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

UNITED STATES ATOMIC ENERGY COMMISSION

APPLICATION FOR BYPRODUCT MATERIAL LICENSE

Form approved. Budget Bureau No. 38-R027

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

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

School of Medicine & University Hospital
School of Medicine
San Juan, Puerto Rico 00905

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

Clinical Research Center
School of Medicine and
Centro Médico de Puerto Rico
San Juan, Puerto Rico 00905

2. DEPARTMENT TO USE BYPRODUCT MATERIAL

Clinical Research Center

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

52-1946-2 (D-66)

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.)*

A.A. Cintrón-Rivera, M.D.
Professor of Medicine and
Program Director, Clinical Research Center

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.)*

A.A. Cintrón-Rivera, M.D.

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

(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.)*

All of the preparations below will be used exclusively for diagnostic and/or tracer studies.

I-131	Iodinated Serum Albumin: Albumotope (Squibb)	2 mc
I-131	Iodinated Fats and Fatty Acids: Trioleotope & Oleotope (Squibb)	3 mc
I-131	Tri-iodothyronine	1 mc
I-131	Antipyrine	1 mc
I-131	Rose Bengal	1 mc
I-131	Diodrast	1 mc
I-131	Sodium Hippurate	1 mc
Fe-59	Radio Ferrous Citrate	1 mc
Fe-59	B_1-Globulin Iron Complex	1 mc
Cr-51	Sodium Chromate - Chromitope (Squibb)	2 mc

(see over)

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: Supplement A (Form A.E.C.-313 a)

Diagnostic and tracer studies in human subjects undergoing studies involving metabolic, cardiovascular, renal, nutritional, hematologic, gastrointestinal diseases and other entities. The Clinical Research Center is a distinct physical entity which is multidisciplinary in nature, and devoted to clinical research. A copy of the existing policies and administrative organization of the Center is enclosed.

70285

(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	1)Univ. of Michigan Clinical Radioisotope Center & U.S.A.E.C. Laboratory for the study of the Biological Effects of Irradiation, University of Michigan, 1953	Basic course Clin. Appl. 6 months	(Yes) No	(Yes) No
b. Radioactivity measurement standardization and monitoring techniques and instruments	2)Also experience at the Radioisotope Laboratory of the School of Medicine, Univ. of P.R. (1957-60) and the Clinical Radioisotope Division, Puerto Rico Nuclear Center (1959-61)	9 years	(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
I-131	100 mc	1. Univ. of Michigan	3 months	Trace, diagnostic and therapeutic
P-32	50 mc	2. Univ. of P.R. School of Med.	3 years	
Cr-51	10 mc	3. Puerto Rico Nuclear Center		
Co-58	50 uc	4. Univ. Hospital Rio Piedras	3 years	Tracer and diagnostic
Co-60	50 uc	(for additional details, please refer to A.E.C. form 313 (a) page 3)		

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)
Scalers	2				measuring
Scint. Counter	3	gamma			measuring
C-M Tube	1	Beta-gamma		3.0 mg/cm²	measuring
Survey Tube	1	Beta-gamma	20mr/hr.	2.0 mg/cm²	monitoring
Liquid Scint. Detector	1	Beta			measurement
Cutie Pie	2	Beta-gamma	2000 mr/hr.	2.0 mg/cm²	monitoring

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

Instrument calibrated and serviced as needed by manufacturer's representative in Puerto Rico.

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

Film Badge Service will be obtained from Nuclear Chicago Corp. badges changed semi-monthly. Pocket dosimeters will be purchased from Nuclear Chicago Corp. self reading type. Consultants available on call from the Puerto Rico Nuclear Center of the University of Puerto Rico.

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.

Hold for decay, then discharge to sewer.

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 (type name in item 1)

Date June 6, 1966

By: O. Higginbotham

Chancellor, Medical Sciences Campus

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—745-582

Cont. Item #6 (a) By Product Material & (b) Chemical and/or Physical Form, etc. - Form AEC-313 (11-63)

Co-58	Cyanocobalamin 58 - Rubratope - 58 (Squibb)	50 uc
Co-60	Cyanocobalamin 60 - Rubratope - 60 (Squibb)	50 uc
Co-57	Cyanocobalamin 57 - Rubratope - 57 (Squibb)	50 uc
P-32	D.F. P-32	2 mc
S-35	Radiosulfate ($S^{35} O_4$)	2 mc
Tritium	Tritiated Thymine and Thymidine	50 uc
	Tritiated folic acid and ascorbic acid	100 uc

Item #9:

Note: For purposes of mailing and receiving materials and supplies, it is preferable to utilize the School of Medicine address in San Juan. Matters can be expedited faster if all communications are sent to the attention of:

Dr. A.A. Cintrón-Rivera
General Clinical Research Center
School of Medicine
San Juan, Puerto Rico 00905

Item #13 - Facilities and Equipment:

18" remote handling tongs, rubber gloves, lead bricks, lead storage containers, trays, absorbent paper, separate laboratory area for isotope work, hood and stainless steel topped cabinets.

Items #14-15 - Radiation Protection Program and Waste Disposal:

Laboratory will be surveyed daily, and work surfaces after each use, or as needed. Wastes will be stored until decayed to low enough levels to be disposed of in sewer. Unused portions will be stored in original shipping containers until ready to be disposed of in sewer. The Health Physics section of the University of Puerto Rico Nuclear Center has on the past helped us in setting up adequate standards of safety, and there is no reason to believe that this advice may not be given when needed. Receipt and disposition of all radioactivity recorded in bound notebook.

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Form AEC-313a (11-63) 10 CFR 30 PAGE 1

UNITED STATES ATOMIC ENERGY COMMISSION

APPLICATION FOR BYPRODUCT MATERIAL LICENSE—MEDICAL

SUPPLEMENT A—HUMAN USE

Form approved. Budget Bureau No. 38-R080

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

A.A. Cintrón-Rivera, M.D.

(b) NAME AND ADDRESS OF APPLICANT (If different from 1(a). Include ZIP Code.)

General Clinical Research Center
School of Medicine and University Hospital
University of Puerto Rico - San Juan, Puerto Rico 00905

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

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

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):

Diagnosis: Plasma volume; blood volume and water space determinations; absorption studies; kidney function studies; liver function studies; diagnosis of pernicious and other related anemias; study of platelet survival; hematologic diagnostic procedures.

(b) CHEMICAL FORM ADMINISTERED:

See: AEC form #313

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

All materials will be secured in assayed forms in amounts necessary for not more than 2 to 3 weeks' work. A radiation physicist will be available for consultation. Handling will be done with radioisotope syringe or pipetter. All materials will be kept in shipping container in which radioisotope are received. For decay, all material will be stored where more than one package is present, behind appropriate lead shield.

(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 BRANCH
REFER TO APPLICATION NO. _____ — 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):

Minimum dosages will be used in tracer and diagnostic work.

-131 Human Serum Albumin - Diagnostic	5-50 uc
-131 Triolein and Oleic Acid - Diagnostic	10-50 uc
-131 Trio-iothyronine - In Vitro diagnostic	10-50 uc
-131 Antipyrine - Diagnostic	40-50 uc
-131 Rose Bengal - Diagnostic	20-50 uc
-131 Diodrast - Diagnostic	20-50 uc
-131 Sodium Hippurate Diagnostic	20-50 uc

(see over)

(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)

If a new project is contemplated, specific request with full details will be made to the U.S.A.E.C.

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:

Material for testing and treatment will always be obtained in individual pre-calibrated and pharmaceutically correct form from either the Abbot Laboratories or Squibb, Inc.

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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

UNITED STATES ATOMIC ENERGY COMMISSION

APPLICATION FOR BYPRODUCT MATERIAL LICENSE—MEDICAL

SUPPLEMENT A—HUMAN USE

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

Cont. No. 5 - Proposed Dosage Schedule (a)

Cr-51	Sodium Chromate Diagnostic	30-100 uc
Co-57	Vitamin B12 Diagnostic	0.5-1.0 uc
Co-60	Vitamin B12 Diagnostic	0.5-1.0 uc
Fe-59	radioferrous citrate Diagnostic	20-50 uc
Fe-59	B1-globulin Iron complex Diagnostic	20-50 uc
P-32	D.F.P. 32-In Vitro platelet labelling	50 uc
S-35	Radiosulfate - Platelet labelling - diagnostic	50 uc

* U.S. GOVERNMENT PRINTING OFFICE : 1966 O—745-382

Form AEC-313a
(11/63)
Page 3

UNITED STATES ATOMIC ENERGY COMMISSION

APPLICATION FOR BYPRODUCT MATERIAL LICENSE—MEDICAL

SUPPLEMENT A—PRECEPTOR STATEMENT

This page is to be completed by the applicant physician's preceptor. If more than one preceptor is necessary to document experience, obtain a separate statement from each. Back of page may be used for comments.

9. NAME AND ADDRESS OF APPLICANT PHYSICIAN (Include ZIP Code)

A.A. Cintrón-Rivera, M.D.
Clinical Research Center
School of Medicine
San Juan, Puerto Rico, 00905

10. CLINICAL TRAINING AND EXPERIENCE OF PHYSICIAN NAMED IN ITEM 9 ABOVE

(A) ISOTOPE	(B) CONDITIONS DIAGNOSED OR TREATED	(C) No. Cases Observed (See 1 in key below)	(D) No. Cases Involving Personal Participation (See 2 in key below)
I-131	Diagnosis of thyroid function	over 2000	over 1500
	Dilution studies	over 1000	over 1000
	Excretion studies Renograms	30	30
	Brain tumor localization Absorption of I^{131} triolein & oleic acid	over 110	over 110
	Scanning studies	50	50
	Treatment of hyperthyroidism	over 100	over 100
	Treatment of cardiac conditions	12	12
	Treatment of thyroid carcinoma	24	24
P-32 Soluble	Treatment of polycythemia	over 40	over 40
	Treatment of leukemia	10	10
	Treatment of bone metastases	10	10
	Tumor localization		
	Intracavitary treatment		
	Interstitial treatment		
Au-198	Intracavitary treatment		
	Interstitial treatment		
	Scanning studies		
Cr-51	Blood determinations	over 50	over 50
	Scanning studies spleen	over 50	over 50
Co-58 or Co-60	Diagnosis of pernicious anemia	over 400	over 400
Co-60	Interstitial treatment		
I-192	Intracavitary treatment		
Co-60 or Cs-137	Teletherapy treatment		
Sr-90	Treatment of superficial diseases of the eye		
Other Isotopes Use back of page	D.F.P. - 32	3	3
	Tri-iodothyronine	over 600	over 300
	I-131 Rose Bengal - scanning & % excretion	40	25

continued

Key to Column (C) and (D) above

1. Observation should consist of observing radioisotope administration techniques and discussion with preceptor the case histories to establish most appropriate diagnostic and/or therapeutic procedure, limitation, contraindications, etc.

2. Personal participation should consist of (a) supervised examination of patients to determine the suitability for radioisotope diagnosis and/or treatment and recommendation on dosage to be prescribed, (b) collaboration in calibration of the dose and the actual administration of the dose to the patient, including calculation of the radiation dose, related measurements, and plotting of data, and (c) adequate period of training to enable the physician to manage radioactive patients and to follow patients through diagnosis and/or the course of treatment.

11. DATES AND TOTAL NUMBER OF HOURS OF CLINICAL RADIOISOTOPE TRAINING 240 hours of training. Practical experience since 1957.

12. THE TRAINING AND EXPERIENCE INDICATED ABOVE WAS OBTAINED UNDER THE SUPERVISION OF Dr. William B. Beierwaltes and the late Dr. Frank H. Bethell at the University of Michigan Medical School. Copy of accredit'ng letters were sent with original application in 1958.

(please See Back of Page.) 3285

AT _____
(Institution) Name and Address

_____
(Byproduct Material License Number)

_____
(Signature of Preceptor)

UNITED STATES ATOMIC ENERGY COMMISSION

APPLICATION FOR BYPRODUCT MATERIAL LICENSE—MEDICAL

SUPPLEMENT A—HUMAN USE

This page may be used for providing additional information.

Cont. Item #10

A Isotope	B Conditions Diagnosed or Treated	C	D
Fe^{59}	Ferrokinetic Studies Iron absorption & excretion studies	over 40	over 40
Tritiated Folic Acid	Metabolism of tritiated Folic acid in Tropical Sprue	3	3
DFP-32	Labelling of platelets for survival studies	7	7

ADDENDUM:

1. Experimental work utilizing animals will be performed at the Basic Science Radioisotope Laboratory run by the Department of Biochemistry of the School of Medicine and the Radiobiology Division of the School of Medicine at the San Juan campus of the School of Medicine.

2. Dr. A.A. Cintrón-Rivera had his original training in 1952 and 1953 at the University of Michigan Radioisotope Center under the preceptorship of Dr. William Beierwaltes and the late Dr. Frank H. Bethell of the Simpson Memorial Institute and the A.E.C. Laboratory for the Study of the Biological Effects of Irradiation of the same School of Medicine.

Dr. Cintrón-Rivera organized the first Clinical Radioisotope Laboratory of the School of Medicine of the University of Puerto Rico with the help of the U.S. Atomic Energy Commission in 1957. In 1959, he organized the Clinical Radioisotope Division of the Puerto Rico Nuclear Center and its training programs for Latin American physicians. As such, he planned the divisional laboratories for the Biomedical Building of the Center. He has been actively engaged in the clinical utilization of radioisotopes for diagnosis, treatment, post graduate training and clinical investigations in human beings since 1952. At the present time he holds the rank of Professor of Medicine and Program Director, Clinical Research Center of the School of Medicine and the University of Puerto Rico. He is also the Chairman of the University Hospital Radioisotope Committee.

A Nigoglioni

Adán Nigoglioni, M.D.
Chancellor, Medical Sciences Campus
School of Medicine
University of Puerto Rico
San Juan, Puerto Rico 00905

* U.S. GOVERNMENT PRINTING OFFICE : 1964 O—745-382