Form AEC-313
(5-58)

ATOMIC ENERGY COMMISSION

APPLICATION FOR BYPRODUCT MATERIAL LICENSE

Form approved.
Budget Bureau No. 38-R027.4

INSTRUCTIONS.–Complete Items 1 through 16 if this is an initial application. If application is for renewal of a license, complete only Items 1 through 7 and indicate new information or changes in the program as requested in Items 8 through 15. Use supplemental sheets where necessary. Item 16 must be completed on all applications. Mail three copies to: U. S. Atomic Energy Commission, Washington 25, D. C. Attention: Isotopes Branch, Division of Licensing and Regulation. 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.)*

Department of the Army
Fitzsimons General Hospital and US
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).)*

FITZSIMONS GENERAL HOSPITAL
DENVER, COLORADO 80240

2. DEPARTMENT TO USE BYPRODUCT MATERIAL

Radioisotope Section, Radiology Service

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

Present License #05-00046-13

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.)*

As specified by Fitzsimons General
Hospital Radioisotope Committee

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.)*

As specified by Fitzsimons General
Hospital Radioisotope Committee

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

Cr^{51}

(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.)*

Na_2CrO_4 6 mc.

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.)*

See Form AEC 313a.

(Continued on reverse side)

Form AEC-313 (5-58) Page Two

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	N/A		Yes No	Yes No
b. Radioactivity measurement standardization and monitoring techniques and instruments	N/A		Yes No	Yes No
c. Mathematics and calculations basic to the use and measurement of radioactivity	N/A		Yes No	Yes No
d. Biological effects of radiation	N/A		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
		N/A		

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 License #05-00046-13					

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

See License #05-00046-13

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

INFORMATION TO BE SUBMITTED ON ADDITIONAL SHEETS

13. FACILITIES AND EQUIPMENT. Describe laboratory facilities and remote handling equipment, storage containers, shielding, fume hoods, etc. Explanatory sketch of facility is attached. *(Circle answer)* Yes No See License #05-00046-13

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, maintenance and repair of the source.

See License #05-00046-13

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 the type and amount of activity involved. See License #05-00046-13

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.

Applicant named in item 1: Dept. of the Army, FGH and US Army Medical and Research & Nutrition Lab. Denver, Colorado 80240

Date 12 October 1967

By: Edwin L. Overholt, Col, MC

Chairman, Radioisotope Committee

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 : 1961 O—615965

Form AEC-313 a (10-61) PAGE 1

UNITED STATES ATOMIC ENERGY COMMISSION

APPLIC..ION FOR BYPRODUCT MATERIAL LIC..SE

SUPPLEMENT A—HUMAN USE

Form approved. Budget Bureau No. 38-R080.1

If byproduct material is for "human use" (internal administration of byproduct material, or the radiation therefrom to human beings), complete this supplement and attach to the application for byproduct material license.

1. (a) USING PHYSICIAN'S NAME

Department of the Army
Fitzsimons General Hospital
USA Med.Research & NutritionLab.

(b) NAME AND ADDRESS OF APPLICANT (If different from 1(a))

FITZSIMONS GENERAL HOSPITAL
DENVER, COLORADO 80240

2. THE USING PHYSICIAN INDICATED ABOVE IS LICENSED TO DISPENSE DRUGS IN THE PRACTICE OF MEDICINE BY A STATE OR TERRITORY OF THE UNITED STATES, THE DISTRICT OF COLUMBIA, OR THE COMMONWEALTH OF PUERTO RICO.

As permitted by Fitzsimons Gen. Hosp.Radioisotope Committee

CIRCLE ANSWER: (YES) NO

3. A STATEMENT OF USING PHYSICIAN'S CLINICAL RADIOISOTOPE EXPERIENCE (PAGE 3 OF THIS SUPPLEMENT) IS SUBMITTED IN SUPPORT OF THIS APPLICATION. IF ANSWER IS NO, USE PAGE 2 OF THIS SUPPLEMENT TO EXPLAIN OR REFER TO OTHER APPLICATION OR RELATED DOCUMENTS ON WHICH THIS INFORMATION APPEARS.

As permitted by Fitzsimons Gen. Hosp. Radioisotope Committee

CIRCLE ANSWER: YES (NO)

PROPOSED DIAGNOSIS OR TREATMENT

4. (a) DESCRIBE PURPOSE FOR WHICH BYPRODUCT MATERIAL WILL BE USED INCLUDING SPECIFIC CONDITIONS OR DISEASES TO BE DIAGNOSED OR TREATED (Use page 2 if necessary):

Cr^{51} will be used to tag platelets to determine platelet survival time.

(b) CHEMICAL FORM ADMINISTERED:

Na_2CrO_4

(c) DESCRIBE PROCEDURES WHICH WILL BE OBSERVED TO MINIMIZE HAZARD FROM HANDLING, STORAGE, AND DISPOSAL OF THE BYPRODUCT MATERIAL:

See License #05-00046-13

(d) DESCRIPTION AND SKETCHES OF SPECIAL DEVICES TO BE USED FOR ADMINISTERING BYPRODUCT MATERIAL TO HUMAN BEINGS ARE

(1) ATTACHED (LITERATURE REFERENCES WILL SUFFICE) — CIRCLE ANSWER: YES (NO)

(2) ON FILE WITH THE ISOTOPES EXTENSION REFER TO APPLICATION NO See License #05-00046-13 — CIRCLE ANSWER: (YES) NO

5. (a) PROPOSED DOSAGE SCHEDULE.—In millicuries for internally administered byproduct material other than discrete fixed sources; and in roentgens or rads, as appropriate, for internal or external irradiation from discrete fixed sources (gold seeds, cobalt needles, etc.) state separately for each condition or disease (use page 2 if necessary):

Proposed dose range 0.015 - 0.003 millicuries.

(b) INVESTIGATIVE PROPOSAL FOR EXPERIMENTAL, NEW OR UNUSUAL HUMAN USES IS ATTACHED. (Attachment should include outline of conditions to be evaluated, including data from animal studies and/or abstract of literature reference if any, number and type of patients (i. e. age group, moribund, etc.)) — CIRCLE ANSWER: YES (NO)

6. IF BYPRODUCT MATERIAL WILL NOT BE OBTAINED IN PRECALIBRATED FORM FOR ORAL ADMINISTRATION OR IN PRECALIBRATED AND STERILIZED FORM FOR PARENTERAL ADMINISTRATION, DESCRIBE IDENTIFICATION, PROCESSING, AND STANDARDIZATION PROCEDURES:

Na_2CrO_4 (Cr^{51}) will be obtained in pre-calibrated form sterilized for parenteral injection from Squibb and Co. or other supplier that meets AEC standards.

7. THE PROPOSED USE OF BYPRODUCT MATERIAL HAS BEEN, OR WILL BE, APPROVED BY THE MEDICAL ISOTOPE COMMITTEE. — CIRCLE ANSWER: (YES) NO

HOSPITAL FACILITIES FOR INDIVIDUAL PRACTICE USE ONLY

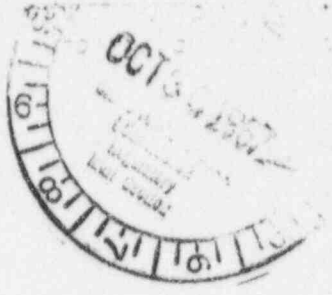
8. (a) THE APPLICANT HAS COMPLETED ARRANGEMENTS FOR A HOSPITAL TO ADMIT RADIOACTIVE PATIENTS WHENEVER ADVISABLE. — CIRCLE ANSWER: YES NO

(b) A COPY OF INSTRUCTIONS TO BE FURNISHED TO THE HOSPITAL AS TO RADIOLOGICAL SAFETY PRECAUTIONS TO BE TAKEN AND AVAILABLE RADIATION INSTRUMENTATION IS ATTACHED. — CIRCLE ANSWER: YES NO

Form AEC-313 a (10-61) PAGE 2	UNITED STATES ATOMIC ENERGY COMMISSION **APPLICATION FOR BYPRODUCT MATERIAL LICENSE** SUPPLEMENT A—HUMAN USE	Form approved. Budget Bureau No. 38-R080.1

This page may be used for providing additional information. Please cross reference to specific items.

*3 See license #05-00046-13



Form WA-[illegible]
(6-60)

U.S. ATOMIC ENERGY COMMISSION
MEDICAL ADVISORY COMMITTEE

APPRAISAL

1. Applicant: Department of the Army

Address: Fitzsimons General Hospital and U. S. Army Medical Research & Nutrition Lab

City: Denver State: Colorado 80240

2. Control No. 96146

3. Department

4. Name and title of trained individual

A. H. Janoski, Captain, MC

Richard P. Carson, Captain, MC

5. Type program:

☐ Private practice.

☐ Private practice in hospital.

☒ Institutional.

6. Review:

☒ First. ☐ Second.

7. Previous application control No.(s)

None

8. Remark on checked items:

☒ A. All radioisotopes and uses stated in application.

☐ B. Use of .... for ....

☒ C. Training and experience of user. To be reviewed by: Drs. Rawson, Greenlaw, Rossi Armstrong, and Christian

☐ D. Dosage(s) indicated.

☐ E. Clinical techniques and procedures outlined.

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

☐ G. Other

RECEIVED
1967 SEP 5 PM 12 34
U.S. ATOMIC ENERGY COMM.
MAIL & FILES SECTION

9. Action of Subcommittee on Human Applications:

☒ Approve. ☐ Disapprove.

Remarks:

August 21, 1967
(Date of approval)

Signature [signature]

Form WA-273
(4-60)

U.S. ATOMIC ENERGY COMMISSION
MEDICAL ADVISORY COMMITTEE

APPRAISAL

1. Applicant: Department of the Army

Address: Fitzsimons General Hospital and U. S. Army Medical Research & Nutrition Lab

City: Denver State: Colorado 80240

2. Control No.
96146

3. Department

4. Name and title of trained individual

A. H. Janoski, Captain, MC

Richard P. Carson, Captain, MC

5. Type program:

☐ Private practice.

☐ Private practice in hospital.

☒ Institutional.

6. Review:

☒ First. ☐ Second.

7. Previous application control No.(s)

None

8. Remark on checked items:

☒ A. All radioisotopes and uses stated in application.

☐ B. Use of ..... for .....

.....

☒ C. Training and experience of user.

To be reviewed by: Drs. Rawson, Greenlaw, Rossi Armstrong, and Christian

☐ D. Dosage(s) indicated.

☐ E. Clinical techniques and procedures outlined.

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

☐ G. Other

RECEIVED
SEP 12 1967
U.S. ATOMIC ENERGY COMMISSION
Regulatory
Mail Section

9. Action of Subcommittee on Human Applications:

☒ Approve. ☐ Disapprove.

Remarks:

Approve.

9/7/67
(Date of appraisal)

Signature R. W. Rawson, M.D.
(Member of subcommittee)

U.S. GOVERNMENT PRINTING OFFICE 16—4809-1

Form WA-272
(4-59)

U.S. ATOMIC ENERGY COMMISSION
MEDICAL ADVISORY COMMITTEE

APPRAISAL

1. Applicant: Department of the Army

Address: Fitzsimons General Hospital and U. S. Army Medical Research & Nutrition Lab

City: Denver State: Colorado 80240

2. Control No. 96146

3. Department

4. Name and title of trained individual

A. H. Janoski, Captain, MC

Richard P. Carson, Captain, MC

5. Type program:

☐ Private practice.

☐ Private practice in hospital.

☒ Institutional.

6. Review:

☒ First. ☐ Second.

7. Previous application control No.(s)

None

8. Remark on checked items:

☒ A. All radioisotopes and uses stated in application.

☐ B. Use of ..... for .....

.....

☒ C. Training and experience of user.

To be reviewed by: Drs. Rawson, Greenlaw, Rossi Armstrong, and Christian

☐ D. Dosage(s) indicated.

☐ E. Clinical techniques and procedures outlined.

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

☐ G. Other

9. Action of Subcommittee on Human Applications:

☒ Approve. ☐ Disapprove.

Remarks:

August 21, 1967
(Date of appraisal)

Signature W. D. Armstrong, M.D.
(Member of subcommittee)

U.S. GOVERNMENT PRINTING OFFICE 16—76889-1

Form WA-272
(4-59)

U.S. ATOMIC ENERGY COMMISSION
MEDICAL ADVISORY COMMITTEE

APPRAISAL

1. Applicant: Department of the Army

Address: Fitzsimons General Hospital and U. S. Army Medical Research & Nutrition Lab

City: Denver State: Colorado 80240

2. Control No.
96146

3. Department

4. Name and title of trained individual

A. H. Janoski, Captain, MC

Richard P. Carson, Captain, MC

5. Type program:

☐ Private practice.

☐ Private practice in hospital.

☒ Institutional.

6. Review:

☒ First. ☐ Second.

7. Previous application control No.(s)

None

8. Remark on checked items:

☒ A. All radioisotopes and uses stated in application.

☐ B. Use of ..... for .....

.....

☒ C. Training and experience of user.

To be reviewed by: Drs. Rawson Greenlaw, Rossi Armstrong, and Christian

☐ D. Dosage(s) indicated.

☐ E. Clinical techniques and procedures outlined.

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

☐ G. Other

9. Action of Subcommittee on Human Applications:

☐ Approve. ☐ Disapprove.

Remarks:

Approved with the understanding that the individual users as requested on Form AEC-313 Item 4 are A.H. Janoski and R.P. Carson

August 16, 1967
(Date of appraisal)

Signature John E. Christian
(Member of subcommittee)

John E. Christian, Ph.D.

U.S. GOVERNMENT PRINTING OFFICE 16—76880-1

Form WA-272
(4-59)

U.S. ATOMIC ENERGY COMMISSION
MEDICAL ADVISORY COMMITTEE

APPRAISAL

1. Applicant: Department of the Army

Address: Fitzsimons General Hospital and U. S. Army Medical Research & Nutrition Lab

City: Denver State: Colorado 80240

2. Control No.
96146

3. Department

4. Name and title of trained individual

A. H. Janoski, Captain, MC

Richard P. Carson, Captain, MC

5. Type program:

☐ Private practice.

☐ Private practice in hospital.

☒ Institutional.

6. Review:

☒ First. ☐ Second.

7. Previous application control No.(s)

None

8. Remark on checked items:

☒ A. All radioisotopes and uses stated in application.

☐ B. Use of ..... for .....

.....

☒ C. Training and experience of user.

To be reviewed by: Drs. Rawson, Greenlaw, Rossi Armstrong, and Christian

☐ D. Dosage(s) indicated.

☐ E. Clinical techniques and procedures outlined.

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

☐ G. Other

9. Action of Subcommittee on Human Applications:

☒ Approve. ☐ Disapprove.

Remarks:

Although I continue in my opposition to research involving appreciable radiation exposure that is carried out by delegated investigators.

Harald H. Rossi

8/16/67
(Date of appraisal)

Signature .....
(Member of subcommittee)

Harald H. Rossi

U.S. GOVERNMENT PRINTING OFFICE 16—74859-1

Form AEC-313
(3-58)

ATOMIC ENERGY COMMISSION

APPLICATION FOR BYPRODUCT MATERIAL LICENSE

Form approved.
Budget Bureau No. 38-R027.4

INSTRUCTIONS.—Complete items 1 through 16 if this is an initial application. If application is for renewal of a license, complete only Items 1 through 7 and indicate new information or changes in the program as requested in Items 8 through 15. Use supplemental sheets where necessary. Item 16 must be completed on all applications. Mail three copies to: U. S. Atomic Energy Commission, Washington 25, D. C. Attention: Isotopes Branch, Division of Licensing and Regulation. 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.)*

Department of the Army
Fitzsimons General Hospital and U. S.
Army Medical Research & Nutrition Lab
Denver, Colo., 80240

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

Fort Lewis, Washington and
Summit of Pikes Peak, Colorado

2. DEPARTMENT TO USE BYPRODUCT MATERIAL

Physiology Division
U.S.Army Medical Research & Nutrition Lab

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

Present application is for amendment to
Lic. No. 05-00046-13

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.)*

As specified and approved by the Radio-
isotope Committee, Fitzsimons General
Hospital

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.)*

Same as 4

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

A. Carbon-14
B. Hydrogen-3

(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.)*

A. 4-^{14}C-cortisol — A. 0.1 millicurie
B. 1,2-^{3}H-aldosterone — B. 0.1 millicurie

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.)*

See Form AEC-313a attached

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90146

(Continued on reverse side)

Form AEC-313 (5-58)

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	Individuals will have appropriate training & experience prior to their approval by the Radioisotope Committee, Fitzsimons General Hospital		Yes No	Yes No
b. Radioactivity measurement stc lardization 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
Same as 8				

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

TYPE OF INSTRUMENTS (Include make and model numbe of each)	NUMBER AVAILABLE	RADIATION DETECTED	SENSITIVITY RANGE (mr/hr)	WINDOW THICKNESS (mg/cm²)	USE (Monitoring, surveying, measuring)
As described in application for renewal of Byproduct Material License No. 05-00046-13 dtd 21 June 66. See also attached protocol.					

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

See License #05-00046-13

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

See License #05-00046-13

INFORMATION TO BE SUBMITTED ON ADDITIONAL SHEETS

13. FACILITIES AND EQUIPMENT. Describe laboratory facilities and remote handling equipment, storage containers, shielding, fume hoods, etc. Explanatory sketch of facility is attached. (Circle answer) Yes No See License #05-00046-13 and attached protocol

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, maintenance and repair of the source.

See License #05-00046-13 and attached protocol

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 the type and amount of activity involved.

See License #05-00046-13 and attached protocol

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.

Dept.of the Army, FGH & USA Med Rsch & Nutr Lab, Denver, Colo 80240
Applicant named in item 1

Date 13 July 67

By: Edwin L. Overholt
EDWIN L. OVERHOLT, Col, MC
Chairman, Radioisotope Committee
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 : 1961 OF—615965

Form AEC-313 a (10-61) PAGE 1

UNITED STATES ATOMIC ENERGY COMMISSION

APPLICATION FOR BYPRODUCT MATERIAL LICENSE

SUPPLEMENT A—HUMAN USE

Form approved. Budget Bureau No. 38-R080.1

If byproduct material is for "human use" (internal administration of byproduct material, or the radiation therefrom to human beings), complete this supplement and attach to the application for byproduct material license.

1. (a) USING PHYSICIAN'S NAME: Dept. of the Army, Fitzsimons Gen Hosp. and US Army Med Rsch & Nutr Lab, Denver, Colo.

(b) NAME AND ADDRESS OF APPLICANT (If different from 1(a)): Same as 1a

2. THE USING PHYSICIAN INDICATED ABOVE IS LICENSED TO DISPENSE DRUGS IN THE PRACTICE OF MEDICINE BY A STATE OR TERRITORY OF THE UNITED STATES, THE DISTRICT OF COLUMBIA, OR THE COMMONWEALTH OF PUERTO RICO. CIRCLE ANSWER: (YES) NO

As permitted by Radioisotope Committee, Fitzsimons Gen Hosp.

3. A STATEMENT OF USING PHYSICIAN'S CLINICAL RADIOISOTOPE EXPERIENCE (PAGE 3 OF THIS SUPPLEMENT) IS SUBMITTED IN SUPPORT OF THIS APPLICATION. IF ANSWER IS NO, USE PAGE 2 OF THIS SUPPLEMENT TO EXPLAIN OR REFER TO OTHER APPLICATION OR RELATED DOCUMENTS ON WHICH THIS INFORMATION APPEARS. CIRCLE ANSWER: (YES) NO

As permitted by Radioisotope Committee. See trng & exp. of Dr. A. Janoski & Dr. R. Carson attached

PROPOSED DIAGNOSIS OR TREATMENT

4. (a) DESCRIBE PURPOSE FOR WHICH BYPRODUCT MATERIAL WILL BE USED INCLUDING SPECIFIC CONDITIONS OR DISEASES TO BE DIAGNOSED OR TREATED (Use page 2 if necessary): For measurement of twenty-four hour urinary aldosterone excretion and twenty-four hour urinary cortisol excretion

(b) CHEMICAL FORM ADMINISTERED:

4 - ^{14}C-cortisol
1, 2-^{3}H-aldosterone

(c) DESCRIBE PROCEDURES WHICH WILL BE OBSERVED TO MINIMIZE HAZARD FROM HANDLING, STORAGE, AND DISPOSAL OF THE BYPRODUCT MATERIAL:

See attached protocol

(d) DESCRIPTION AND SKETCHES OF SPECIAL DEVICES TO BE USED FOR ADMINISTERING BYPRODUCT MATERIAL TO HUMAN BEINGS ARE

(1) ATTACHED (LITERATURE REFERENCES WILL SUFFICE) CIRCLE ANSWER: YES (NO)

(2) ON FILE WITH THE ISOTOPES EXTENSION REFER TO APPLICATION NO _____ CIRCLE ANSWER: YES (NO)

5. (a) PROPOSED DOSAGE SCHEDULE.—In millicuries for internally administered byproduct material other than discrete fixed sources; and in roentgens or rads, as appropriate, for internal or external irradiation from discrete fixed sources (gold seeds, cobalt needles, etc.) state separately for each condition or disease (use page 2 if necessary):

Two injections of 1.0 microcurie each of 4-^{14}C- cortisol and two injections of 2.0 microcuries each of 1, 2-^{3}H-aldosterone

(b) INVESTIGATIVE PROPOSAL FOR EXPERIMENTAL, NEW OR UNUSUAL HUMAN USES IS ATTACHED. (Attachment should include outline of conditions to be evaluated, including data from animal studies and/or abstract of literature reference if any, number and type of patients (i. e. age group, moribund, etc.)) CIRCLE ANSWER: (YES) NO

6. IF BYPRODUCT MATERIAL WILL NOT BE OBTAINED IN PRECALIBRATED FORM FOR ORAL ADMINISTRATION OR IN PRECALIBRATED AND STERILIZED FORM FOR PARENTERAL ADMINISTRATION, DESCRIBE IDENTIFICATION, PROCESSING, AND STANDARDIZATION PROCEDURES: The isotopes will be tested for purity by chromatography on three separate systems. The purified isotopes will be dissolved in absolute ethanol and sterilized rendering them pyrogen free by Millipore filtration. The isotopes will be kept as a 10% solution of ethanol in sterile water in a sterile, multidose stoppered vial. They will be administered to the subjects by a medical officer.

7. THE PROPOSED USE OF BYPRODUCT MATERIAL HAS BEEN, OR WILL BE, APPROVED BY THE MEDICAL ISOTOPE COMMITTEE. CIRCLE ANSWER: (YES) NO

HOSPITAL FACILITIES FOR INDIVIDUAL PRACTICE USE ONLY

8. (a) THE APPLICANT HAS COMPLETED ARRANGEMENTS FOR A HOSPITAL TO ADMIT RADIOACTIVE PATIENTS WHENEVER ADVISABLE. CIRCLE ANSWER: YES NO

(b) A COPY OF INSTRUCTIONS TO BE FURNISHED TO THE HOSPITAL AS TO RADIOLOGICAL SAFETY PRECAUTIONS TO BE TAKEN AND AVAILABLE RADIATION INSTRUMENTATION IS ATTACHED. CIRCLE ANSWER: YES NO

Form AEC-313 a (10-61) PAGE 2	UNITED STATES ATOMIC ENERGY COMMISSION **APPLICATION FOR BYPRODUCT MATERIAL LICENSE** SUPPLEMENT A—HUMAN USE	Form approved. Budget Bureau No. 38-R080.1

This page may be used for providing additional information. Please cross reference to specific items.

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March 1967

USAMRNL
PHYSIOLOGY DIVISION PROTOCOL

Project No. 3A104501B71R Research in Biomedical Sciences
Task No. 05: Environmental Medicine
Work Unit No. 82: Metabolic Effect of Altitude
Study No. 4: Endocrine Effects of Altitude

I. INTRODUCTION

It has been established that acute exposure of man to high altitude causes the onset of a distressing, incapacitating syndrome, termed "mountain sickness." (1, 2, 3) This syndrome is characterized by impaired physical and psychomotor performance. The transitory effects of high altitude exposure - the most debilitating symptoms - severe headache, nausea and vomiting, extreme fatigue and anorexia usually last up to 5 - 6 days in most subjects. These symptoms are variable in intensity in different people or in the same person at different times.

Various theories have been advanced in the attempt to explain the etiology of mountain sickness. Research has been concerned primarily with the evaluation of cardiopulmonary and acid-base alterations in man. Still, all of the reported, established alterations do not explain the phenomenon of acclimatization that occurs in most subjects within 5 - 7 days. Recently, in the attempt to discover the cause of mountain sickness and the mechanisms of adaptation, investigators have focused on endocrine function, shifts in body fluids, and electrolyte balance in man at high altitude. The following sections summarize the observed alterations of endocrine function, body fluids and electrolytes in man at high altitude. There is a wealth of literature of similar observations conducted on animals which is essentially consistent with the reports on man (4 - 14).

Body Fluids and Electrolytes in Man at High Altitude

When man ascends rapidly to high terrestrial locations, there is a continuous decrease in plasma volume, a decrease in extracellular fluid volume, and a rise in intracellular fluid volume. Total body water increases (15). Total body potassium obtained from body scanning for K^{40} is noted to be increased by one research group (16) but similar measurements made by USAMRNL show that total body potassium decreases (15). Excessive urinary excretion of sodium, potassium and chloride ions has been documented (15, 17). There is a significant rise in salivary sodium to potassium ratio (18) and urinary sodium to potassium ratio (17). In addition to electrolyte changes, urine volume increases at high altitude (19).

These observed effects of altitude on man resulting in body fluid shifts and electrolyte alterations suggest diminished aldosterone secretion by the adrenal glands. Very recently it has been reported that urinary aldosterone excretion does decrease at altitude, approaching zero within three days of high altitude exposure (19). These findings appear to be consistent with the observed pattern of urinary electrolyte excretion. Additional investigation is necessary in order to establish and correlate the electrolyte changes with aldosterone secretion at high altitude by means of balance studies with human volunteers. If aldosterone excretion is indeed diminished at high altitude in the face of sodium loss, diminished plasma and extracellular fluid volumes, the mechanism is unknown and is contrary to accepted physiological controls of aldosterone secretion.

Adrenocortical Function in Man at High Altitude

Various investigators using intermittent chamber studies in man (20, 21), or actual field studies at high altitude (17, 22, 23),

have observed a rise in the 24-hour urinary excretion of 17-ketosteroids and 17-hydroxycorticosteroids during acute exposure. One research group did note a difference in the excretion pattern of 17-hydroxy-corticosteroids and 17-ketosteroids. The latter decreased initially. Adrenal function has been studied in a group of high altitude natives, and is the same as a comparable group living at sea level (24).

These studies are generally consistent with the known physiological control of pituitary adrenal function during stress. The correlation of adrenocortical function to "mountain sickness" and the magnitude of environmental adrenocortical steroid secretion and ACTH release during stress require additional investigation. The accurate measurement of these hormones during acute altitude exposure can determine the desirability of a possible therapeutic means of controlling the symptoms of high altitude stress in man.

Glucose Tolerance in Man at High Altitudes

Studies in man (25, 26, 27, 28) have established that there is a lower fasting blood glucose level and greater utilization of glucose at high altitude. Whether the cause of enhanced glucose utilization is secondary to increased insulin secretion or the effect of adreno-corticosteroids on glucose metabolism, is not known, and should be determined.

II. OBJECTIVE

The objectives of the present proposal to study human subjects at high altitude are (1) to evaluate through balance studies, the nature of electrolyte alterations; (2) to determine the magnitude of the stress response at altitude by evaluation of pituitary and adrenocortical function; (3) to measure and correlate the aldosterone secretion and excretion in relationship to electrolyte changes; and (4) to investigate the mechanism for increased glucose utilization.

The purpose of the study will be to correlate these findings with the severity of mountain sickness symptoms at 14, 100 feet.

III. JUSTIFICATION

Reports concerning the Indian Army (29) have furnished alarming evidence of incapacitating medical and personnel problems resulting from altitude sickness, when a military force attempts to function on mountain locations. An understanding of the physiological alterations during altitude acclimatization and the relationship of these to various mountain sickness symptoms might lead to successful methods of pre-selecting or pre-conditioning troops.

Knowledge of the endocrine function in man at high altitude would shed light on the adaptive changes that occur during the stress of hypoxia. Significantly patho-physiological alterations in hormone secretion can be dealt with therapeutically. Recent Army Research Office conferences (30, 31) have pointed to a military need for studies on physiology, pharmacology and performance in high terrestrial environments.

IV. EXPERIMENTAL DESIGN

A. The subjects will be ten U. S. Army volunteers (19 to 25 years old) who have signed a volunteer form indicating their knowledge of the scope of the procedures planned, including the intravenous administration of tracer quantities of radioactive steroid compounds and their willingness to serve as subjects. The radioactive concentration of these isotopes will be recorded in the subjects' Army Health Records. The subjects will be interviewed, examined and selected by a medical officer after review of their health records to exclude cardiopulmonary, renal or endocrine disorders. A medical officer is to be present during the entire study and is authorized to terminate the experiment at any time continuation would be detrimental to the health of the subject.

The study will be conducted for a total period of 21 days beginning 11 September 1967. The sea level studies will be conducted at Fort Lewis, Washington. This site meets the requirements that the sea level site be located in a temperate climate. A hot, humid climate would make electrolyte balance studies inaccurate. In addition, heat exposure alters blood volume and this would interfere with studies on aldosterone secretion.

During the sea level test period, constituting days 1 to 14, the subjects will be started on a constant metabolic diet which will require eight days of equilibration of body electrolytes prior to initiating balance studies. This diet will be continued until the end of the study on day 21. On day 15 the subjects will be flown to Colorado Springs or Denver and transferred by Army vehicle to the Army mobile laboratory on Pikes Peak (14,100 ft). The altitude test phase will be conducted there with living quarters provided for the subjects.

B. Clinical Study

1. Plan of study

a. Sea level test period - 0900 hours day 1 to 0900 hours day 15.

b. Travel period - day 15.

c. Altitude test period - 0900 hours day 16 to 0900 hours day 21.

2. Diet

A prepared liquid diet comprising daily consumption of 2,800 calories as 55% carbohydrate, 15% protein, and 30% fat. The daily electrolyte and mineral intake will be 100 mEq. of sodium, 80 mEq. of potassium, 1600 mg of calcium, and 1200 mg of phosphorous.

The diet and water content are to be constant and analysed. During the day of travel, the subjects will be maintained on this diet. On days 5 and 19, the subjects will fast from 21:00 hours until 14:00 hours the following day (glucose tolerance test). There will be no smoking during this interval.

3. Water intake

Distilled water will be used for drinking purposes. Daily water intake will be measured and recorded. A minimum of 1500 ml of water per subject per day is to be consumed.

4. Medications

a. Glucose - 100 grams in distilled water administered orally on days 6 and 20 at 09:00 hours

b. 4-C^{14} - cortisol (1μc) and 1, 2-H^{3} - aldosterone (2μc) - administered intravenously in 10 ml sterile solution of 10% ethanol in water at 09:00 hours on days 9 and 17.

c. Sodium chloride - 500 mg in gelatin capsules in the event of diminished dietary intake to maintain constant daily sodium intake.

d. Potassium replacement elixir (5 ml contains 10 mEq. of potassium as gluconate and citrate salts) - to maintain constant daily potassium intake if intake of food diminishes when anoretic.

e. Calcium gluconate tablets - 500 mg if food intake diminishes when anoretic to maintain constant daily intake of calcium.

f. Aspirin and Darvon - administered orally at the discretion of the medical officer for headache. The dosage and time of administration are to be recorded.

g. Intravenous infusions of isotonic sodium chloride and potassium will be administered if severe vomiting occurs in order to maintain electrolyte and water balance.

5. Collections

a. Urine

Total 24-hour urine collections will be obtained from each subject starting at 09.00 hours each day. Each collection period will end on 09:00 hours the following day with the subjects voiding at this time and adding this specimen to the previous day's collection. The days of collection are 8 through 14 and 16 through 20. The urine will be stored in large plastic bottles and kept under refrigeration at all times during collection. At the end of each 24-hour collection period, all urine collected will be frozen and will be kept in this state until analysed at the USAMRNL. All specimen bottles will be labeled with name of subject, and the starting and ending dates of the 24-hour collection. Radioactivity labels will be affixed to all 24-hour urine samples collected after the administration of radioisotopes to the subjects.

b. Blood

(1) Plasma insulin and glucose

At 08:30 hours on days 6 and 20, 5 ml of venous blood will be drawn into fluoride-oxalate vacuum tubes. Following oral glucose administration, similar samples will be taken at 15, 30, 45, 60, 90, 120, 240, and 300 minutes. The tubes will be labeled and the contents frozen. The subjects are to refrain from smoking from the period of fasting until the final blood sample is drawn.

(2) Plasma ACTH and cortisol

On days 9, 10, 13, 16, 17 and 18, venous blood will be taken at 08:45 hours. Thirty ml of blood will be drawn into a syringe containing heparin and transferred to centrifuge tubes and centrifuged. The plasma will be transferred to screw-cap glass tubes, labeled "cortisol" and frozen. Forty ml

of venous blood will be collected through sterile plastic tubing directly into a large centrifuge tube containing heparin. The centrifuge tube will remain immersed in an ice-water bath during the collection, then immediately centrifuged at 12 degrees centigrade. The plasma will be transferred to screw-cap tubes labeled "ACTH" and frozen. All tubes will be labeled with name of subject, time and date.

3) Fifteen ml of venous blood will be taken at 15:00 hours on days 8, 9, 10, 13, 14, 16, 17, 18, 19, and 20. Following centrifugation, the serum will be transferred to labeled test tubes and frozen.

c. Feces

Feces will be collected in plastic bags on days 8, 9, 10, 11, 12, 13, 14, 16, 17, 18, 19 and 20.

d. Vomitus

Any vomitus will be collected in plastic bags for analysis.

C. Measurements

1. Electrolytes

Concentrations of sodium and potassium in the diet, venous blood, stools and urine will be determined by AutoAnalyzer or flame photometry. Calcium will be measured by atomic absorption spectrophotometry. Chloride and creatinine will be measured by the Auto-Analyzer. The Fiske and Subbarow method will be used for phosphate concentrations.

2. Nitrogen

Urinary nitrogen content will be determined by the Auto-Analyzer. The macro-Kjeldahl technique will be used for nitrogen in the diet and in the feces.

3. Fat

Diet and stool fat will be determined by routine analytical methods.

4. Glucose and insulin

Plasma glucose will be measured by AutoAnalyzer. Plasma insulin will be determined by Captain J. Anderson, Metabolic Division of the USAMRNL employing the method of Morgan and Lazarow (32).

5. Steroids

a. Plasma cortisol by the Peterson modification (33) method of Silber and Porter (34) using the Beckman DU Spectrophotometer.

b. Total 24-hour urinary 17-ketosteroids and 17-ketogenic steroids by the Sobel (35) modification of the Norymberski method. Gas-liquid chromatography will be used to determine individual 17-ketosteroids.

c. Twenty-four hour urinary aldosterone excretion by a modification of the double isotope technique of Kliman and Peterson (36) using 1,2-H^3-aldosterone, 1,2-H^3-tetrahydroaldosterone, and acetic-1-C^{14} anhydride.

d. Twenty-four hour urinary cortisol excretion by the method of Erlich (37), using 1,2-H^3-cortisol and acetic-1-C^{14} anhydride.

6. Plasma adrenocorticotropic hormone

ACTH levels in plasma will be determined by the method of Vernikos-Danellis (38) by means of bioassay in hypophysectomized rats.

7. Plasma and urine osmolality

Osmolality will be determined by means of the Fiske osmometer.

D. Radioactive Steroids as Tracers in Human Subjects

1. Purification

4-C^{14}-cortisol (specific activity SA 15-30 mc/millimole)

and 1, 2-H^3-aldosterone (SA 35 curies/millimole) obtained commercially from New England Nuclear Corporation will be tested for purity by chromatography on three separate systems. The purified isotopes will be dissolved in absolute ethanol, and sterilized rendering them pyrogen-free by Millipore filtration. The isotopes will be kept as a 10% solution of ethanol in sterile water in a sterile, multi-dose, stoppered vial. They will be administered intravenously to the subjects by a medical officer.

2. Dosage considerations and calculations

It has been determined that over 90% of injected radioactively labeled cortisol is excreted by human subjects via the kidney within the first 48 hours (39, 40). Furthermore, no radioactivity can be detected in the body fluids in four days (39). The biological half-life of radioactive cortisol in the human bloodstream is 60 - 80 minutes (41). Similarly, over 90% of radioactive aldosterone injected into human subjects is excreted in the urine within 48 hours (42). The location of the tritium and carbon-14 labels in the steroid nucleus is such that the labels remain an integral part of the compound in the body and are excreted intact as steroid metabolites without degradation. (43). This factor has enabled numerous investigators to employ these isotopically labeled steroids in clinical research without the hazards of critical organ concentration, the random labeling of body water by tritium, or the expiration of carbon-14 carbon dioxide in human subjects.

Based on knowledge gained from reports in the literature, one can make the safe assumption that the effective half-life (T 1/2) of these isotopes in man is one day (an over-assumption). The total body burden would be calculated as follows: (44)

1. 4-C^{14}-cortisol. 1 μc injected into a 70 kg man assuming total body distribution with an effective T 1/2 of one day.

$$D\beta \sim 73.8 \times C \times \bar{E}\beta \times T \text{ rads}$$

$\bar{E}\beta \approx 0.050$ Mev. for C^{14}

$C \approx 1.0/70,000$

$T \approx 1$ day

$D\beta \approx 73.8 \times 1.0/70,000 \times 0.050 \times 1$ rads

$D\beta \approx 5.27 \times 10^{-5}$ rads

2. 1, 2-H^3 - aldosterone. Two μc injected into a 70 kg man assuming total body distribution with an effective T 1/2 of one day.

$D\beta \approx 73.8 \times C \times \bar{E}\beta \times T$ rads

$\bar{E}\beta \approx 0.006$ Mev. for H^3.

$C \approx 2.0/70,000$

$T \approx 1$ day

$D\beta \approx 72.8 \times 2.0/70,000 \times 0.006 \times 1$ rads

$D\beta \approx 1.26 \times 10^{-5}$ rads

During the control period 1.0 μc of 4-C^{14}-cortisol and 2.0 μc of 1, 2-H^3-aldosterone will be injected simultaneously (6.53×10^{-5} rads). This will be repeated once at high altitude the following week. The total radiation dose received by each individual will be no more than 1.3×10^{-4} rads which is considerably below the limits generally agreed upon for an internal emitter - approximately 0.1 rem per week (5 rem per year).

3. Monitoring radioactivity

During the experimental studies, after the administration of radioisotopes all excreta will be collected until levels of radioactivity are equal to background levels. All samples containing radioactivity will be returned to the U.S. Army Medical Research and Nutrition Laboratory at Denver, Colorado for analysis. All radioactive waste will be transported to Denver and disposed of by the Radioisotope Section of the USAMRNL as outlined in "Procedures for Use of Radioactive Material" (See Appendix E Application for Renewal and Amendment to AEC Byproduct Material License No. 5-46-13 (A66) dated June 1966). All areas where radioisotopes are used will be monitored by means of a PAC-3G with a beta probe (Eberline Instrument Company, Serial No. 1226). Also periodic wipes will be taken with moist gauze and returned to the U.S. Army Medical Research

and Nutrition Laboratory for counting in a Packard Model 3314 liquid scintillation counter (Serial No. A3314-05-00712).

All rules, regulations and limitations set forth by Army AEC and local authorities, including those embodied in AR 70-25; AR 40-37; Title 10, Part 20, Code of Federal Regulations "Standards for Protection Against Radiation"; and Handbook 69 of the National Bureau of Standards will be complied with.

Enclosed and attached to this protocol is the Voluntary Consent Statement relating to the intravenous administration of radioisotopically labeled steroid compounds as tracers. (See Appendix I)

4. Determination of the Secretory Rates of Cortisol and Aldosterone

a. Cortisol secretion rate

The cortisol secretion rate will be determined by the method of Roginsky, et al. (45) from the combined 48-hour urine collection following isotope injection.

b. Aldosterone secretion rate

This will be determined by the method of Kelly, et al. (46) using the double isotope derivative method.

V. ADMINISTRATION

A. The study will be the responsibility of the Physiology Division of USAMRNL.

B. The personnel and their responsibilities will be assigned as follows:

1. Captain A. H. Janoski, MC: Project leader; responsible medical officer.

2. John P. Hannon, Ph. D.: Project Co-leader.

3. J. L. Shields, Ph. D.: Project Co-leader.

4. Captain R. P. Carson, MC: Medical Officer
5. Captain B. Whitten, MSC: Administrative officer
6. George J. Klian, Ph. D.: Technical supervisor
7. Major C. G. Liddle, V. C.: Radiation officer
8. One NCOIC: Subject control and dietary supervisor
9. Four enlisted military technicians
10. Two civilian technicians

C. Continuous physician coverage during the study will be the responsibility of Captains A.H. Janoski and R. P. Carson of the U. S. Army Medical Corps.

D. Cost

1.	Equipment	800.00
2.	Chemicals, including solvents	$4,000.00
3.	Per diem for subjects	210.00
4.	Travel for subjects	1,500.00
5.	Diet for subjects	500.00
6.	Air freight (samples collected during study)	700.00
7.	Class A Funds	600.00
8.	Travel for project personnel (7 investigators, 5 enlisted men, 2 civilians). Includes one round trip to Seattle	2,100.00
9.	Rental truck for equipment (30 days)	900.00
10.	GSA vehicles (2 for 21 days)	400.00
11.	Lab rats for bioassay (250 rats)	800.00
12.	Per diem for investigators	2,400.00
13.	Per diem for enlisted men	
	a. Sea level site - 14 days (government quarters available, government mess not available).	560.00

14.	Per diem for civilian technicians (21 days)	$672.00
15.	Three investigators' per diem for three-day site survey	144.00
16.	Three investigators' travel to Seattle for site survey (3 round trips)	450.00
17.	Additional per diem for 3 investigators for four days at sea level site to set up study	192.00
18.	Additional per diem for 4 enlisted men for four days at sea level site to set up study (government quarters available; government mess not available)	128.00
19.	Miscellaneous expendable items	$,200.00
	Total	$18,816.00

E. Miscellaneous

Since the final approval by the AEC for the use of isotopes in human studies rests on the approval of the protocol and definite site selection for sea level studies, it is requested that final action on this protocol be no later than 5 June 1967. If the protocol is approved at this time, application would then be made to the AEC for action on the license amendment. Furthermore, final action on the protocol at this date would enable the investigators to prepare the isotopes for human administration and to obtain the necessary chemical supplies for the field study.

F. Additional Information

See Appendix I and Appendix II.

A. H. JANOSKI
Captain, MC

VOLUNTARY CONSENT STATEMENT

Military _____ Military Patient _____ Civilian _____ Civilian Patient _____

I, _____, having the capacity to consent, voluntarily and without force or duress consent to participate in research involving the use of tracer amounts of radioisotopes. I have been informed of, and understand, the nature, duration, and purpose of the experiment, the method and means by which it is to be conducted, the inconveniences and hazards to be expected, and the effects upon my health and person which may possibly come from participation in the experiment.

Specifically, I agree to receive (intravenously / orally) a small quantity of _____ containing _____ microcuries of _____. I also agree to furnish urine and stool samples for the period following until no detectable radioactivity is present and submit to measurements of expired gases if Carbon-14 has been received.

I understand that I may at any time during the course of the experiment revoke my consent and withdraw from the experiment without prejudice.

I do not at this time have any physical diseases, except for the following _____ _____, or mental disease, to the best of my knowledge.

_____ _____

DATE SIGNATURE

_____

SIGNATURE OF WITNESS

APPROVAL

I have personally ascertained that the quality of the foregoing consent is sufficient to permit the volunteer to participate in the experiment.

_____ _____

ATTENDING PHYSICIAN PROJECT LEADER

APPENDIX II

SUBJECT STATEMENT

Date _____

I voluntarily agree to participate as a subject in the experiment to be conducted on high altitude. I am aware that I may withdraw from the experiment at any time without prejudice or penalty of any kind. It has been explained to me that constant medical supervision will be maintained and that neither the exposure to high altitude nor the experimental techniques used in this study are unduly hazardous. I realise that in some subjects the high altitude may cause any or all of the following symptoms: dryness of the mouth and nose, excitement, blurring of vision, dizziness, tiredness, tremor, lack of appetite, mild cramps, thirst, confusion, a sense of well-being, sleepiness, muscular aches, ringing in my ears, nausea, runny nose, headache, hunger, sleeplessness, coughing, rapid heart beat, chest pains, fatigue, constipation, fever, muscular stiffness, stomach ache, itching or sneezing.

The nature and purpose of the experiment have been explained to me and I sign this statement fully understanding the project, any hazards connected with it, and my rights.

_____

(Name)

BIBLIOGRAPHY

1. C. W. Harris and J. E. Hansen. Electrocardiographic changes during exposure to high altitude. Amer. J. of Cardiology 18: 183-190, 1966.

2. Stickney, J. C. and E. J. Van Liere. Acclimatization to low oxygen tension. Physiology Reviews 33: 13, 1953.

3. Harris, C. W., J. L. Shields and J. P. Hannon. Acute altitude sickness in females. Aerospace Med. 37: 1163, 1966.

4. Sundstrom, E. S. and G. Michaels. The adrenal cortex in adaptation to altitude, climate and cancer. Memoirs of the University of California, Vol. 12, 1942. University of California Press, Berkeley, California.

5. Langley, L. L. and R. W. Clarke. The reaction of the adrenal cortex to low atmosphere pressure. Yale Journal of Biology and Medicine 14: 529, 1941-1942.

6. Dohan, F. C. Effects of low atmosphere pressure on the adrenals, thymus and testes of rats. Proc. Soc. Exper. Biol. and Med. 49: 404, 1942.

7. Darrow, D. C. and E. L. Sarason. Some effects of low atmosphere pressure on rats. Journal of Clinical Investigations 23: 11, 1944.

8. Hailman, H. F. The effect of preventing acapnia on adrenal cortical hypertrophy under conditions of decreased barometric pressure. Endocrinology 34: 187, 1944.

9. Demopoulos, H. B., B. Highman, P. D. Altland, M. A. Gerving and G. Kaley. Effects of high altitude on granular juxtaglomerular cells and their possible role in erythropoietin production. American Journal of Pathology 46: 497, 1965.

10. Thorn, G. W., M. Clinton, Jr., S. Farber and H. W. Edmonds. Studies on Altitude Tolerance, I. Bulletin of Johns Hopkins Hospital 79: 59, 1946.

11. Thorn, G. W., M. Clinton, Jr., B. M. Davis and R. A. Lewis Effect of adrenal cortical hormone therapy on altitude tolerance. Endocrinology 36: 381, 1945.

12. Lewis, R. A., G. W. Thorn, G. F. Koepf and S. S. Dorrance. The role of the adrenal cortex in acute anoxia. Journal of Clinical Investigation 21: 33, 1942.

13. Reeves, J. L. Influence of intermittent exposure to simulated altitude on pla ma and tissue electrolytes in rats. USAF Aerospace Medicine Center Pamphlet 61-37, February, 1961.

14. Marks, B. H., A. N. Bhattacharya and J. Vernikos-Danellis. Effect of hypoxia on secretion of ACTH in the rat. American Journal of Physiology 208: 1021, 1965.

15. Unpublished data. Physiology Division of the United States Army Medical Research and Nutrition Laboratory, Fitzsimons General Hospital, Denver, Colorado.

16. Ayres, P. J., R. C. Hunter and E. S. Williams. Aldosterone excretion and potassium retention in subjects living at high altitude. Nature 191: 78, 1961.

17. Pugh, L. G. Physical and medical aspects of the Himalayan Scientific and Mountaineering Expedition, 1960-1961. British Medical Journal 2: 621, 1962.

18. Williams, E. S. Salivary electrolyte composition at high altitude. Clinical Science 21: 37, 1961.

19. Williams, E. S. Electrolyte regulation during the adaptation of humans to life at high altitude. Proc. Royal Society, Series B: 266, 1966.

20. Pincus, G., and H. Hoagland. Steroid excretion and the stress of flying. Journal of Aviation Medicine 14: 173, 1943.

21. Clinton, Jr., M., G. W. Thorn and V. D. Davenport. Studies on Altitude Tolerance. II. Bulletin of Johns Hopkins Hospital 79: 70, 1946.

22. Timeras, P. S., W. Pace and C. A. Hwang. Plasma and urine 17-hydroxycorticosteroid levels in man during acclimatization to high altitude. Fed. Proc. 16: 340, 1957.

23. Hornbein, T. F. Adrenal cortical response to chronic hypoxia. Journal of Applied Physiology 17: 246, 1962.

24. Moncloa, F. and E. Pretell. Cortisol secretion rate, ACTH and methopyrapone tests in high altitude natives. Journal of Clin. Endo. and Metab. 24: 915, 1964.

25. Forbes, W. H. Blood sugar and glucose tolerance at high altitude. American Journal of Physiology 116: 309, 1936.

26. Picon-Reategui, E. Studies in the metabolism of carbohydrates at sea level and at high altitude. Metabolism 11: 1148, 1962.

27. Picon-Reategui, E. Intravenous glucose tolerance test at sea level and at high altitude. Journal of Clin. Endo. and Metab. 23: 1256, 1963.

28. Calderon, R. and L. A. Llerema. Carbohydrate metabolism in people living in chronic hypoxia. Diabetes 14: 100, 1965.

29. Evans, W. O. and J. E. Hansen. Troop performance in high altitude. Army: February, 1966

30. Army Research Office Symposium on High Altitude March 1963.

31. Army Research Office Symposium on High Altitude September 1963.

32. Morgan, C. R. and A. Lazarow. Immunoassay of insulin using a two-antibody system. Proc. Society Exp. Biology and Medicine 110: 29, 1962.

33. Peterson, R. E., A. Karrer and S. L. Guerra. Evaluation of Silber-Porter procedure for determination of plasma hydrocortisol. Anal. Chemistry 29: 144: 1957.

34. Silber, R. H. and C. C. Porter. The determination of 17, 21-dihydroxy-20-ketosteroids in urine and plasma. Jour. of Biol. Chemistry 210: 923, 1954.

35. Sobel, C., O. J. Golub, R. J. Henry, S. L. Jacobs and G. K. Basu. Study of the Norymberski methods for determination of 17-ketogenic steroids (17-hydroxycorticosteroids) in urine. Jour. of Clinical Endocrinology and Metabolism 18: 208, 1958.

36. Kliman, B. and R. E. Peterson. Double isotope derivative assay of aldosterone in biological extracts. Jour. of Biol. Chemistry 235: 1639, 1960.

37. Erlich, E. N. Reciprocal variations in urinary cortisol and aldosterone in response to increased salt intake. Jour. of Clinical Endocrinology and Metabolism 26: 1160, 1966.

38. Vernikos-Danellis, J. and E. Anderson. Changes in adrenal corticosterone concentration in rats: Method of bioassay for ACTH. Endocrinology 79: 624, 1966.

39. Peterson, R. E., J. B. Wyngaarden, S. L. Guerra, B. B. Brodie and J. J. Bunim. The physiological disposition and metabolic fate of hydrocortisone in man. J. of Clin. Investigation 34: 1779, 1955.

40. Cope, C. L. and E. G. Black. The behavior of 14^{C}-cortisol and estimation of cortisol production rate in man. Clinical Science 17: 147, 1958.

41. Kumagai, L. F., E. L. Simons, H. Brown and C. D. West. The transformation of radioactive cortisol in normal humans. Steroids Supplement II: 119, 1965.

42. Kelly, W. G. and J. Laragh. In: Advances in Metabolic Disorders. Vol. I, 1964, New York, Academic Press.

43. Kowarski, A., J. Finkelstein, B. Lopas and C. J. Migeon. The in vivo stability of the tritium label in 1, 2-H^{3}-d-aldosterone when used for measurement of aldosterone secretion rate by the double isotope dilution technique. Steroids 3: 95, 1964.

44. Quimby, E. H. and S. Feitelberg. Radioactive isotopes in medicine and biology. Lea and Febiger, Philadelphia 1963.

45. Roginsky, M., J. Shaver and N. P. Christy. A study of adrenocortical function in acromegaly. Jour. of Clinical Endocrinology and Metabolism 26: 1101, 1966.

46. Kelly, W. G., L. Bandi, J. N. Shoolery and S. Lieberman. Isolation and characterization of aldosterone metabolites from human urine; two metabolites bearing a bicyclic structure. Biochemistry 1: 172, 1962.

TRAINING AND EXPERI E OF EACH INDIVIDUAL NAMED IN ITEM 4 (U. pplemental 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	Columbia Univ College of Physicians & Surgeons	2 yrs	(Yes) No	(Yes) No
b. Radioactivity measurement standardization and monitoring techniques and instruments	Mt Sinai Hosp (Radiophysics Dept)	1 yr	(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
H^3	5 Mc	Columbia Univ College of Physicians & Surgeons	2 yrs	Purification, Human metabolism, Isolation & Synthesis
C^{14}	10 Mc	"	"	"

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/cm^2)	USE (Monitoring, surveying, measuring)

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

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

INFORMATION TO BE SUBMITTED ON ADDITIONAL SHEETS

13. FACILITIES AND EQUIPMENT. Describe laboratory facilities and remote handling equipment, storage containers, shielding, fume hoods, etc. Explanatory sketch of facility is attached. *(Circle answer)* Yes No

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, maintenance and repair of the source.

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 the type and amount of activity involved.

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.

Alfonso H. Janoski Capt MC
Applicant named in item 1

Date _____ By: _____

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 : 1961 OF—615960

Form AEC-313 a (10-61) PAGE 3

UNITED STATES ATOMIC ENERGY COMMISSION

APPLICATION FOR BYPRODUCT MATERIAL LICENSE

SUPPLEMENT A—HUMAN USE

Form approved. Budget Bureau No. 38-R080.1

This page may be completed by the physician's preceptor (if any) in the medical use of radioisotopes. When the information is not furnished by the preceptor, the name and present address of the preceptor (if any) should be shown in item 12 below.

9. (a) USING PHYSICIAN'S NAME	(b) NAME AND ADDRESS OF APPLICANT (If different from 9(a))
Alfonso H. Janoski Capt MC USAMRNL Denver, Colo. 80240	

10. CLINICAL TRAINING AND EXPERIENCE OF PHYSICIAN WHO WILL USE BYPRODUCT MATERIAL

(A) ISOTOPE	(B) CONDITION(S) DIAGNOSED OR TREATED	(C) NUMBER OF CASES	(D) TYPE OF PARTICIPATION FOR ALL CASES IN COLUMN B (circle applicable numbers of items in accordance with key set forth below)
I-131	Diagnosis of thyroid function	50	(1) 2 (3) (4)
	Treatment of hyperthyroidism	15	(1) 2 (3) (4)
	Treatment of thyroid cancer	4	(1) 2 (3) (4)
	Treatment of cardiac conditions		1 2 3 4
	Brain tumor localization	5	1 2 3 (4)
	Blood determinations		1 2 3 4
	Kidney function		1 2 3 4
	Others:		1 2 3 4
P-32 Soluble	Treatment of polycythemia and leukemia	10	(1) 2 3 (4)
	Brain tumor localization		1 2 3 4
	Treatment of bone metastases	2	1 2 3 (4)
	Others:		1 2 3 4
			1 2 3 4
P-32 $CrPO_4$	Treatment of prostatic cancer		1 2 3 4
	Treatment of cervical cancer		1 2 3 4
	Treatment of pleural effusions and/or ascites		1 2 3 4
	Others:		1 2 3 4
			1 2 3 4
Au-198 Colloid	Treatment of prostatic cancer		1 2 3 4
	Treatment of cervical cancer		1 2 3 4
	Treatment of pleural effusions and/or ascites	2	1 2 3 (4)
	Others:		1 2 3 4
			1 2 3 4
Cr-51	Blood determinations	25	(1) 2 (3) (4)
	Others:		1 2 3 4
			1 2 3 4
Other Isotopes	Tritium labelled & Carbon-14 labelled	6	(1) (2) 3 (4)
	Steroids - Research		1 2 3 4
			1 2 3 4

Key to above numbers (column D)

Active Participation and Discussion in the:

1. Examination of patients to determine suitability for radioisotope diagnosis and/or treatment and recommendations on dosage to be prescribed.
2. Collaboration in calibration and administration of dosages including related measurements and plotting of data.
3. Active period of training and experience of sufficient duration to permit followup of patients through treatment and posttreatment period including reevaluation as to effectiveness and complications.
4. Study and discussion of case histories to establish most efficacious diagnostic and/or therapeutic techniques for this radioisotope use.

11. TOTAL NUMBER OF HOURS OF PARTICIPATION IN CLINICAL TRAINING 240 hours

12. THE TRAINING AND EXPERIENCE INDICATED ABOVE WAS OBTAINED UNDER THE SUPERVISION OR GUIDANCE OF Dr Sergei Feitelberg - Mt Sinai Hosp New York; Dr Sidney Werner - Columbia-Presbyterian Med Center N.Y.; Dr Nicholas P. Christy - Roosevelt Hospital, NY. AT _____ _____

(Name of physician (preceptor)) (Institution) (Signature)

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	Nuclear Medicine Dept Univ. Hospital, Ann Arbor, Mich.	1 mo.	(Yes) No	(Yes) No
b. Radioactivity measurement standardization and monitoring techniques and instruments	"	1 mo.	(Yes) No	(Yes) No
c. Mathematics and calculations basic to the use and measurement of radioactivity	"	1 mo.	(Yes) No	(Yes) No
d. Biological effects of radiation	"	1 mo.	(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
I^{131}	10 Mc	Univ. of Mich. Med. Center	1 Month	Diagnostic and Therapeutic
Xe^{133}	1 Curie	Univ. of Mich. Med. Center	1 Year	Research

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/cm^2)	USE (Monitoring, surveying, measuring)

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

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

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 is attached. (Circle answer) Yes No

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, maintenance and repair of the source.

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 the type and amount of activity involved.

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.

Richard P. Carson, Capt., M.C.
Applicant named in item 1

Date _____ By: _____

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 : 1964 O—748-382

Form AEC-313 a (10-61) PAGE 3

UNITED STATES ATOMIC ENERGY COMMISSION

APPLICATION FOR BYPRODUCT MATERIAL LICENSE

SUPPLEMENT A—HUMAN USE

Form approved. Budget Bureau No. 38-R080.1

This page may be completed by the physician's preceptor (if any) in the medical use of radioisotopes. When the information is not furnished by the preceptor, the name and present address of the preceptor (if any) should be shown in item 12 below.

9. (a) USING PHYSICIAN'S NAME	(b) NAME AND ADDRESS OF APPLICANT (If different from 9(a))
Richard P. Carson, Capt MC USAMRNL Denver, Colo.	

10. CLINICAL TRAINING AND EXPERIENCE OF PHYSICIAN WHO WILL USE BYPRODUCT MATERIAL

(A) ISOTOPE	(B) CONDITION(S) DIAGNOSED OR TREATED	(C) NUMBER OF CASES	(D) TYPE OF PARTICIPATION FOR ALL CASES IN COLUMN B (circle applicable numbers of items in accordance with key set forth below)
I-131	Diagnosis of thyroid function	24	(1) (2) 3 (4)
	Treatment of hyperthyroidism	6	(1) (2) (3) (4)
	Treatment of thyroid cancer	3	(1) (2) (3) (4)
	Treatment of cardiac conditions	1	1 2 3 (4)
	Brain tumor localization		1 2 3 4
	Blood determinations	3	(1) (2) 3 (4)
	Kidney function		1 2 3 4
	Others:		1 2 3 4
P-32 Soluble	Treatment of polycythemia and leukemia	3	(1) (2) (3) (4)
	Brain tumor localization		1 2 3 4
	Treatment of bone metastases		1 2 3 4
	Others:		1 2 3 4
			1 2 3 4
P-32 $CrPO_4$	Treatment of prostatic cancer		1 2 3 4
	Treatment of cervical cancer		1 2 3 4
	Treatment of pleural effusions and/or ascites		1 2 3 4
	Others:		1 2 3 4
			1 2 3 4
Au-198 Colloid	Treatment of prostatic cancer		1 2 3 4
	Treatment of cervical cancer		1 2 3 4
	Treatment of pleural effusions and/or ascites		1 2 3 4
	Others:		1 2 3 4
			1 2 3 4
Cr-51	Blood determinations	3	(1) (2) 3 (4)
	Others:		1 2 3 4
			1 2 3 4
Other Isotopes	Hg^{197} Brain and Renal scanning	15	(1) (2) 3 (4)
	Na^{24} Dilution study	1	(1) (2) 3 (4)
			1 2 3 4

Key to above numbers (column D)

Active Participation and Discussion in the:

1. Examination of patients to determine suitability for radioisotope diagnosis and/or treatment and recommendations on dosage to be prescribed.
2. Collaboration in calibration and administration of dosages including related measurements and plotting of data.
3. Active period of training and experience of sufficient duration to permit followup of patients through treatment and posttreatment period including reevaluation as to effectiveness and complications.
4. Study and discussion of case histories to establish most efficacious diagnostic and/or therapeutic techniques for this radioisotope use.

11. TOTAL NUMBER OF HOURS OF PARTICIPATION IN CLINICAL TRAINING 160 hours

12. THE TRAINING AND EXPERIENCE INDICATED ABOVE WAS OBTAINED UNDER THE SUPERVISION OR GUIDANCE OF

Wm. H. Beirwaltes, MD, AT Univ. of Mich Med Center
Ann Arbor, Mich

(Name of physician (preceptor)) (Institution) (Signature)

U. S. ARMY MEDICAL RESEARCH AND NUTRITION LABORATORY
FITZSIMONS GENERAL HOSPITAL
DENVER, COLORADO, 80240

IN REPLY REFER TO

MEDEN-PH

7 July 1967

SUBJECT: Application for Amendment to AEC Byproduct Material License No. 05-00046-13

THRU: Commanding General
U. S. Army Medical Research and Development Command
ATTN: Chief, Medical Rsch Br.
Office of The Surgeon General TED 13 July 1967
Department of the Army
Washington, D. C. 20315

TO: The Surgeon General
ATTN: MEDPS-PO
Department of the Army
Washington, D. C. 20315

1. Submitted herewith is application for renewal and amendment to Byproduct Material License No. 05-00046-13 in six copies for appropriate processing.

2. Approval has been granted by the Office of The Secretary of the Army for the use of radioisotopes in human volunteers; therefore, this application is for an AEC amendment to use radioisotopes in humans and to use them at Ft. Lewis, Washington and Pikes Peak, Colo.

3. Request expeditious handling of the request to permit meeting the deadline imposed by the limited period of availability of the 14,100 ft altitude area of Pikes Peak for this study.

JAMES C. SYNER
Colonel, MC
Commanding

3 Incls:
1. AEC Forms 313 & 313a
2. Protocol
3. Trng & Exp

96146

DEPARTMENT OF THE ARMY
OFFICE OF THE SURGEON GENERAL
WASHINGTON, D.C. 20315

IN REPLY REFER TO:
MEDPS-PO

2 August 1967

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

Gentlemen:

Recommend that the inclosed application for amendment to AEC Byproduct Material License for Fitzsimons General Hospital be approved.

Sincerely,

HERSCHEL E. GRIFFIN
Colonel, M. C.
Chief, Preventive Medicine Division

1 Incl
as (in trip)

96146

6-13 HB

Form AEC-313 (5-58)	ATOMIC ENERGY COMMISSION **APPLICATION FOR BYPRODUCT MATERIAL LICENSE**	Form approved. Budget Bureau No. 38-R027.4

INSTRUCTIONS.–Complete Items 1 through 16 if this is an initial application. If application is for renewal of a license, complete only Items 1 through 7 and indicate new information or changes in the program as requested in Items 8 through 15. Use supplemental sheets where necessary. Item 16 must be completed on all applications. Mail three copies to: U.S. Atomic Energy Commission, Washington, D.C., 20545. Attention: Isotopes Branch, Division of Licensing and Regulation. 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.)*

Department of the Army
Fitzsimons General Hospital and
U. S. Army Med. Rsch. & Nutrition Lab.
Denver, Colorado 80240

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

Same as 1 a

2. DEPARTMENT TO USE BYPRODUCT MATERIAL

Radioisotope Clinic
Cardiac Catheterization Laboratory

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

Present application is for amendment to Lic. No. 05-00046-13 (A66)

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.)*

As specified and approved by the Radioisotope Committee, Fitzsimons General Hospital

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.)*

Same as 4

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

Xenon-133

(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.)*

1) Xenon-133 gas dissolved in saline
2) 50 millicuries in precalibrated ampules of 3-4 millicuries each, obtained from Union Carbide Corporation, Sterling Forest Research Center.

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.)*

See Form AEC 313a attached.

93940 T10

(Continued on reverse side)

Form AEC-313 (5-58) Page Two

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	Individuals will have appropriate training and experience prior to their approval by the Radioisotope Committee, Fitzsimons General Hospital.		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
Same as 8.				

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/cm^2)*	USE *(Monitoring, surveying, measuring)*
As described in application for renewal of Byproduct Material License No. 05-00046-13 (A66) dated 21 June 1966.					

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

See License # 05-00046-13 (A66)

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

See License # 05-00046-13 (A66)

INFORMATION TO BE SUBMITTED ON ADDITIONAL SHEETS

13. FACILITIES AND EQUIPMENT. Describe laboratory facilities and remote handling equipment, storage containers, shielding, fume hoods, etc. Explanatory sketch of facility is attached. *(Circle answer)* Yes No See License # 05-00046-13 (A66)

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, maintenance and repair of the source.

See License # 05-00046-13 (A66)

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 the type and amount of activity involved. See attachment 1

CERTIFICATE (This item must be completed by applicant)

16. THE APPLICANT AND ANY OFFICIAL EXECUTING THIS CERTIFICATION 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.

Dept of the Army, FGH&US Army Med Rsch & Nutr Lab, Denver, Colo 80240
Applicant named in item 1

Date _____ By: Edwin L Overholt

EDWIN L OVERHOLT, Col., MC
Chairman, Radioisotope Committee
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.

GPO 865-815

Form AEC-313 a (10-61) PAGE 1

UNITED STATES ATOMIC ENERGY COMMISSION

APPLICATION FOR BYPRODUCT MATERIAL LICENSE

SUPPLEMENT A—HUMAN USE

Form approved. Budget Bureau No. 38-R080.1

If byproduct material is for "human use" (internal administration of byproduct mat[illegible] or the radiation therefrom to human beings), complete this supplement and attach to the application for byproduct material license.

1. (a) USING PHYSICIAN'S NAME

Dept of the Army, Fitzsimons Gen Hosp & USA Med Rsch & Nutr Lab, Denver, Colo 80240

(b) NAME AND ADDRESS OF APPLICANT (If different from 1(a))

Same as 1a

2. THE USING PHYSICIAN INDICATED ABOVE IS LICENSED TO DISPENSE DRUGS IN THE PRACTICE OF MEDICINE BY A STATE OR TERRITORY OF THE UNITED STATES, THE DISTRICT OF COLUMBIA, OR THE COMMONWEALTH OF PUERTO RICO.

As permitted by Radioisotope Committee, Fitzsimons Gen Hosp

CIRCLE ANSWER: (YES) NO

3. A STATEMENT OF USING PHYSICIAN'S CLINICAL RADIOISOTOPE EXPERIENCE (PAGE 3 OF THIS SUPPLEMENT) IS SUBMITTED IN SUPPORT OF THIS APPLICATION. IF ANSWER IS NO, USE PAGE 2 OF THIS SUPPLEMENT TO EXPLAIN OR REFER TO OTHER APPLICATION OR RELATED DOCUMENTS ON WHICH THIS INFORMATION APPEARS.

As permitted by Radioisotope Committee, Fitzsimons Gen Hosp

CIRCLE ANSWER: YES (NO)

PROPOSED DIAGNOSIS OR TREATMENT

4. (a) DESCRIBE PURPOSE FOR WHICH BYPRODUCT MATERIAL WILL BE USED INCLUDING SPECIFIC CONDITIONS OR DISEASES TO BE DIAGNOSED OR TREATED (Use page 2 if necessary): Xenon-133 - For measurement of myocardial blood flow in patients with (or suspected) coronary artery disease.

(b) CHEMICAL FORM ADMINISTERED:

Xenon-133 - gas dissolved in saline

(c) DESCRIBE PROCEDURES WHICH WILL BE OBSERVED TO MINIMIZE HAZARD FROM HANDLING, STORAGE, AND DISPOSAL OF THE BYPRODUCT MATERIAL:

See attachment 1

(d) DESCRIPTION AND SKETCHES OF SPECIAL DEVICES TO BE USED FOR ADMINISTERING BYPRODUCT MATERIAL TO HUMAN BEINGS ARE

(1) ATTACHED (LITERATURE REFERENCES WILL SUFFICE) See attachment 2 — CIRCLE ANSWER: (YES) NO

(2) ON FILE WITH THE ISOTOPES EXTENSION REFER TO APPLICATION NO _____ — CIRCLE ANSWER: YES (NO)

5. (a) PROPOSED DOSAGE SCHEDULE.—In millicuries for internally administered byproduct material other than discrete fixed sources; and in roentgens or rads, as appropriate, for internal or external irradiation from discrete fixed sources (gold seeds, cobalt needles, etc.) state separately for each condition or disease (use page 2 if necessary):

Four injections of 50 - 100 microcuries each of Xenon-133 (Total dose per subject - less than 500 Microcuries)

(b) INVESTIGATIVE PROPOSAL FOR EXPERIMENTAL, NEW OR UNUSUAL HUMAN USES IS ATTACHED. (Attachment should include outline of conditions to be evaluated, including data from animal studies and/or abstract of literature reference if any, number and type of patients (i. e. age group, moribund, etc.)) — CIRCLE ANSWER: (YES) NO

6. IF BYPRODUCT MATERIAL WILL NOT BE OBTAINED IN PRECALIBRATED FORM FOR ORAL ADMINISTRATION OR IN PRECALIBRATED AND STERILIZED FORM FOR PARENTERAL ADMINISTRATION, DESCRIBE IDENTIFICATION, PROCESSING, AND STANDARDIZATION PROCEDURES: Xenon-133 will be obtained from Union Carbide Corp., Sterling Forest Research Center in precalibrated ampules containing the gas dissolved in saline. Sterilization of the solution will be accomplished by drawing up aliquots of the solution thru a millipore filter into an airtight sterile syringe prior to use.

93940

7. THE PROPOSED USE OF BYPRODUCT MATERIAL HAS BEEN, OR WILL BE, APPROVED BY THE MEDICAL ISOTOPE COMMITTEE. — CIRCLE ANSWER: (YES) NO

HOSPITAL FACILITIES FOR INDIVIDUAL PRACTICE USE ONLY

8. (a) THE APPLICANT HAS COMPLETED ARRANGEMENTS FOR A HOSPITAL TO ADMIT RADIOACTIVE PATIENTS WHENEVER ADVISABLE. — CIRCLE ANSWER: YES NO

(b) A COPY OF INSTRUCTIONS TO BE FURNISHED TO THE HOSPITAL AS TO RADIOLOGICAL SAFETY PRECAUTIONS TO BE TAKEN AND AVAILABLE RADIATION INSTRUMENTATION IS ATTACHED. — CIRCLE ANSWER: YES NO

Form AEC-313 a
(10-61)
PAGE 2

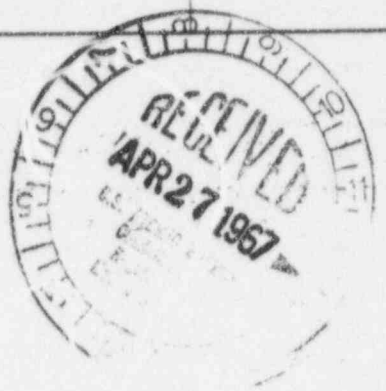
UNITED STATES ATOMIC ENERGY COMMISSION

APPLICATION FOR BYPRODUCT MATERIAL LICENSE

SUPPLEMENT A — HUMAN USE

Form approved.
Budget Bureau No. 38-R080.1

This page may be used for providing additional information. Please cross reference to specific items.



Item 3. See license # 05-00046-13 (A66)

U.S. GOVERNMENT PRINTING OFFICE : 1961 O-615965

ATTACHMENT 1 (AEC 313, item 15 and 313a, item 4c)

The Xenon-133 gas dissolved in saline will be obtained in precalibrated ampules from Union Carbide Corp. The solution will be sterilized by passage through a Millipore filter as it is drawn up into a sterile airtight syringe just prior to use. The material will be stored in a shielded hood in the Radioisotope Clinic. The lead shielding will be of one centimeter or more thickness to keep exposure rate below 2.5 mrad/hour. Disposable gloves will be used to handle the material. Used syringes will be handled by the Radioisotope Clinic as described in application for License No. 05-00046-13 (A66). Any Xenon-133 solution remaining at the end of the study will be allowed to decay for 2 months (10 half-lives) and then disposed of by pouring down a sink drain.

The injected Xenon is excreted from the body by the lungs, therefore expired air of the patients receiving the material will be collected in meterological balloons and subsequently released outside in an open area. As the volume of the catheterization laboratory is 88.5 cubic meters (88,500 liters), the release of 250 microcuries of Xenon-133 gas into the room air would produce a concentration of less than 3×10^{-6} microcuries/ml of air (exempt concentration under Title 10, Chap. 1, Section 30.70, Sched. A of the Federal Register). Because of the above and the low dose to be administered (less than 500 microcuries) contamination of laboratory air will be negligible.

ATTACHMENT 2 (AEC 313a, item 4d)

A complete description of the procedure for measuring myocardial blood flow by selective coronary injection of Xenon-133 in saline can be found in the following reference:

Ross, R.S., Ueda, K., Lichtlen, P.R., and Rees, J.R.: Measurement of Myocardial Blood Flow in Animals and Man by Selective Injection of Radioactive Inert Gas into the Coronary Arteries. Circ. Res. 15: 28, 1964.

Results of a clinical study utilizing this technique has also been reported:

Bernstein, L., Friesinger, G.C., Lichtlen, P.R. and Ross, R.S.: The Effect of Nitroglycerin on the Systemic and Coronary Circulation in Man and Dogs. Circ. 33:107, 1966.

6 April 1967

PROTOCOL: Effects of Selective Coronary Arteriography on Myocardial Blood Flow in Man

INTRODUCTION

Selective coronary arteriography has become an important addition to the list of diagnostic procedures available for the detection and evaluation of coronary artery disease. Studies of the coronary circulation utilizing this technique have materially aided our understanding of various aspects of this disease. The hemodynamic consequences of injection of radiopaque agents directly into the coronary circulation have been studied both in animals and man (1 - 3). Changes in myocardial blood flow (MBF) have been observed in opened-chest dogs (4, 5) and more recently in intact dogs, as well (6). However, we are not aware of any studies reporting the effect of coronary arteriography on MBF in man. The study to be described in this protocol is designed to fill this gap in our knowledge.

METHODS

MBF will be measured by selective intracoronary injection of Xenon-133 gas dissolved in sterile saline and calculated in ml/min/100 gm from the precordial disappearance of radioactivity. The details of the procedure to be followed have been fully described by Ross, et al. (7). In addition, one of the investigators (Captain R. P. Carson) has had a year's experience with this technique, both in animals and man, while a postdoctoral fellow at the University of Michigan. Enclosed are three figures from his studies illustrating the method of calculating MBF from the precordial radioactivity curve (fig. 1), the reliability of the method for measuring MBF (fig. 2), and the results of sublingual administration of nitroglycerin on MBF in nine patients (fig. 3).

Subjects will consist of patients with suspected or known coronary artery disease undergoing selective coronary arteriography during cardiac catheterization. Patient consent will be obtained after they are informed of the procedures to be performed and the risks involved from the study and the use of a radioisotope.

The study will be conducted in the cardiac catheterization laboratory of Fitzsimons General Hospital. Four measurements of MBF will be made on each subject, two during a control period and then 30 seconds and again 300 seconds following coronary injection of contrast agent. Each measurement will require an injection of 50 - 100 microcuries of Xenon-133. the total amount of radioactivity administered to each subject being less than 500 microcuries.

It has been estimated that 90-95% of an administered dose of Xenon-133 is expired during the first passage through the lungs. Captain Carson was able to confirm this in a dog study. Because of this and the small doses used, the systemic radiation dose to the subject is small. The organs receiving the largest exposure are the heart and lungs. Lassen (3) has calculated the exposure dose from an intra-arterial injection of 5 millicuries of a saline solution of Xenon-133 as follows: tracheal mucosa - 96.8 mrad, lung - 17.5 mrad, adipose tissue - 8.8 mrad, gonads - 1.1 mrad, and other tissues - 1.6 mrad. For the local organ being studied: brain (400 gm tissue exposed) - 86 mrad, kidney (150 gm tissue exposed) - 31 mrad. The average weight of an adult human heart is 300 gm. We will be injecting one tenth this dose of Xenon-133; thus, the exposure dose will be correspondingly reduced.

Since the injected Xenon is excreted from the body through the lungs, the expired air of the subjects will be collected in suitable containers such as meteorological balloons or other large-capacity containers and subsequently

released outside in an open area. As the total dose to be administered is low and the expired air will be collected, contamination of laboratory air will be negligible. In animal studies at the University of Michigan, no appreciable increase in room background could be detected using an ionizing chamber monitor under the conditions described.

The Xenon-133 will be obtained precalibrated in saline solution from the Sterling Forest Research Center, Union Carbide Corporation, New York. It will be stored in the Radioisotope Clinic in a hood with lead shielding of 1 cm or more thickness to keep the exposure rate below 2.5 mrad/hr. Disposable gloves will be used to handle the material. Aliquots of the solution will be drawn up through a Millipore filter into sterile airtight syringes and transported in lead shielded containers to the cardiac catheterization laboratory the day of the study. Contaminated syringes, gloves, etc., will be handled through the Radioisotope Division. Any Xenon solution remaining at the end of the study will be allowed to decay for two months (10 half-lifes) and then be disposed of by pouring down a sink drain.

The detecting and recording equipment will be mounted on a portable cart and will consist of a 2 x 3 inch sodium iodide crystal in an adjustable probe, a linear ratemeter, and a strip chart recorder. A portable instrument will be available for continuous monitoring of the room air during the study.

INVESTIGATORS

Principal investigator for this study will be: Captain Richard P. Carson, MC.

Associate investigators will be: Captain Charles Peterson, MC; Lt. Colonel Robert Jones, MC; Major David Preston, MC.

RICHARD P. CARSON
Captain, MC

REFERENCES

1. Friesinger, G. C., et al.: Hemodynamic effects of the injection of radiopaque material. Circulation 31: 730, 1965.

2. Benchimol, A. and McNally, E. M.: Hemodynamic and electrocardiographic effects of selective coronary angiography in man. N. Eng. J. Med. 274: 1217, 1966.

3. Ross, R. S., et al.: Electrocardiographic and hemodynamic observations during selective coronary cineangiocardiography. J. Clin. Invest. 41: 1395, 1962. (Abst.)

4. Griggs, D. M., Jr., et al.: Effects of radiopaque material on phasic coronary flow and myocardial oxygen consumption. Clinical Res. 14: 274, 1966 (Abst.)

5. Guzman, S. V. and West, J. W.: Cardiac effects of intracoronary arterial injections of various roentgenographic contrast media. Am. Heart J. 58: 597, 1959.

6. Carson, R. P.: Unpublished data.

7. Ross, R. S., et al.: Measurement of myocardial blood flow in animals and man by selective injection of radioactive inert gas into the coronary arteries. Circ. Res. 15: 28, 1964.

8. Lassen, N. A.: Assessment of tissue radiation dose in clinical use of radioactive inert gases with examples of absorbed doses from H_2 - 3, Kr - 85 and Xe - 133. Minerva Nucleare 8: 211, 1964.

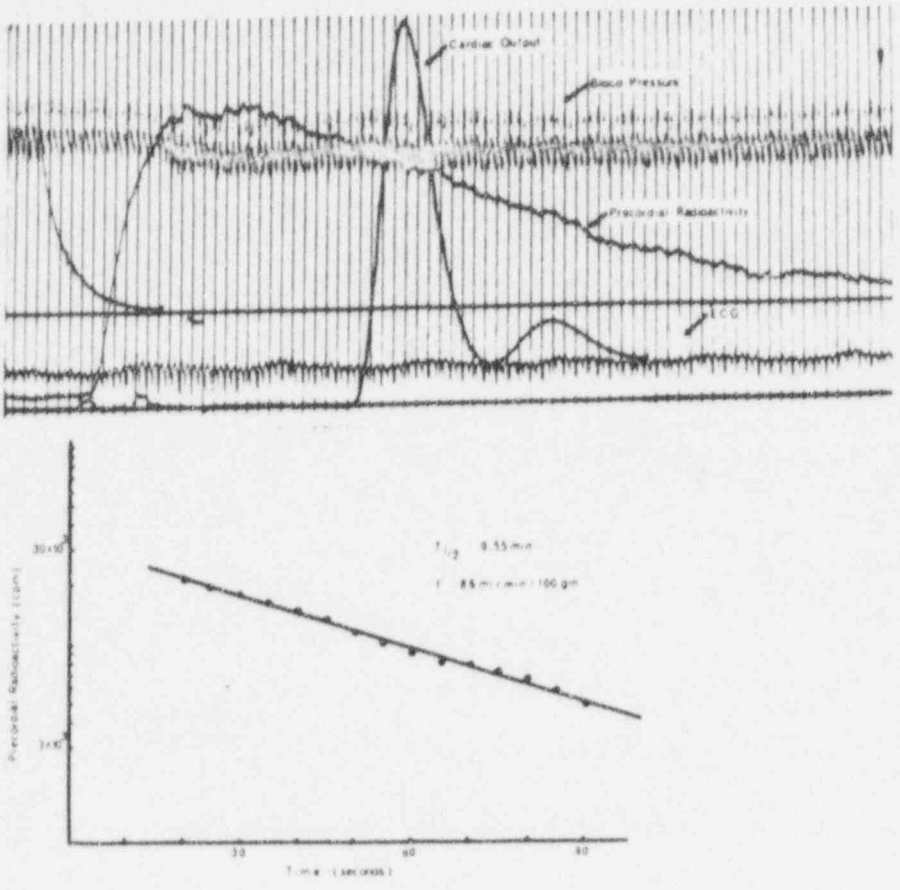


FIG. 1

Above: Portion of record from closed-chest dog experiment showing typical precordial radioactivity curve following injection of Xenon-133 in saline through a catheter positioned within the ostium of the left coronary artery. Vertical lines represent 1 second time intervals.

Below: Semilogarithmic replot of the washout portion of the curve (after subtracting background). The half time of this line is used to calculate flow from the formula

$$\text{Flow} = \frac{\frac{\log 2 \times 100}{T_{\frac{1}{2}}}}{G}$$

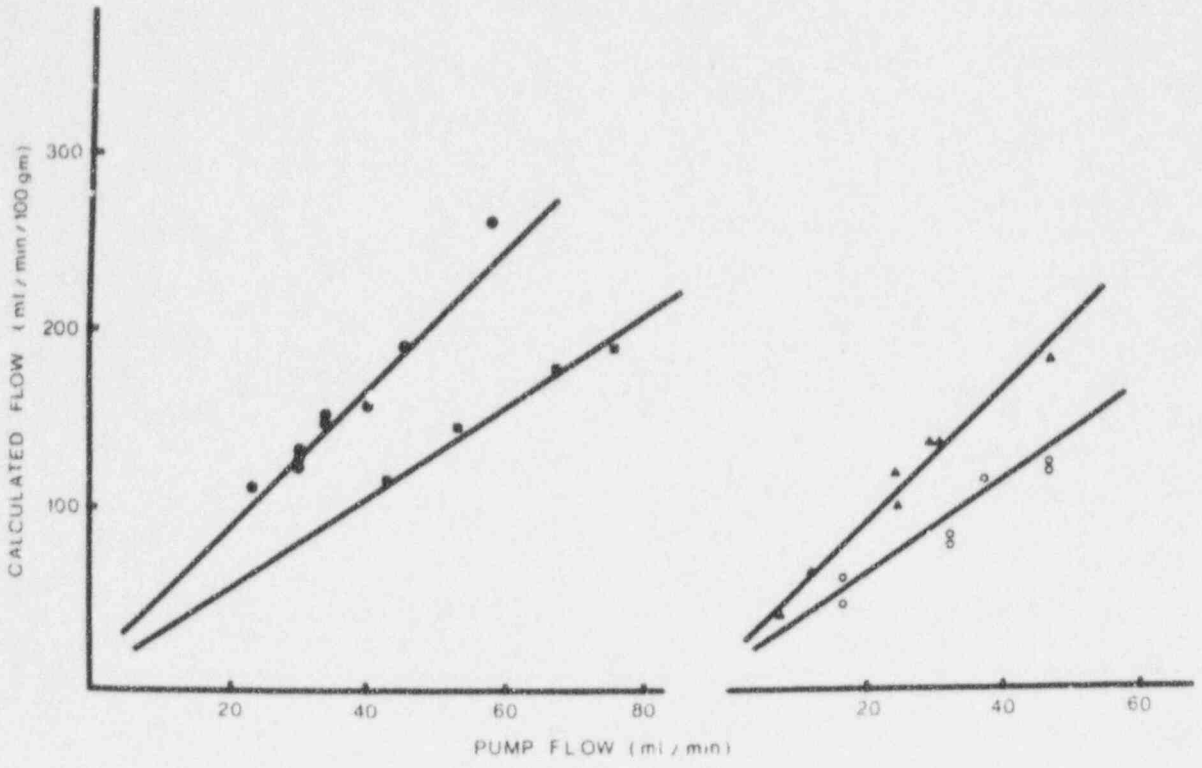


FIG. 2

Results of 4 opened-chest dog experiments in which posterior circumflex branch of left coronary artery was cannulated and blood supplied from femoral artery via an externally controlled rotor pump. Xenon-133 in saline was injected through a side arm in the tubing between the pump and the coronary vessel. The scintillation probe was positioned over the thoracotomy at the level of the anterior chest wall. MBF was determined by the Xenon method at various pump speeds. Flow rates calculated from the Xenon washout curves were then plotted against the corresponding pump flow rates.

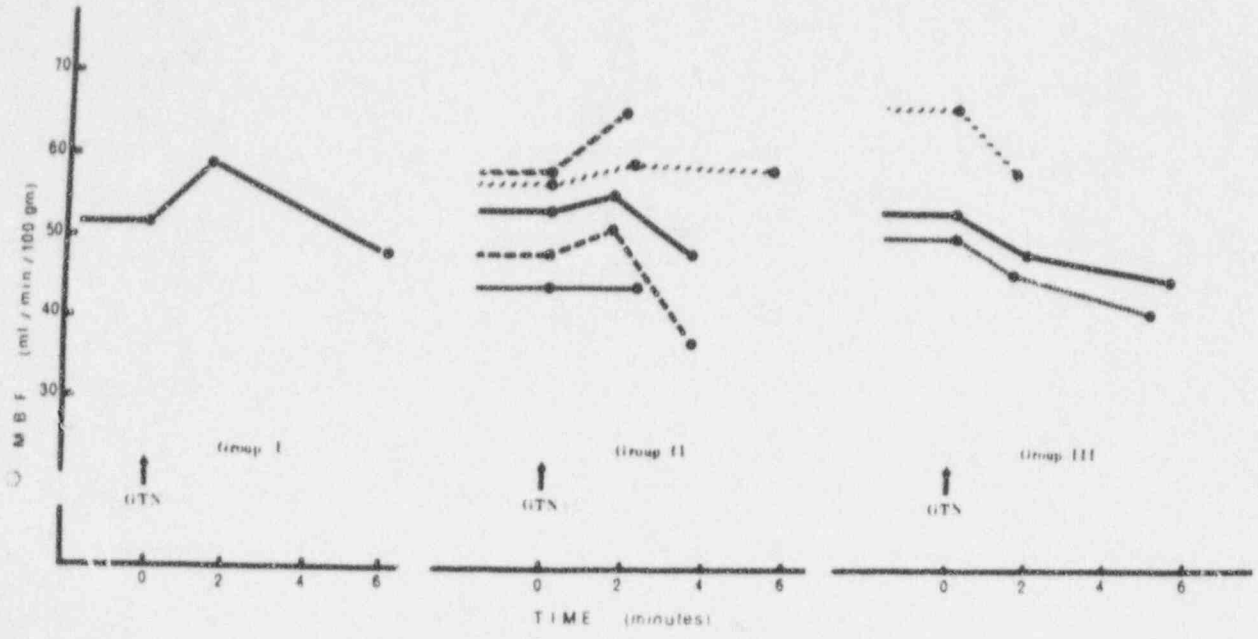


FIG. 3

Effects of sublingual administration of 0.3 mg nitroglycerin in 9 male subjects. MBF was calculated from the disappearance rate of precordial radioactivity following selective injection of Xenon-133 in saline into the right coronary artery.
Group I - One patient with no cardiac disease.
Group II - Five patients with coronary artery disease.
Group III - Three patients with myocardial hypertrophy.

MEDDO-X 13 April 1967

SUBJECT: Application for Amendment of Byproduct Material License

TO: The Surgeon General
ATTN: MEDPS-P
Department of the Army
Washington, D. C. 20315

Submitted herewith is Application for Amendment of Byproduct Material License Number 5-46-13 to permit the use of pre-calibrated Xenon-133 gas dissolved in saline for measurement of myocardial blood flow. AEC Form 313 and 313a are submitted in six copies for appropriate processing.

Incl
as

ROBERT E. BLOUNT
Major General, MC
Commanding

DEPARTMENT OF THE ARMY
OFFICE OF THE SURGEON GENERAL
WASHINGTON, D.C. 20315

IN REPLY REFER TO:
MEDPS-PO

20 April 1967

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

Gentlemen:

Recommend approval of the inclosed application for amendment to AEC Byproduct Material License Number 5-46-13, Fitzsimons General Hospital, Denver, Colorado.

Sincerely,

WILLIAM E. FROEMMING
Colonel, M. C.
Preventive Medicine Division

1 Incl
as (in trip)

93940

Form AEC-313 (5-58)

ATOMIC ENERGY COMMISSION

APPLICATION FOR BYPRODUCT MATERIAL LICENSE

Form approved. Budget Bureau No. 38-R027.4

INSTRUCTIONS.--Complete Items 1 through 16 if this is an initial application. If application is for renewal of a license, complete only Items 1 through 7 and indicate new information or changes in the program as requested in Items 8 through 15. Use supplemental sheets where necessary. Item 16 must be completed on all applications. Mail three copies to: U.S. Atomic Energy Commission, Washington, D.C., 20545. Attention: Isotopes Branch, Division of Licensing and Regulation. 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.)*

Department of the Army
Fitzsimons General Hospital 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).)*

Same as 1(a.)

2. DEPARTMENT TO USE BYPRODUCT MATERIAL

U. S. Army Medical Research and
Nutrition Laboratory

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

05-00046-13

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.)*

Users approved by the Radioisotope
Committee

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.)*

As designated by Radioisotope Committee

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

A. Strontium-90

(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.)*

A. Strontium sulfate sealed source manufactured by United States Radium Corporation, 4150 Old Berwick Rd., Bloomsburg, Pa. 17815.
Source will be in a Model AD-10 cell for a gas chromatograph manufactured by the Glowall Corp. (See item #7)

A. 13 millicuries

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.)*

For use in a Model 310 gas chromatograph manufactured by the Glowall Corp.,
2530 Wyandotte Rd., Willow Grove, Pa., 19090.

31213

(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	Individuals will be approved by the Radioisotope Committee, Fitzsimons General Hospital		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
As above				

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 attached Form AEC 313b					

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

Calibrated every 6 months or as needed with Strontium-90 standard.

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

Film badges processed at 4-week intervals by Lexington Army Depot

INFORMATION TO BE SUBMITTED ON ADDITIONAL SHEETS

13. FACILITIES AND EQUIPMENT. Describe laboratory facilities and remote handling equipment, storage containers, shielding, fume hoods, etc. Explanatory sketch of facility is attached. (Circle answer) Yes No

As specified in Application for AEC Byproduct Material License 05-00046-13 dated 21 June 6

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, maintenance and repair of the source.

As specified in Application for AEC Byproduct Material License 05-00046-13 dated 21 June 66

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 the type and amount of activity involved.

As specified in Application for AEC Byproduct Material License 05-00046-13 dated 21 June 6

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.

Department of the Army
FGH & USAMRNL
Denver, Colorado 80240
Applicant named in Item 1

Date 22 November 1966

By: Edwin L. Overholt
EDWIN L. OVERHOLT
Chief, Radioisotope Committee
Title of certifying official

FGH & USAMRNL

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.

Form AEC-313b (7-66)

APPLICATION FOR BYPRODUCT MATERIAL LICENSE
SUPPLEMENT B—SEALED SOURCES

Form approved
Budget Bureau No. 38-R028.3

If application is for byproduct material to be used in or manufactured as a "sealed source" complete this supplement and attach to the application for byproduct material license. Applicant for *use* of sealed source should complete Section I. An applicant desiring to *manufacture* a sealed source should complete Section II. If information has been submitted previously and there are no changes in the sealed source and/or device design or other changes in information submitted previously, details requested below may be omitted *provided* reference is made on line below to the application or other document on which this information appears:

SECTION I—USE (*See instructions*) Sealed Source:

1. IF SEALED SOURCE OR DEVICE CONTAINING SEALED SOURCE IS MANUFACTURED COMMERCIALLY, GIVE FOLLOWING INFORMATION:
   A. Manufacturer or supplier of sealed source and/or device: U.S. Radium Corp., 4150 Old Berwick Rd., Bloomsburg, Pa. Glowall Corp., 2530 Wyandotte Rd., Willow Grove, Pa.
   B. Make and model number of sealed source and/or device: Model AD-10 for use in Model 310 Gas Chromatograph
   C. Person who will hold legal title to sealed source: Fitzsimons General Hospital and U.S. Army Medical Research and Nutrition Laboratory, Denver, Colo.

2. (a) NAME OF PERSON WHO WILL PERFORM NECESSARY PERIODIC LEAKAGE TESTS (*6-month intervals for beta-gamma; 3-month period for alpha emitters. See instructions*): Radiation Safety Officer, U.S. Army Medical Research & Nutrition Laboratory, Denver, Colo. (Charles G. Liddle, Capt., VC)

   (b) IF ABOVE PERSON IS NOT THE SUPPLIER, MANUFACTURER, NOR A COMMERCIAL LABORATORY ROUTINELY OFFERING SUCH SERVICES, GIVE BRIEF STATEMENT OF EXPERIENCE OR TRAINING OF SUCH PERSON IN TECHNIQUES TO BE EMPLOYED, A STATEMENT OF LEAK TESTING PROCEDURES INCLUDING EVIDENCE OF ITS EFFICACY AND INSTRUMENTATION TO BE USED:

See attached for training and experience of individual who will perform leak tests.

Leak tests will be performed using wet gauze swipes. Swipes will be placed in vials containing a toluene scintillation solution and counted in a liquid scintillation counting system (either a Packard Model 314EX, a Packard Model 3314, or a Nuclear Chicago Mark I Liquid scintillation counter). The instruments can readily detect levels of contamination above 5×10^{-5} microcuries.

3. ARRANGEMENTS WHICH WILL PREVAIL FOR PERFORMING INITIAL RADIATION SURVEY (*if appropriate*), SERVICING, MAINTENANCE, REPAIR, CONTROL, AND DISPOSAL, ETC., OF THE SOURCE:

Initial radiation survey will be performed by U. S. Radium Corporation. Servicing maintenance or repair will be performed by The Glowall Corp. or the U. S. Radium Corp. Control and/or disposal will be carried out as with other radioisotopes possessed and used by this Laboratory under AEC License No. 05-00046-13.

SECTION II—MANUFACTURE

4. IF SEALED SOURCE TO BE MANUFACTURED OR FABRICATED BY THE APPLICANT IS DESIGNED TO TRANSMIT ONLY GAMMA RAYS AND CONTAINS IN ELEMENTAL FORM (*but not powders*) COBALT 60, IRIDIUM 192, GOLD 198, TANTALUM 182, OR THULIUM 170, GIVE FOLLOWING INFORMATION AND DISREGARD QUESTIONS 5 THROUGH 12 ON THIS SUPPLEMENT:
   (a) Quantity of byproduct material per source and model number
   (b) Leak testing procedure to be employed;
   (c) Attach annotated engineering drawing of source container and holder, if any;
   (d) Describe label to be affixed to source container and/or source holder (*or attach copy. See instructions*):

91213

(*Continued on reverse side*)

Training and Experience: Charles G. Liddle, Capt VC

Form AEC-313

Item 8 Type of Training:	Where Trained	Duration of Training	
a. Principles and practices of radiation protection	Walter Reed Army Institute of Research	2 weeks	Formal
	Taft Sanitary Engineering Center	4 weeks	Formal
	University of Rochester	1 year	Formal
b. Radioactivity measurement standardization and monitoring techniques and instruments	"	"	"
c. Mathematics and calculations basic to the use and measurement of radioactivity	"	"	"
d. Biological effects of radiation	"	"	"

Item 9 Experience with radiation

Isotope	Maximum amount	Where experience gained	Duration	Type of Use
H^3	1 Mc	Fourth U S Army Med Lab	1 yr	research
		Walter Reed Army Institute of Research	2 yrs	research
		USAMRNL	1 yr	research
C^{14}	"	"	"	"
P^{32}	"	"	"	"
S^{35}	"	"	"	"
Ca^{45}	"	"	"	"
Cr^{51}	"	"	"	"
Fe^{59}	"	"	"	"
Co^{60}	"	"	"	"
Zn^{65}	"	"	"	"
Sr^{85}	"	"	"	"
Sr^{90}	"	"	"	"
I^{125}	"	"	"	"
I^{131}	"	"	"	"
Cs^{137}	"	"	"	"
$Ba\text{-}La^{140}$	"	"	"	"
Hg^{197}	"	"	"	"
Hg^{203}	"	"	"	"

Form AEC-313 (5-58)	ATOMIC ENERGY COMMISSION **APPLICATION FOR BYPRODUCT MATERIAL LICENSE**	Form approved Budget Bureau No. 38-R027.4.

INSTRUCTIONS.—Complete Items 1 through 16 if this is an initial application. If application is for renewal of a license, complete only Items 1 through 7 and indicate new information or changes in the program as requested in Items 8 through 15. Use supplemental sheets where necessary. Item 16 must be completed on all applications. Mail three copies to: U.S. Atomic Energy Commission, Washington, D.C., 20545. Attention: Isotopes Branch, Division of Licensing and Regulation. 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.)*

Department of the Army
Fitzsimons General Hospital 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).)*

Same as 1(a)

2. DEPARTMENT TO USE BYPRODUCT MATERIAL

U. S. Army Medical Research and
Nutrition Laboratory

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

03-00046-13

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.)*

Users approved by the Radioisotope
Committee

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.)*

As designated by Radioisotope Committee

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

A. Strontium-90

(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.)*

A. Strontium sulfate sealed source manufactured by United States Radium Corporation, 4150 Old Berwick Rd., Bloomsburg, Pa. 17815.
Source will be in a Model AB-10 cell for a gas chromatograph manufactured by the Glenall Corp. (See Item #7)

A. 13 millicuries

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.)*

For use in a Model 310 gas chromatograph manufactured by the Glenall Corp., 4530 Wyndotte Rd., Willow Grove, Pa., 19090.

01213

(Continued on reverse side)

Form AEC-313 (5-58) Page Two

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	Individuals will be approved by the Radiological Committee, Pitsburg General Hospital		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
As above				

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/cm^2)	USE (Monitoring, surveying, measuring)
See attached Form AEC 313b					

11. METHOD, FREQUENCY, AND STANDARDS USED IN CALIBRATING INSTRUMENTS LISTED ABOVE.
Calibrated every 6 months or as needed with Strontium-90 standard.

12. FILM BADGES, DOSIMETERS, AND BIO-ASSAY PROCEDURES USED. *(For film badges, specify method of calibrating and processing, or name of supplier.)*
Film badges processed at 4-week intervals by Lexington Army Depot

INFORMATION TO BE SUBMITTED ON ADDITIONAL SHEETS

13. FACILITIES AND EQUIPMENT. Describe laboratory facilities and remote handling equipment, storage containers, shielding, fume hoods, etc. Explanatory sketch
As specified in Application for AEC Byproduct Material License 03-00016-13 dated 21 June

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, serv-
As specified in Application for AEC Byproduct Material License 03-00016-13 dated 21 June

15. WASTE DISPOSAL. If a commercial waste disposal service is employed, specify name of company. Otherwise, submit detailed description of methods which will
As specified in Application for AEC Byproduct Material License 03-00016-13 dated 21 June

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.

Department of the Army
FOR A MAJOR
Denver, Colorado Depot
Applicant named in item 4

Date 22 November 1966

By [signature]
Chief, Radiological Committee
Title of certifying official

FOR A MAJOR

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.

GPO 865-815

Form AEC-313b (2-55)

APPLICATION FOR BYPRODUCT MATERIAL LICENSE

SUPPLEMENT B—SEALED SOURCES

Form approved. Budget Bureau No. 38-R028.3

If application is for byproduct material to be used in or manufactured as a "sealed source" complete this supplement and attach to the application for byproduct material license. Applicant for *use* of sealed source should complete Section I. An applicant desiring to *manufacture* a sealed source should complete Section II. If information has been submitted previously and there are no changes in the sealed source and/or device design or other changes in information submitted previously, details requested below may be omitted *provided* reference is made on line below to the application or other document on which this information appears:

SECTION I—USE (*See instructions*)

Sealed Source:

1. IF SEALED SOURCE OR DEVICE CONTAINING SEALED SOURCE IS MANUFACTURED COMMERCIALLY, GIVE FOLLOWING INFORMATION:

A. Manufacturer or supplier of sealed source and/or device: U.S.Radium Corp., 4150 Old Berwick Rd.,Bloomsburg,Pa. Glowall Corp.,2530 Wyandotte Rd.,Willow Grove,Pa.

B. Make and model number of sealed source and/or device: Model AD-10 for use in Model 310 Gas Chromatograph

C. Person who will hold legal title to sealed source: Fitzsimons General Hospital and U.S. Army Medical Research and Nutrition Laboratory, Denver, Colo.

2. (a) NAME OF PERSON WHO WILL PERFORM NECESSARY PERIODIC LEAKAGE TESTS (*6-month intervals for beta-gamma; 3-month period for alpha emitters. See instructions*):
Radiation Safety Officer, U.S. Army Medical Research & Nutrition Laboratory, Denver, Colo. (Charles G. Liddle, Capt., VC)

(b) IF ABOVE PERSON IS NOT THE SUPPLIER, MANUFACTURER, NOR A COMMERCIAL LABORATORY ROUTINELY OFFERING SUCH SERVICES, GIVE BRIEF STATEMENT OF EXPERIENCE OR TRAINING OF SUCH PERSON IN TECHNIQUES TO BE EMPLOYED, A STATEMENT OF LEAK TESTING PROCEDURES INCLUDING EVIDENCE OF ITS EFFICACY AND INSTRUMENTATION TO BE USED:

See attached for training and experience of individual who will perform leak tests.

Leak tests will be performed using wet gauze swipes. Swipes will be placed in vials containing a toluene scintillation solution and counted in a liquid scintillation counting system (either a Packard Model 314EX, a Packard Model 3314, or a Nuclear Chicago Mark I Liquid scintillation counter). The instruments can readily detect levels of contamination above 5×10^{-5} microcuries.

3. ARRANGEMENTS WHICH WILL PREVAIL FOR PERFORMING INITIAL RADIATION SURVEY (*if appropriate*), SERVICING, MAINTENANCE, REPAIR, CONTROL, AND DISPOSAL, ETC., OF THE SOURCE:

Initial radiation survey will be performed by U. S. Radium Corporation. Servicing maintenance or repair will be performed by The Glowall Corp. or the U. S. Radium Corp. Control and/or disposal will be carried out as with other radioisotopes possessed and used by this Laboratory under AEC License No. 05-00046-13.

SECTION II—MANUFACTURE

4. IF SEALED SOURCE TO BE MANUFACTURED OR FABRICATED BY THE APPLICANT IS DESIGNED TO TRANSMIT ONLY GAMMA RAYS AND CONTAINS IN ELEMENTAL FORM (*but not powders*) COBALT 60, IRIDIUM 192, GOLD 198, TANTALUM 182, OR THULIUM 170, GIVE FOLLOWING INFORMATION AND DISREGARD QUESTIONS 5 THROUGH 12 ON THIS SUPPLEMENT:

(a) Quantity of byproduct material per source and model number

(b) Leak testing procedure to be employed:

(c) Attach annotated engineering drawing of source container and holder, if any.

(d) Describe label to be affixed to source container and/or source holder (*or attach copy. See instructions*):

91213

(Continued on reverse side)

16—61441-2

Training and Experience: Charles G. Liddle, Capt VC

Form AEC-313

Item 8 Type of Training:	Where Trained	Duration of Training	
a. Principles and practices of radiation protection	Walter Reed Army Institute of Research	2 weeks	Formal
	Taft Sanitary Engineering Center	4 weeks	Formal
	University of Rochester	1 year	Formal
b. Radioactivity measurement standardization and monitoring techniques and instruments	"	"	"
c. Mathematics and calculations basic to the use and measurement of radioactivity	"	"	"
d. Biological effects of radiation	"	"	"

Item 9 Experience with radiation

Isotope	Maximum amount	Where experience gained	Duration	Type of Use
H^3	1 Mc	Fourth U S Army Med Lab	1 yr	research
		Walter Reed Army Institute of Research	2 yrs	research
		USAMRNL	1 yr	research
C^{14}	"	"	"	"
P^{32}	"	"	"	"
S^{35}	"	"	"	"
Ca^{45}	"	"	"	"
Cr^{51}	"	"	"	"
Fe^{59}	"	"	"	"
Co^{60}	"	"	"	"
Zn^{65}	"	"	"	"
Sr^{85}	"	"	"	"
Sr^{90}	"	"	"	"
I^{125}	"	"	"	"
I^{131}	"	"	"	"
Cs^{137}	"	"	"	"
$Ba\text{-}La^{140}$	"	"	"	"
Hg^{197}	"	"	"	"
Hg^{203}	"	"	"	"

HEADQUARTERS
DEPARTMENT OF THE ARMY
OFFICE OF THE SURGEON GENERAL
WASHINGTON, D.C. 20315

IN REPLY REFER TO
MEDPS-PM

22 December 1966

Isotopes Branch
Division of Material Licensing
U.S. Atomic Energy Commission
Washington, D. C. 20545

Gentlemen:

It is recommended that the attached application for amendment to Byproduct Material License No. 05-00046-13 be approved.

Sincerely,

HERSCHEL E. GRIFFIN
Colonel, MC
Chief, Preventive Medicine Division

1 Incl
as

Form AEC-313 (5-58)

ATOMIC ENERGY COMMISSION

APPLICATION FOR BYPRODUCT MATERIAL LICENSE

Form approved. Budget Bureau No. 38-R027.3

INSTRUCTIONS.–Complete Items 1 through 16 if this is an initial application. If application is for renewal of a license, complete only Items 1 through 7 and indicate new information or changes in the program as requested in Items 8 through 15. Use supplemental sheets where necessary. Item 16 must be completed on all applications. Mail three copies to: U. S. Atomic Energy Commission, Washington 25, D. C. Attention: Isotopes Branch, Division of Licensing and Regulation. 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.)*

Department of the Army
Fitzsimons General Hospital and
US Army Medical Research & Nutrition
Laboratory, Denver, Colorado 80240

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

Same as 1a.

2. DEPARTMENT TO USE BYPRODUCT MATERIAL

Radioisotope Section, Radiology Service

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

License #5-46-13

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.)*

As specified by Fitzsimons General Hospital
Radioisotope Committee

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.)*

Same as 4.

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

43 Technetium 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.)*

Pertechnate Ion 280mc, Squibb Molybdenum generator 400mc

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.)*

See Form AEC 313a.

(Continued on reverse side)

Form AEC-313 (5-58) Page Two

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	N/A		Yes No	Yes No
b. Radioactivity measurement standardization and monitoring techniques and instruments	N/A		Yes No	Yes No
c. Mathematics and calculations basic to the use and measurement of radioactivity	N/A		Yes No	Yes No
d. Biological effects of radiation	N/A		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
		N/A		

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 License #5-46-13 See Form AEC 313a, continuation of Para 4d, 3, c, (2)					

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

See License #5-46-13

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

See License #5-46-13

INFORMATION TO BE SUBMITTED ON ADDITIONAL SHEETS

13. FACILITIES AND EQUIPMENT. Describe laboratory facilities and remote handling equipment, storage containers, shielding, fume hoods, etc. Explanatory sketch of facility is attached. (Circle answer) Yes No

See License #5-46-13

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, maintenance and repair of the source.

See License #5-46-13

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 the type and amount of activity involved.

See License #5-46-13

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.

Dept of the Army, FGH & U. S. Army Med. Resch. & Nutr. Lab., Denver, Colo.

Applicant named in item 1

Date NOV 28 1966 By: Edwin L. Overholt

EDWIN L. OVERHOLT, COLONEL MC
Chairman, Radioisotope Committee

Title of certifying official

RECEIVED NOV 28 1966 U.S. ATOMIC ENERGY COMMISSION DIVISION OF REGULATION

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 - 568572

Form AEC-313 a (3-56)
PAGE 1

UNITED STATES ATOMIC ENERGY COMMISSION

APPLICATION FOR BYPRODUCT MATERIAL LICENSE

SUPPLEMENT A—HUMAN USE

Form approved. Budget Bureau No. 38-R080.1

If byproduct material is for "human use" (internal administration of byproduct material, or the radiation therefrom to human beings), complete this supplement and attach to the application for byproduct material license.

1. (a) USING PHYSICIAN'S NAME
Department of the Army
Fitzsimons General Hospital and
USA Med. Rsch. & Nutr. Lab.

(b) NAME AND ADDRESS OF APPLICANT (If different from 1(a))
Fitzsimons General Hospital
Denver, Colorado 80240

2. THE USING PHYSICIAN INDICATED ABOVE IS LICENSED TO DISPENSE DRUGS IN THE PRACTICE OF MEDICINE BY A STATE OR TERRITORY OF THE UNITED STATES, THE DISTRICT OF COLUMBIA, OR THE COMMONWEALTH OF PUERTO RICO. As permitted by Fitzsimons General Hospital Radioisotope Committee CIRCLE ANSWER	(YES)	NO
3. A STATEMENT OF USING PHYSICIAN'S CLINICAL RADIOISOTOPE EXPERIENCE (PAGE 3 OF THIS SUPPLEMENT) IS SUBMITTED IN SUPPORT OF THIS APPLICATION. IF ANSWER IS NO, USE PAGE 2 OF THIS SUPPLEMENT TO EXPLAIN OR REFER TO OTHER APPLICATION OR RELATED DOCUMENTS ON WHICH THIS INFORMATION APPEARS. As permitted by Fitzsimons General Hospital Radioisotope Committee CIRCLE ANSWER See License #5-46-13	YES	(NO)

PROPOSED DIAGNOSIS OR TREATMENT

4. (a) DESCRIBE PURPOSE FOR WHICH BYPRODUCT MATERIAL WILL BE USED INCLUDING SPECIFIC CONDITIONS OR DISEASES TO BE DIAGNOSED OR TREATED (Use page 2 if necessary): Technicium 99m will be used for the detection of brain tumors.

(b) CHEMICAL FORM ADMINISTERED:
Pertechnetate Ion

(c) DESCRIBE PROCEDURES WHICH WILL BE OBSERVED TO MINIMIZE HAZARD FROM HANDLING, STORAGE, AND DISPOSAL OF THE BYPRODUCT MATERIAL:
See Supplement A

(d) DESCRIPTION AND SKETCHES OF SPECIAL DEVICES TO BE USED FOR ADMINISTERING BYPRODUCT MATERIAL TO HUMAN BEINGS ARE (1) ATTACHED (LITERATURE REFERENCES WILL SUFFICE) See Supplement A CIRCLE ANSWER	(YES)	NO
(2) ON FILE WITH THE ISOTOPES EXTENSION REFER TO APPLICATION NO See License #5-46-13 CIRCLE ANSWER	(YES)	NO

5. PROPOSED DOSAGE SCHEDULE
(a) In millicuries for internally administered byproduct material other than discrete fixed sources; and in roentgens or rads, as appropriate, for internal or external irradiation from discrete fixed sources (gold seeds, cobalt needles, etc.) state separately for each condition or disease (use page 2 if necessary):
Dosage range will be 5-10 millicuries for brain scan.

See Supplement A

(b) INVESTIGATIVE PROPOSAL FOR EXPERIMENTAL, NEW OR UNUSUAL HUMAN USES IS ATTACHED. (Attachment should include outline of conditions to be evaluated, including data from animal studies and/or abstract of literature reference if any, number and type of patients (i. e. age group, moribund, etc.)) CIRCLE ANSWER	YES	(NO)

6. IF BYPRODUCT MATERIAL WILL NOT BE OBTAINED IN PRECALIBRATED FORM FOR ORAL ADMINISTRATION OR IN PRECALIBRATED AND STERILIZED FORM FOR PARENTERAL ADMINISTRATION, DESCRIBE IDENTIFICATION, PROCESSING, AND STANDARDIZATION PROCEDURES:
See Form AECa, page 2, continuation of Para 4d, 1, 2.

7. THE PROPOSED USE OF BYPRODUCT MATERIAL HAS BEEN, OR WILL BE, APPROVED BY THE MEDICAL ISOTOPE COMMITTEE. CIRCLE ANSWER	(YES)	NO

HOSPITAL FACILITIES FOR INDIVIDUAL PRACTICE USE ONLY

8. (a) THE APPLICANT HAS COMPLETED ARRANGEMENTS FOR A HOSPITAL TO ADMIT RADIOACTIVE PATIENTS WHENEVER ADVISABLE. CIRCLE ANSWER	YES	NO
(b) A COPY OF INSTRUCTIONS TO BE FURNISHED TO THE HOSPITAL AS TO RADIOLOGICAL SAFETY PRECAUTIONS TO BE TAKEN AND AVAILABLE RADIATION INSTRUMENTATION IS ATTACHED. CIRCLE ANSWER	YES	NO

This page may be used for providing additional information. Please cross reference to specific items.

4c continued.

Radiation Protection.

Technetope sterile generators will be used as directed by E. R. Squibb and Sons and the generator will not be removed from its protective shielding.

Para.4d continued.

1. Purity.

a. The procedure we use to determine the amount of molybdenum 99 in the Technetium 99m eluate will be as follows:

Mo^{99} emits a gamma of 0.740 and 0.780 MEV, which together represent 16.8% of all Mo^{99} disintegrations. By setting Pulse Height Analyzer with a base of 700KEV only the emission above 700KEV will be recorded. From these counts a quantitative check can be made by comparison of a known standard of I-131 (with a gamma of 722 KEV which represents 3% of all its disintegrations.

$$\frac{(\text{uc of } I^{131})(\text{CPM of } Mo^{99})(Mo^{99} \text{ Dil. factor})}{\text{CPM I-131})(5)}$$

The Mo^{99} dilution factor will be 1000, as taken from Tc Assay step No. 1.

b. R. E. Squibb & Sons will be the sole supplier for the Technetium generator.

c. Testing for alumina leakage through the filtrate will be done according to instructions from R. E. Squibb & Sons.

2. Assaying Technetium 99m activity:

a. Assay of $Tc^{99}m$ can be accomplished by using the Squibb Cobalt-57 standard (Cobaltous Chloride Co^{57}) provided with the generator.

(1) Withdraw 0.5cc. from the vial of $Tc^{99}m$ and dilute with water to make 500 cc. (Solution A)(Dilution Factor = 1000)

(2) Transfer 1.0cc. of this dilution (Solution A) to a 500cc. volumetric flask and dilute to volume with water. (Solution B)

(3) Transfer 1.0cc. of the final dilution to a test tube (Solution B) and count it in a well-type scintillation counter.

(4) Transfer 1.0cc. from the vial of Cobalt-57 Standard to a second test tube and count it in a well-type scintillation counter.

(5) Calculate $Tc^{99}m$ activity using the following formula:

$$Tc^{99}m \text{ Activity (mc/cc.)} = \frac{A \times B \times 10^4 \times 50}{C \times 0.885}$$

Where:

A = net counts per minute of diluted $Tc^{99}m$ (Solution B)
B = activity (in millicuries) of Cobalt-57 Standard, taken from the label and corrected for decay.
C = net counts per minute of Cobalt-57 standard

$10^4 \times 50$ = dilution factor for $Tc^{99}m$.
0.885 = factor for converting Cobalt-57 activity to equivalent $Tc^{99}m$ activity.

3. Equipment to be used:

a. Equipment for assay will be sterile tuberculin syringes 1cc. volumetric pipettes and 500ml glass flask with glass stoppers.

b. Counting equipment.

(1) Twin scaler #2 model, #600-125, manufacturer, Picker-Nuclear.
(2) Magna Well, Model #610-050, manufacturer, Picker-Nuclear.

c. Diagnostic equipment.

(1) Magnascanner, Model #6184D, modified to 120 cm/min.
(a) An additional low energy medium focus collimator has been purchased and is on hand, manufacturer, Picker-Nuclear.
(2) Pho/Gamma Scintillation Camera, Model #6401, manufacturer, Nuclear-Chicago.

U.S. GOVERNMENT PRINTING OFFICE: 1959 O - 528228

Para 5a, continued . . .

RADIATION ABSORBED DOSAGES FOR Tc^{99m}

ORGAN	DOSE	FORM OF Tc^{99m}	METHOD OF ADMINISTRATION	RAD DOSE
Whole Body	1 mc	Pertechnetate	IV or Oral	13.2 MRads
Brain	1 mc	Pertechnetate	IV	5.6 MRads
Brain	1 mc	Pertechnetate	Oral	0.8 MRads
Thyroid	1 mc	Pertechnetate	IV or Oral	235 MRads
Stomach	1 mc	Pertechnetate	IV	230 MRads
Stomach	1 mc	Pertechnetate	Oral	31.8 MRads
Liver	1 mc	Pertechnetate	IV	32 MRads
Liver	1 mc	Pertechnetate	Oral	157 MRads
Large Bowel	1 mc	Pertechnetate	IV	142 MRads
Large Bowel	1 mc	Pertechnetate	Oral	226 MRads