the instrument was calibrated in this range of activity, the assay would be off (on the low side) by approximately 22%. Calculated as follows:

$$\% \text{ error} = \frac{\text{True activity} - \text{Observed activity}}{\text{True activity}} \times 100$$

$$= \frac{169\text{-}132}{169} \times 100$$

$$= 22\%$$

If an error of greater than 5% is observed in conducting the above assay check, it will be necessary in routine assays to either assay an aliquot of the eluate that can be accurately measured, or construct a curve to correct for counting losses at higher counting rates. Such a curve can be constructed by assaying various aliquots of a high activity milking—e.g. 1, 2, 3, 4, and 5 cc.—and plotting the activity assayed versus the true activity (calculated for assay of 1 cc. aliquot).

DIRECTIONS FOR ASSAYING ^{99}Mo ACTIVITY

A. Whole Vial Assay Method

1. Determination of the ^{99}Mo factor

Use the Whole Vial Assay components previously described and set the discriminator to the 0.6 Mev to 1.0 Mev range. Calculate the ^{99}Mo factor by dividing the activity (in μCi) of the Cesium 137 Standard by the net count rate (gross cpm minus background cpm) of the Cesium 137 Standard and multiplying by a factor of 4.5 to convert ^{137}Cs activity to equivalent ^{99}Mo activity. (NOTE: The Cesium 137 Standard is provided on request in a collecting vial with a total volume of 5 cc. If the Squibb Standard is not used, be certain that the substitute ^{137}Cs standard is used in a container having the same geometry as the collecting vial.)

Calculate as follows:

$$^{99}\text{Mo factor} = \frac{\text{Cesium 137 activity (total } \mu\text{Ci)} \times 4.5}{\text{net count rate of Cesium 137 Standard (cpm)}}$$

NOTE: The ^{99}Mo factor remains the same for each assay if the instrument calibration is not altered; if there is a change in calibration, a new factor must be determined.

2. For each assay:

   a. Place the lead shield on top of the well of a scintillation spectrometer; if the well aperture is too large for support, place the shield in the middle of the Whole Vial Assay platform and center over the well.
   b. Set the discriminator to the 0.6 Mev to 1.0 Mev range. Record the background activity (cpm).
   c. Insert the vial containing the ^{99m}Tc sample into the lead shield and cover with the ring and top lids.
   d. Record the net count rate (cpm) of the ^{99m}Tc sample (gross cpm minus background cpm).
   e. Calculate the ^{99}Mo activity as follows:

^{99}Mo activity = ^{99}Mo factor (from step 1) × net count rate (cpm) of ^{99m}Tc sample

Example:

net count rate of ^{99m}Tc sample
(as determined in step 2 d) = 1700 cpm
^{99}Mo factor = 0.003 μCi/cpm
^{99}Mo activity = 0.003 μCi/cpm × 1700 cpm
= 5.1 μCi

   f. Calculate the concentration of ^{99}Mo per millicurie of ^{99m}Tc sample by dividing the ^{99}Mo activity (from step 2 e) by the total ^{99m}Tc activity.

Example:

$$\frac{^{99}\text{Mo activity (in } \mu\text{Ci)}}{^{99m}\text{Tc activity (in mCi)}} = \frac{5.1}{51} = \frac{0.1 \ \mu\text{Ci Molybdenum 99}}{\text{per mCi Technetium 99m}}$$

B. Alternate Method

1. Place the collecting vial containing the total ^{99m}Tc eluate in a ¼-inch lead container and set this on the surface of a well-type scintillation detector or scintillation probe. (The lead container is provided on request with the Cesium 137 Standard mentioned below.)

2. Determine the activity in the 0.6—1.0 Mev range. Record net counts/minute.

3. Remove the vial of ^{99m}Tc from the lead container and replace it with a Cesium 137 Standard. Determine the activity in the 0.6—1.0 Mev range, maintaining constant geometry with previous count. Record net counts/minute. (The Cesium 137 Standard is provided on request in a collecting vial with a total volume of 5 cc. If the Squibb Standard is not used, be certain that the substitute ^{137}Cs standard is used in a container having the same geometry as the collecting vial.)

4. Calculate ^{99}Mo activity using the following formula:

$$^{99}\text{Mo Activity } (\mu\text{Ci/cc.}) = \frac{A \times B \times 4.5}{C}$$

Where:

A = net cpm of ^{99m}Tc sample
B = activity (in microcuries per cc.) of ^{137}Cs Standard
C = net cpm of ^{137}Cs Standard
4.5 = factor for converting ^{137}Cs activity to equivalent ^{99}Mo activity

^{99m}Tc DECAY FACTORS

The activity of ^{99m}Tc can be calculated by using the appropriate factor in the table below.

		0	5	10	15	20	25	30	35	40	45	50	55
		MINUTES											
0		1.000	990	981	972	962	953	944	935	926	917	908	899
1	H	891	882	872	865	857	849	841	833	825	817	809	801
2	O	794	786	778	771	764	756	749	742	735	728	721	714
3	U	707	700	693	687	680	674	667	661	655	648	642	636
4	R	630	624	618	612	606	600	595	589	583	577	572	566
5	S	561	556	550	545	540	535	530	524	519	514	509	504
6		500											

Example

If the known radioactivity of the ^{99m}Tc eluate sample tested is 10.072 mCi and the time elapsed after the activity was determined is 3 hours and 35 minutes, the activity of the sample is calculated as follows:

(10.072 mCi) × (0.661) = 6.666 mCi

COBALT 57 DECAY FACTORS

To determine the activity of ^{57}Co for the calculation of ^{99m}Tc activity, multiply the assay value stated on the label of the Cobalt 57 Standard by the appropriate factor in the following table:

Weeks	Factor	Weeks	Factor	Weeks	Factor	Weeks	Factor
1	0.980	14	0.776	27	0.614	40	0.486
2	0.962	15	0.762	28	0.603	41	0.477
3	0.945	16	0.748	29	0.592	42	0.469
4	0.928	17	0.735	30	0.582	43	0.461
5	0.911	18	0.722	31	0.571	44	0.452
6	0.895	19	0.709	32	0.561	45	0.444
7	0.880	20	0.696	33	0.551	46	0.436
8	0.864	21	0.684	34	0.541	47	0.429
9	0.848	22	0.672	35	0.532	48	0.421
10	0.833	23	0.660	36	0.522	49	0.414
11	0.819	24	0.648	37	0.513	50	0.406
12	0.804	25	0.636	38	0.504	51	0.399
13	0.790	26	0.625	39	0.495	52	0.392

PHYSICAL PROPERTIES

Technetium 99m has a half-life of 6 hours. The scintillation spectrum of ^{99m}Tc shows a photopeak at 0.14 Mev from its gamma emission; it does not emit a beta particle.

Molybdenum 99 has a half-life of 67 hours. Its two major photopeaks are at 0.74 Mev and 0.78 Mev, from two of its numerous gamma emissions; in addition, the isotope emits several beta particles.

The half-life of Cobalt 57 is 270 days. The scintillation spectrum of ^{57}Co shows essentially only one photopeak at 0.123 Mev from its principal gamma emission. ^{57}Co also emits an X-ray, but has no beta emission.

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