701631 PNL-9086

UNIVERSITY OF WASHINGTON
Seattle, Washington 98105

April 7, 1966

REPOSITORY PNL
COLLECTION Prisoner Study
BOX No. 3156
FOLDER Walla Walla Project

United States Atomic Energy Commission
Isotopes Branch
Division of Materials Licensing
Washington, D. C. 20545

Attention: Mr. Richard E. Cunningham, Chief

Dear Mr. Cunningham:

I am hereby submitting for your approval, an application for license of three nominal five curie sources of tritium to be used as fixed titanium tritide targets for generation of neutrons in a neutron generator. This application is unusual in that the purpose of the target is the controlled production of neutron injury by doses of .5 to 40 rads to the testes of human volunteer subjects to be carried out at the Washington State Penitentiary at Walla Walla. The 14 MEV neutron irradiation research is complementary to a program of 250 KVP x-ray irradiation studies now almost complete and a program of 2.5 MEV neutrons research which has utilized deuteron targets to produce the same range of doses. In view of the unusual features of this experimental program, every effort has been made to supply complete supporting information to aid in expediting action on our application by the Division of Materials Licensing.

The study of effects of irradiation on human testes was first undertaken by C. Alvin Paulsen, M.D. following the criticality accident at Hanford Atomic Products Operation, Richland, Washington, in April, 1962. Clinical followups on the three exposed men gave clear indication that spermatogenesis, chromosome morphology, and pituitary gonadal control was altered by the accidental exposure which produced barely discernable effects elsewhere in the body and at absorbed doses expected to be below the limit of biological observation. Two questions posed by these clinical observations are 1) what is the "special" vulnerability of testicular tissue, and its physiology, and 2) to what extent was this attributable to neutron irradiation.

Following presentation and publication of the clinical findings regarding the Hanford accident under the auspices of the Colorado State University meeting of the International Symposium on the Effects of Ionizing Radiation to the Reproductive system (edited by W. D. Carlson, F. X. Gassner, New York, The MacMillan Company, 1964, pp 305-307; reprint enclosed: Appendix I), an increased awareness of the significance of the findings was expressed and as a result the Hanford clinical team under Dr. Paulsen was encouraged to undertake additional controlled research. AEC Grant No. AT(45-1)1781 was awarded to the University of Washington in support of this research. Mr. Paul Henshaw

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of the AEC Division of Biology and Medicine is the contract administrator. Dr. Paulsen bears the primary responsibility as senior investigator and will perform the clinical studies necessary to evaluate biological response of the tissue. Dr. William C. Roesch has supervised development of the physical apparatus necessary to perform the irradiation and accurately establish the dosages. As Manager of Radiological Physics at Battelle-Northwest Pacific Northwest Laboratories, Dr. Roesch directs a competent staff and has available whatever equipment or facilities may be deemed necessary for successful completion of these studies. (Curriculum Vitae for Drs. Paulsen and Roesch are attached as Appendices II and III to this application.) Under Dr. Roesch's direction, Mr. Kenneth Swinth, Research Scientist in the Radiological Physics Unit, Battelle-Northwest has been assigned to maintain and operate the physical facility at Walla Walla and perform experimental dosimetry and health physics measurements. Mr. Swinth is qualified for this responsibility by reason of his academic training (Master of Sciences, Radiological Science) and his work during developmental stages of this experiment at Hanford.

The present status of this research program is as follows:

1) Formal arrangements have been completed with the Superintendent of the Washington State Penitentiary at Walla Walla, Mr. B. J. Rhay; the Penitentiary Medical Director, Dr. Carroll Heffron; and the Director of the Washington State Department of Institutions, Dr. Garrett Heyns, for the use of the Walla Walla State Penitentiary hospital facilities and prisoner volunteer subjects. (See letter to C. Alvin Paulsen, M.D. from Dr. Garrett Heyns, dated March 12, 1963, Appendix IV.)

2) Necessary medico-legal arrangements for use of volunteer subjects have been negotiated by Dr. Paulsen and reviewed by the University Hospital Clinical Investigation Committee of the University of Washington.

3) The Texas-Nuclear Corporation Model 9591 Neutron Generator has been set up in the Radiological Physics Section at Battelle-Northwest Pacific Northwest Laboratories (Hanford) and shielding and dosimetry pilot studies have been performed using appropriate human phantoms. By this means the most effective use of the neutron generator has been established, that is, exposure of the gonads has been optimized and unnecessary exposure of the bowel and bladder minimized. In addition, actual operating experience has been gained and shielding design requirements have been determined.

Excerpts from Mr. Swinth's pilot neutron survey and shielding study and a floor plan of the installed facility are presented in Appendix V. The surveys were made using a tritium target and 400 microamperes of beam current. In order to satisfy state fire inspection regulation, the specifications were changed at the time of final assembly of the facility at Walla Walla. Sixty-two inches of concrete was substituted for the 23" of concrete plus 18" of inflammable parafin. For the same reason, the 40" wood beam top shield was replaced by nine inches of concrete and a 40" deep water tank.

4) The nominal five curie tritium targets which are the subject of this license have been employed in the pilot study at Hanford. Tritium containment experience to date has been satisfactory in that while the

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presence of contamination within the system has been verified, there is no excessive buildup. Also, tritium air monitoring has shown no detectable concentration in room air during suspect procedures. This evidence notwithstanding special ventilation ducting and blowers will vent vacuum pump exhaust including tritium and ozone to the building exterior. Gloves will be worn during target changes and urine samples will be taken on those research personnel most subject to contamination during operation.

5) Room B-01, one of three adjacent storage rooms in a corner of the Penitentiary Hospital basement, has been prepared for the installation of the neutron generator and necessary shielding. The research staff constitutes the only regular occupants of the basement area. Since studies are to be carried out only on alternating Wednesdays each month, there is no question of continuous exposure to either neutrons or tritium gas. Nevertheless protective design has been conservative so that occupied areas will not exceed 2 mrem/hr. Immediately above Room B-01 is the office of the Chief Medical Supervisor, Mr. Lester Harlow. Mr. Harlow, as well as five members of the regular research staff, will be assigned a neutron-beta-gamma film badge. A monitor badge will be placed in Mr. Harlow's office to indicate exposure levels.

6) X-ray studies of volunteer subjects has been carried out at the Washington State Penitentiary Hospital at Walla Walla with doses ranging from 6 to 400 rads. Dr. Robert Parker of the Department of Radiology at the University of Washington Hospital is serving as technical consultant for these x-ray studies. Data already obtained by Dr. Paulsen has shown that the kind of information expected on the basis of the earlier Hanford results will be obtained from the experiment as designed.

The neutron generator tritium target is required to complete the study of neutron exposure effects. Neutron exposures which are to be made at 0.5, 1.0, 2.0, 10, 20, and 40 rads from deuterium target must be duplicated with the higher energy tritium target neutrons. Specific objectives are (1) determination of the maximum dose which does not significantly alter spermatogenesis; (2) approximation of the dose which permits full recovery; (3) applicability of protection afforded by an altered dietary regimen such as ketogenic regimen; (4) by microscopic examination of seminiferous tubule damage, the LET concepts of Rossi can be confirmed.

Forty to sixty healthy volunteers between the ages of 21 to 45 whose sentences will exceed the experiment period by five years will be recruited with the assistance of the Medical Director of the Washington State Penitentiary at Walla Walla. The aims of the experiment and its implication with respect to local injury and in the future to fertility will be discussed and documented with each volunteer. A schedule of stipends for services has been established (i.e. $10.00 per month during the experiment and $25.00 during the month when testicle biopsy is performed).

Control observations of the subjects will precede neutron exposures. Parameters of the experiment are urinary-gonadotrophin excretion titre, urinary-estrogen excretion titre as an index of Leydig cell function, repeated seminal fluid examinations, microscopic examination of testicular

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biopsy specimen plus tissue culture and subsequent evaluation of the chromosomal pattern and morphology (i.e. "breaks" and changes in chromosomal number).

Following exposure, the subjects will be followed by repeated examinations of the control parameters for up to two years.

Sincerely,

Ralph M. Baltzo

Mr. Ralph M. Baltzo
Director
Radiological Safety Division

RMB:bbc

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.)*

C. Alvin Paulsen, M. D.
Associate Professor of Medicine
University of Washington School of Medicine
Seattle, Washington 98105

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

Washington State Penitentiary
Walla Walla, Washington

2. DEPARTMENT TO USE BYPRODUCT MATERIAL

AEC Contract Research AT(45-1)1781
(Prison Inmate Volunteer Studies)
Penitentiary Hospital

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

None

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.)*

Supervisor: C. Alvin Paulsen, M.D.
Operator: Mr. Kenneth Swinth

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.)*

Mr. Ralph M. Baltzo, Director
Radiological Safety Division
University of Washington
Seattle, Washington 98105

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

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(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.)*

Three neutron generator targets - nominal 5 curies each
Texas Nuclear Model 9591

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.)*

Neutron generator target (Texas Nuclear Model 9700) to supply adequate flux of nominal 14 MEV neutrons to complete study AT(45-1)1781 of effects of x-ray, 4 MEV and 15 MEV neutron doses on human testicular physiology.

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(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 Mr. Kenneth Swinth	WHERE TRAINED	DURATION OF TRAINING	ON THE JOB (Circle answer)	FORMAL COURSE (Circle answer)
a. Principles and practices of radiation protection	University of Wash. Radiological Sciences, M. S. Degree	Two Years	(Yes) No	(Yes) No
b. Radioactivity measurement standardization and monitoring techniques and instruments	and Radiological Physics Operation, Battelle-Northwest, Richland, Wn.	"	(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
Neutron exposure studies and general radiation studies		Radiological Physics Operation, Battelle-Northwest "	Three Years "	Pilot studies of current research project "

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)
Depangher Double Moderator (BF^3 detector in moderator) with RIDL counter.	1	Fast Neutrons	.2 mrem/hr and up	---	Monitor
Texas Nuclear Tritium "Sniffer"	1	Tritium	1 MPC and up	None	Monitor

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

Neutron meter calibrated against Van de Graaff generator. Texas-Nuclear tritium monitor calibrated against radium check source daily.

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

R. S. Landauer, Jr. & Co., neutron, beta-gamma film badges supplied to six staff members and one monitor position.

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.

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.

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