Form AEC-313
(8-64)
10 CFR 30

UNITED STATES ATOMIC ENERGY COMMISSION

APPLICATION FOR BYPRODUCT MATERIAL LICENSE

Form approved.
Budget Bureau No. 38-R0027

INSTRUCTIONS.—Complete Items 1 through 16 if this is an initial application or an application for renewal of a license. Information contained in previous applications filed with the Commission with respect to Items 8 through 15 may be incorporated by reference provided references are clear and specific. Use supplemental sheets where necessary. Item 16 must be completed on all applications. Mail two copies to: U.S. Atomic Energy Commission, Washington, D.C., 20545, Attention: Isotopes Branch, Division of Materials Licensing. Upon approval of this application, the applicant will receive an AEC Byproduct Material License. An AEC Byproduct Material License is issued in accordance with the general requirements contained in Title 10, Code of Federal Regulations, Part 30, and the Licensee is subject to Title 10, Code of Federal Regulations, Part 20.

1. (a) NAME AND STREET ADDRESS OF APPLICANT. *(Institution, firm, hospital person, etc. Include ZIP Code.)*

Department of the Army
Fitzsimons Army Medical Center and U.S.
Army Medical Research and Nutrition
Laboratory
Denver, Colorado 80240

(b) STREET ADDRESS(ES) AT WHICH BYPRODUCT MATERIAL WILL BE USED. *(If different from 1(a). Include ZIP Code.)*

Department of the Army
Fitzsimons Army Medical Center and U. S.
Army Medical Research and Nutrition
Laboratory
Denver, Colorado 80240

2. DEPARTMENT TO USE BYPRODUCT MATERIAL

Department of Radiology
Nuclear Medicine Service

3. PREVIOUS LICENSE NUMBER(S). *(If this is an application for renewal of a license, please indicate and give number.)*

Amendment to Existing License No. 05-00046-13 (30 Apr 1974)

4. INDIVIDUAL USER(S). *(Name and title of individual(s) who will use or directly supervise use of byproduct material. Give training and experience in Items 8 and 9.)*

See Application Dated
12 March 1973 (Control No. 35871)

5. RADIATION PROTECTION OFFICER. *(Name of person designated as radiation protection officer if other than individual user. Attach resume of his training and experience as in Items 8 and 9.)*

See Application dated 12 March 1973
(Control No. 35871)

6. (a) BYPRODUCT MATERIAL. *(Elements and mass number of each.)*

Tc-99m

(b) CHEMICAL AND/OR PHYSICAL FORM AND MAXIMUM NUMBER OF MILLICURIES OF EACH CHEMICAL AND/OR PHYSICAL FORM THAT YOU WILL POSSESS AT ANY ONE TIME. *(If sealed source(s), also state name of manufacturer, model number, number of sources and maximum activity per source.)*

Tc-99m - Fe - Ascorbate - DTPA, 100 mCi, prepared by use of RENOTEC. 99m Tc - Iron-Ascorbate- DTPA kit, E.R. Squibb and Sons, Inc., P.O. Box 4000, Princeton, New Jersey 08540

Tc-99m Sodium Pertechnetate obtained as eluate from E.R. Squibb and Sons, Generator Model 08871 (See para 60 of existing AEC Byproduct Material License 05-00046-13.

7. DESCRIBE PURPOSE FOR WHICH BYPRODUCT MATERIAL WILL BE USED. *(If byproduct material is for "human use," supplement A (Form AEC-313a) must be completed in lieu of this item. If byproduct material is in the form of a sealed source, include the make and model number of the storage container and/or device in which the source will be stored and/or used.)*

Human Use - Kidney Imaging
see supplement A (Form AEC - 313a)

42903

(Continued on reverse side)

TRAINING AND EXPERIENCE OF EACH INDIVIDUAL NAMED IN ITEM 4 (Use supplemental sheets if necessary)

8. TYPE OF TRAINING	WHERE TRAINED	DURATION OF TRAINING	ON THE JOB (Circle answer)	FORMAL COURSE (Circle answer)
a. Principles and practices of radiation protection	See application dated 12 March 1973 (Control No. 35871)		Yes No	Yes No
b. Radioactivity measurement standardization and monitoring techniques and instruments			Yes No	Yes No
c. Mathematics and calculations basic to the use and measurement of radioactivity			Yes No	Yes No
d. Biological effects of radiation			Yes No	Yes No

9. EXPERIENCE WITH RADIATION (Actual use of radioisotopes or equivalent experience)

ISOTOPE	MAXIMUM AMOUNT	WHERE EXPERIENCE WAS GAINED	DURATION OF EXPERIENCE	TYPE OF USE
	See application dated 12 March 1973 (Control No. 35871)			

10. RADIATION DETECTION INSTRUMENTS (Use supplemental sheets if necessary)

TYPE OF INSTRUMENTS (Include make and model number of each)	NUMBER AVAILABLE	RADIATION DETECTED	SENSITIVITY RANGE (mr/hr)	WINDOW THICKNESS (mg/cm²)	USE (Monitoring, surveying, measuring)
See application dated 12 March 1973 (Control No. 35871) and application dated 25 June 1968.					

11. METHOD, FREQUENCY, AND STANDARDS USED IN CALIBRATING INSTRUMENTS LISTED ABOVE.

See application dated 12 March 1973 (Control No. 35871) and application dated 25 June 1968.

12. FILM BADGES, DOSIMETERS, AND BIO-ASSAY PROCEDURES USED. (For film badges, specify method of calibrating and processing, or name of supplier.)

See application dated 12 March 1973 (Control No. 35871) and application dated 25 June 1968.

INFORMATION TO BE SUBMITTED ON ADDITIONAL SHEETS IN DUPLICATE

13. FACILITIES AND EQUIPMENT. Describe laboratory facilities and remote handling equipment, storage containers, shielding, fume hoods, etc. Explanatory sketch of facility may be submitted. (See application dated 12 March 1973 (Control No. 35871) and application dated 25 June 1968.)

14. RADIATION PROTECTION PROGRAM. Describe the radiation protection program including control measures. If application covers sealed sources, submit leak testing procedures where applicable, name, training, and experience of person to perform leak tests, and arrangements for performing initial radiation survey, servicing and maintenance. (See application dated 12 March 1973 (Control No. 35871) and application dated 25 June 1968.)

15. WASTE DISPOSAL. If a commercial waste disposal service is employed, specify name of company. Otherwise, submit detailed description of methods which will be used for disposing of radioactive wastes and estimates of kind, type and amount of activity involved. (See application dated 12 March 1973 (Control No. 35871) and application dated 25 June 1968.)

CERTIFICATE (This item must be completed by applicant)

16. THE APPLICANT AND ANY OFFICIAL EXECUTING THIS CERTIFICATE ON BEHALF OF THE APPLICANT NAMED IN ITEM 1, CERTIFY THAT THIS APPLICATION IS PREPARED IN CONFORMITY WITH TITLE 10, CODE OF FEDERAL REGULATIONS, PART 30, AND THAT ALL INFORMATION CONTAINED HEREIN, INCLUDING ANY SUPPLEMENTS ATTACHED HERETO, IS TRUE AND CORRECT TO THE BEST OF OUR KNOWLEDGE AND BELIEF.

Fitzsimons Army Medical Center
Denver, Colorado 80240
Applicant named (Item 1)

Date 30 Oct 73

By: H.F. COWGILL, M.D.
Colonel, MC

Title of certifying official

WARNING.—18 U. S. C., Section 1001, Act of June 25, 1948, 62 Stat. 749, makes it a criminal offense to make a willfully false statement or representation to any department or agency of the United States as to any matter within its jurisdiction.

* U.S. GOVERNMENT PRINTING OFFICE : 1966 O—333-213

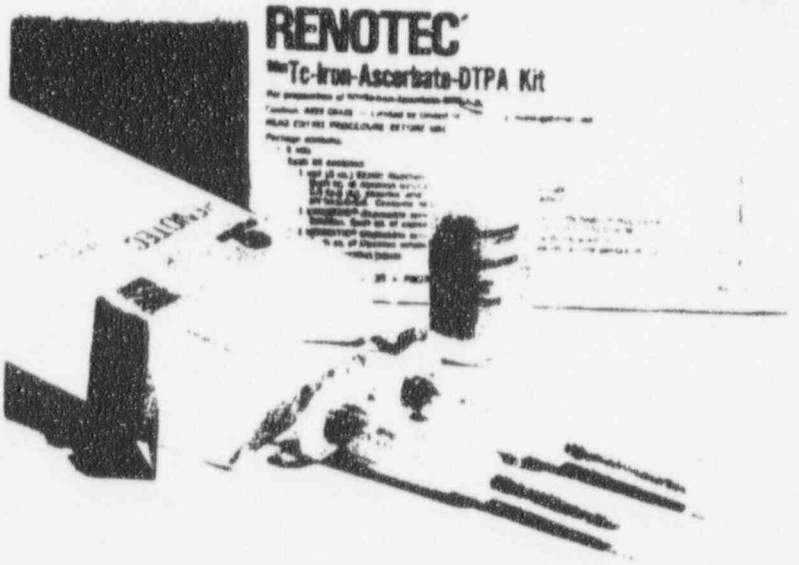
A NEW SQUIBB 'SETUP' TO COMPLEMENT YOUR WORK-UP

New
More
Efficient Packaging

- Holds 5 kits
- Saves refrigerator storing space
- Cutout window provides view of expiration date

New
Easy-to-use, Unimatic® Preassembled Syringes

- No leaking
- With rubber diaphragm seal—prevents needle-liquid contact until ready for use
- Color-coded—for easy identification
- Completely disposable



With premeasured reaction vial

SQUIBB HOSPITAL DIVISION

RENOTEC® (Technetium 99m-Iron-Ascorbate-DTPA KIT)
For Kidney Imaging

RENOTEC®
Technetium 99m-Iron-Ascorbate-DTPA Kit

Description

Renotec provides the nonradioactive reagents needed to prepare a sterile, nonpyrogenic solution of technetium 99m-iron-ascorbate-diethylenetriamine pentaacetic acid. Renotec does not require complex laboratory facilities for radiopharmaceutical synthesis of ^{99m}Tc-Fe-ascorbate-DTPA.

NOTE: The sterile ^{99m}Tc-sodium pertechnetate to be used in the reaction is obtained by elution from a Squibb technetium 99m generator.

Actions

The ^{99m}Tc-Fe-ascorbate-DTPA prepared from Renotec (Technetium 99m-Iron-Ascorbate-DTPA Kit) is not a true chelate. It has been theorized that the radioactive component which localizes in the kidneys is a hydrolized form of technetium similar to that formed by the ^{99m}Tc-Fe-ascorbic acid complex; both are alike in biological behavior.

The ^{99m}Tc-Fe-ascorbate-DTPA is not excreted purely by glomerular filtration as are the chelates ^{99m}Tc-DTPA (Ferrous) and ^{99m}Tc-DTPA (Sn), and is retained in higher amounts in the kidney. As a result, quantitative renal function studies are not possible with ^{99m}Tc-Fe-ascorbate-DTPA, but the greater concentration in the kidney makes the product ideal for renal imaging.

Indications

The ^{99m}Tc-Fe-ascorbate-DTPA, prepared from the Renotec (Technetium 99m-Iron-Ascorbate-DTPA Kit) reagents, is intended for use as a scanning agent for kidneys and as an aid in detecting kidney lesions.

Contraindications

At present, there are no known contraindications to the use of ^{99m}Tc-Fe-ascorbate-DTPA.

Warnings

The contents of the syringes provided in the kit are intended *only* for use in the preparation of ^{99m}Tc-Fe-ascorbate-DTPA *and are NOT to be directly injected into a patient.*

This radiopharmaceutical should not be administered to patients who are pregnant, or during lactation, unless the benefits to be gained outweigh the potential hazards.

Ideally, examinations using radiopharmaceuticals, especially those elective in nature, of a woman of childbearing capability, should be performed during the first few (approximately 10) days following the onset of menses.

Since ^{99m}Tc is excreted in human milk, formula-feedings should be substituted for breast-feeding if the agent must be administered to the mother during lactation.

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

Note: Renotec (Technetium 99m-Iron-Ascorbate-DTPA Kit) is not radioactive. However, after ^{99m}Tc is added, adequate shielding of the resulting preparation should be maintained.

Precautions

To assure adequate urinary flow, the patient should be sufficiently hydrated. To minimize radiation dose to the bladder, the patient should be encouraged to void when the examination is completed and as often thereafter as possible for the next 4-6 hours.

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

NOTE: Renotec (Technetium 99m-Iron-Ascorbate-DTPA Kit) was designed for use with the sterile ^{99m}Tc sodium pertechnetate eluate obtained from a Squibb technetium 99m generator; it is recommended that only a Squibb technetium 99m generator be used as the source of sodium pertechnetate.

Adverse Reactions

At present, adverse reactions have not been reported following the administration of ^{99m}Tc-Fe-ascorbate- DTPA.

Dosage and Administration

The ^{99m}Tc-Fe-ascorbate-DTPA is administered intravenously. The suggested adult dose range for renal scanning is 3 to 5 mCi.

The patient dose should be measured by a suitable radioactivity calibration system immediately prior to administration (suitable dose calibrators are available from Squibb).

Physical Characteristics of ^{99m}Tc

Table I
Transition Data
(Sodium Pertechnetate ^{99m}Tc)

Mode	% Disintegration	Transition Energy (Mev)
Gamma-1	98.6	0.0022
Gamma-2	98.6	0.1405
Gamma-3	1.4	0.1427

Specific gamma dose rate constant (Γ) = 0.72 R/mCi—hr. at 1 cm.
Local energy deposition (E_β) = 0.014 Mev/disintegration.

Radiation Dosimetry

Method of Calculation: Absorbed dose estimates, J. Nucl. Med., Suppl. 2, Pamphlet No. 4 (March 1969)

Maximum Dose: 5 mCi, intravenously injected. The effective half-time is taken to be equal to the physical half-life of 6.0 hours. The doses to the gonads are considered to be proportional to the whole-body dose, with a backscatter factor of 1.2 for the female gonads.

Table II
Renotec (Technetium 99m-Iron-Ascorbate-DTPA Kit)
Radiation Doses of ^{99m}Tc for 5 mCi/70 kg Man

Organ	Whole-body	Kidneys	Bladder	Gonads	
				Male	Female
Dose (rads)	0.06	0.21	2.8	0.06	0.10

To correct for radioactive decay, multiply the assay value stated on the label by the fraction remaining at the time of administration. The fraction remaining at selected time intervals before and after the calibration day can be found in Table III.

Table III
Decay Chart Technetium 99m
Half-life 6.0 hr.

Hours	Fraction Remaining	Hours	Fraction Remaining
−5	1.779	5	.562
−4	1.587	6	.500
−3	1.414	7	.446
−2	1.260	8	.397
−1	1.122	9	.354
0	1.000	10	.315
1	.891	11	.281
2	.794	12	.250
3	.707	18	.125
4	.630	24	.063

Preparation of ^{99m}Tc-Fe-Ascorbate-DTPA

Important: Renotec (Technetium 99m-Iron-Ascorbate-DTPA-Kit) should be used with the sterile ^{99m}Tc-sodium pertechnetate eluate obtained from a Squibb technetium 99m generator. See the instruction sheet provided with the generator for complete directions on eluting and assaying ^{99m}Tc. Do not use the eluate if there is any evidence of foreign matter. NOTE: During preparation of ^{99m}Tc-Fe-ascorbate-DTPA the solution will undergo color changes ranging from light brown to yellow.

Procedure: 1. Swab the rubber closure of the Sterile Reaction Solution vial with germicide. 2. Aseptically inject the proper volume (1 to 5 cc.) of sterile ^{99m}Tc eluate into the Sterile Reaction Solution vial. The volume is determined by the dosage required (the number of mCi) and the activity of the eluate at the time of preparation of the complex (see also Step 6). Relieve the excess pressure in the vial (created by the injection of the eluate) by withdrawing a volume of air approximately equal to the volume of eluate injected. Shake the vial gently to mix the contents. 3. Assemble Syringe 1, containing sterile 0.07N sodium hydroxide solution, and aseptically inject the entire contents into the Sterile Reaction Solution vial. Relieve the excess pressure by withdrawing approximately 2 cc. of air. Shake the vial gently to mix the contents. 4. Assemble Syringe 2, containing sterile DTPA solution, and aseptically inject the entire contents into the Sterile Reaction Solution vial. Relieve the excess pressure by withdrawing approximately 2 cc. of air. Shake the vial gently to mix the contents. 5. Affix the accompanying pressure-sensitive label to the Sterile Reaction Solution vial. Maintain adequate shielding for the radioactive ^{99m}Tc-Fe-ascorbate-DTPA. 6. The radioactivity concentration of the final ^{99m}Tc-Fe-ascorbate-DTPA may be calculated by the following formula: $C = A \div (6 + V)$, where C = radioactivity concentration of ^{99m}Tc-Fe-ascorbate-DTPA (mCi/cc.), A = ^{99m}Tc activity added to Sterile Reaction Solution vial (cc.), and V = volume of ^{99m}Tc eluate added to Sterile Reaction Solution vial (cc.). Withdrawals from the Sterile Reaction Solution vial should be made with a 22-26 gauge needle.

How Supplied

Renotec is available in cartons containing 5 Kits. Each Kit contains:

- 1 vial (2 cc.) of Sterile Reaction Solution. Each cc. of aqueous solution provides 5 mg. ferric chloride, 2.5 to 5 mg. ascorbic acid, and sodium hydroxide to adjust pH to 2.0-4.0. Contains no preservative.
- 1 Unimatic® disposable syringe (2 cc.) Syringe 1—Sterile 0.07N Sodium Hydroxide Solution. Each cc. of aqueous solution provides 2.8 mg. sodium hydroxide.
- 1 Unimatic® disposable syringe (2 cc.) Syringe 2—Sterile DTPA Solution. Each cc. of aqueous solution provides 2.5 mg. diethylenetriamine pentaacetic acid.
- An adequate supply of pressure-sensitive labels.

SQUIBB HOSPITAL DIVISION
E. R. Squibb & Sons, Inc.
P.O. Box 4000
Princeton, N.J. 08540

42903

AEC-272
(10-64)

U.S. ATOMIC ENERGY COMMISSION
MEDICAL ADVISORY COMMITTEE

APPRAISAL

1. Applicant: Department of the Army Address: City: Denver State: Colorado	2. Control No.: 39841 3. Department:
4. Name and title of trained individual Dr. John E. Canham	5. Type Program: ☐ Private practice ☐ Private practice in hospital ☐ Institutional
6. Review ☐ First ☐ Second	7. Previous application control No (s)

8. Remark on checked items

☐ A. All radioisotopes and uses stated in application

☐ B. Use of _____ for _____

☐ C. Training and experience of user

☐ D. Dosage(s) indicated

☐ E. Clinical techniques and procedures outlined

☐ F. Type patient used (i.e., terminal, infants, normal)

☐ G. Other

FOR YOUR INFORMATION

9. Action of Subcommittee on Human Applications

☐ Approve ☐ Disapprove

Remarks

Thank you.

October 1, 1973
(Date of appraisal)

Signature: John E Christian
(Member of subcommittee)
John E. Christian, Ph.D.