

File

BATTELLE-NORTHWEST

PACIFIC NORTHWEST LABORATORIES a Division of BATTELLE MEMORIAL INSTITUTE
P. O. Box 999 Richland, Washington 99352

H. M. PARKER

5/10/67

The attached report from Dr. Paulsen has a bearing on the work of the ad hoc committee on the use of humans in experimentation.

Copies to:

- WJ Bair
- LL Burger
- CE Newton
- WD Norwood
- RC Thompson

BB-1950-026

REPOSITORY PNL
 COLLECTION Prisoner Study
 BOX No. 2947
 FOLDER HSC 67-2

0009024

BATTELLE-NORTHWEST



PACIFIC NORTHWEST LABORATORIES a division of BATTELLE MEMORIAL INSTITUTE
P. O. Box 999 Richland, Washington 99352

RSP
HMP

H. M. PARKER

As you will see from p 2
of the WWR Rad' Count, I think
they wd have turned down
the expt if they had been
operative from the start.

This is my only copy
- pl. return.

BB-1950-024

0009025

UNIVERSITY OF WASHINGTON

U.S.P.H.S. HOSPITAL

Box 3145

SEATTLE, WASHINGTON 98114

School of Medicine

Department of Medicine

CHIEF, DIVISION OF ENDOCRINOLOGY

May 9, 1967

Mr. Herbert Parker
Battelle-Northwest
P. O. Box 999
Richland, Washington 99352

Dear Mr. Parker:

Enclosed is a copy of the minutes of the Radiation Safety and Radioisotope Committee of the University. As you can see from reading the material, careful deliberation was carried out and our proposal was approved with the limitations so stated. Due to the fact that our mannikin dosimetry studies have not been completed, we still have not exposed the inmate volunteers. The committee has been so informed, and the limitation of one year has been extended and will start at the time that our dosimetry data has been approved by this same committee.

One additional factor that I did not mention on the phone is that our proposal has also been reviewed and passed on by the Clinical Investigation Committee of the University. A letter from the chairman of that committee is also enclosed for your information.

Finally, I am sending you a copy of our Atomic Energy Commission license for the tritium foils which we use for the 15 MeV energy level.

If there is any further information you would like, please let me know. Thank you again for your help in expediting this aspect of our research project.

Sincerely yours,



C. Alvin Paulsen, M. D.
Associate Professor of Medicine

CAP:gg

0009026

UNIVERSITY OF WASHINGTON
SEATTLE, WASHINGTON 98105

Department of Chemistry

July 13, 1966

*Send copy of
this to Kenneth
Smith.*

Dr. C. A. Paulsen
1121 U. S. Public Health Service Hospital
1131 - 4th South
Seattle, Washington

Dear Dr. Paulsen:

As you probably know, on June 22 Dean McCarthy approved the recommendation of the Radiation Safety and Radioisotope Committee that your application to obtain a byproduct license be approved with the following limitations:

- 1) The maximum neutron dose to the center of the testicles is to be limited to 15 Rads.
- 2) No more than 20 volunteer subjects are to be irradiated in the course of neutron exposure studies.
- 3) Mannikin studies will be made to establish the pattern of neutron dose distribution in other nearby organs. This data will be submitted to the Radiation Safety & Radioisotopes Committee for review before proceeding with human exposure.
- 4) Irradiation of human subjects is to be complete within one year of the approval of the mannikin studies. (item 3).

Should higher level of exposure become desirable as a result of these studies, consideration will then be given to recommending the original schedule of exposure limits.

I was informed by telephone on July 11 by Mr. Hanson of the AEC that the license application has been granted.

I wish to thank you for your cooperation in discussing your interesting project with our committee.

Sincerely yours,

Robert Vandembosch

Robert Vandembosch, Chairman
Radiation Safety and Radioisotope
Committee

RV:cl

cc - Ralph Baltzo

0009027

MINUTES, RADIATION SAFETY & RADIOISOTOPES COMMITTEE
MAY 31, 1966

Attendance: Dr. Robert Vandembosch, Department of Chemistry, Chairman
Mr. Ralph M. Ealtzo, Radiological Safety Division, ex officio
Dr. Benjamin Hall, Department of Genetics
Dr. Wil B. Help, Division of Nuclear Medicine
Dr. Kenneth L. Jackson, Radiological Sciences
Dr. Ralph W. Moulton, The Graduate School, ex officio
Dr. G. L. Woodruff, Nuclear Engineering
Mr. Peter Wootton, Department of Radiology

The meeting was called to order by the Committee Chairman, Dr. Robert Vandembosch, at 1:30 p.m., to give final consideration of the request by Dr. C. Alvin Paulsen, Department of Medicine.

Dr. Help conveyed a statement from Dr. Paulsen to the effect that a limited approval by the Committee subject to later experimental confirmation of human dosimetry would be acceptable at this time.

Dr. Vandembosch stated that the deliberations by the Committee should go beyond this, that there should be some expression of whether the Committee would be inclined to approve the research program on human subjects if the dosimetry data was approximately as described in Dr. Paulsen's earlier submission.

Dr. Jackson made the following points relevant to somatic risk from x-radiation exposures of the area of the testes in the dosage range 10 - 50 R. There are no adequate human data that bear directly on this problem and one must estimate the risk by indirect means. Physiological tests have been carried out on whole-body irradiation Japanese survivors in attempts to detect accelerated aging (e.g., hair greying and skin changes, Geriatrics 16:27, 1961). No reports on these surviving individuals have appeared which implicate late testicular lesions as a problem. Thus, if these exposures caused practical physiological dysfunction to the scrotum and its internal structures the probability for this must be low.

At the present time the best estimate of the risk can be made by consideration of malignancy as the end point. Increased mortality among male Japanese survivors who were heavily whole body irradiated show a vague but statistically insignificant increase in neoplasms, excluding leukemia (Rad. Res. 25:25, 1965). Increased mortality from all causes among the high dose male survivors was observed six years after exposure (increased about 24%) and has declined thereafter.

Other pertinent data are those involving radiation therapy of patients for ankylosing spondylitis (British Med. J. 2:1327, 1955). The 12,161 male patients of this study were lightly irradiated in the area of testes and at certain other sites (Health Physics 12:239, 1966). (These exposures probably equal or exceed the rad doses proposed for approval in Dr. Paulsen's project). Mortality resulting from malignancy in lightly irradiated tissues appeared to be increased about 10 per cent but this difference was not statistically significant. Of the total irradiated patients in this study (14,554) only 60 died as a result of disease associated with the lightly irradiated tissues, as compared to 52 expected deaths.

The REE for testicular damage (sterility) for acute fast neutron exposure is estimated to be less than two (Late Testicular Lesions in Irradiated Monkeys, USAP SAM 61-72, 1961). The REE for acute exposure high LET radiation carcinogenesis in the mouse has been reported in the range of 0.4 to 5 (Health Physics 9:357, 1965).

Dr. Hall broached the question of balancing risk against benefit in the following terms. Committee consideration of Dr. Paulsen's proposal prior to the x-ray studies might well have resulted in a recommendation not to proceed because of the risks involved - the small but finite risk to the irradiated prisoners and the risk to the University's standing. However, consideration by this Committee was not deemed necessary, and the work was begun. At this point, the testicles of 40 humans have been x-irradiated, these risks have been incurred, and some useful data on dose vs. response have been obtained. The value of these data may be diminished if some similar irradiation equipment with neutrons are not performed. Since the additional risks inherent in these experiments need not be large as compared to those already incurred, the Committee might wish to consider approval of Dr. Paulsen's request subject to limitations on the following: (1) The maximum dose to be received by any subject; (2) the total number of persons to be irradiated; (3) the time period within which all the neutron irradiation will be completed.

Mr. Wootton proposed that the Committee limit its approval to a dosage figure related to ICRP pronouncements. As an example, a one-time exposure of 25 Rem encountered during emergency operations was admitted by the ICRP to not unduly prejudice future health and safety. After discussion of this point, a figure of 30 Rem was suggested because Dr. Paulsen's x-ray data has shown that this is the minimum dose which will cause aspermiia which is a useful criterion for establishing the neutron REE. Higher doses which would be necessary to reach the point of aspermiia with no recovery appear to entail significantly more risk for relatively less data. In view of earlier discussion of the REE and the expected inverse square diffusion of neutrons, this was interpreted to mean 15 Rads of neutrons to center of the testicles and a maximum of 4 Rads to the body organs at 10 cm. A motion to limit the exposure on this basis was approved unanimously. After further discussion, the Committee approved exposure of no more than 20 persons to neutron radiation for determination of the REE. The results of hemiklin studies of dosimetry are to be sent to the Committee as it becomes available. The Committee will review progress of the experiment in one year and urges that neutron exposures be completed by that time or as soon as circumstances permit.

On the basis of the above considerations, the Committee's position was summarized by Dr. Jackson as follows. Some risk is involved in irradiation of the testes, principally of carcinogenesis. However, the probability of any one individual developing cancer as a result of irradiation must be exceedingly low. Because the number of subjects is small, it is very unlikely that any measurable increase in carcinogenesis will be detectable.

Respectfully submitted,

UNIVERSITY OF WASHINGTON
SEATTLE, WASHINGTON 98105

June 20, 1966

School of Medicine
Department of Surgery

File

C. Alvin Paulsen, M.D.
U.S.P.H.S. Hospital
1131 - 14th Avenue S.
Seattle 44, Washington

Dear Dr. Paulsen:

As you are aware, the Clinical Investigation Committee reviewed your proposal entitled "The Study of Irradiation Effects on the Human Testis: Including Histologic, Chromosomal and Hormonal Aspects" on June 16, 1966. The committee members in attendance included Drs. Nyhus, Chairman, Nelp, Fink and Robertson.

The Committee had in hand the minutes of the Radiation Safety and Radioisotopes Committee meetings of May 13, 1966 and May 31, 1966.

The members of the Clinical Investigation Committee were in general agreement with the recommendations of the Radiation Safety and Radioisotopes Committee pertaining to your studies and their nuclear implications. The C.I.C. committee members were interested to hear your personal views (which were corroborated by Dr. Nelp) that there is absolutely no proof of risk relative to carcinogenesis in the male testis as implied by Dr. Jackson in the May 31, 1966 minutes of the RS & R committee meeting. To reiterate, the statement was placed on record that there is "no evidence in the animal that there is any carcinogenic problem."

Since your informed consent procedure is itemized in your proposal of May 20th, to the RS & R Committee, it will not be repeated here. Your verbal report of the procedure to the C.I.C. Committee was succinct and indeed without obvious flaw. It was suggested by one of the Committee members that at each orientation session the specific instructions might be placed on recording tape and kept for reference if necessary at a later date.

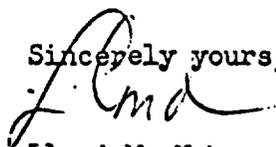
The matter of significance of the study was then discussed. It is apparent that there is absolutely no data available in this regard relative to humans. Your point that the kinetics of spermatogenesis has been proven to be markedly different in various species indicates a real need for these studies. Specific information in this area becomes increasingly important due to current considerations of work in atomic energy centers as well as considerations of space travel.

After complete review and deliberation, the C.I.C. Committee agrees that the studies proposed by you should be done within the confines of the limitations proposed by the Radiation Safety and Radioisotopes Committee. Because of the importance of these studies, the Committee wishes to review the progress of the study yearly.

LMN:st

cc: Dean Hogness
Mr. Ralph Baltzo
Dr. Robert Vandenbosch
Dean Mc Carthy
C.I.C. Members

Sincerely yours,



Lloyd M. Nyhus, M.D.
Chairman
Clinical Investigation Committee

0009030

This Copy is For Your Files

Pursuant to the Atomic Energy Act of 1954 and Title 10, Code of Federal Regulations, Chapter 1, Parts 30, 32, 33, 34, and 35, and in reliance on statements and representations heretofore made by the licensee, a license is hereby issued authorizing the licensee to receive, acquire, own, possess, transfer and import byproduct material listed below; and to use such byproduct material for the purpose(s) and at the place(s) designated below. This license shall be deemed to contain the conditions specified in Section 183 of the Atomic Energy Act of 1954, and is subject to all applicable rules, regulations, and orders of the Atomic Energy Commission now or hereafter in effect and to any conditions specified below.

Licensee			
1. Name	University of Washington School of Medicine	3. License number	46-01662-05
2. Address	Seattle, Washington 98105	4. Expiration date	June 30, 1968
		5. Reference No.	

6. Byproduct material (element and mass number)	7. Chemical and/or physical form	8. Maximum amount of radioac- tivity which licensee may pos- sess at any one time
A. Hydrogen 3	A. Tritium foils (Texas Nuclear Model No. 9591)	A. 15 curies

9. Authorized Use:

A. To be used in a Texas Nuclear Model No. 9700 neutron generator.

CONDITIONS

- 10. Byproduct material shall only be used at Washington State Penitentiary, Walla Walla, Washington.
- 11. In accordance with Section 20.501, the licensee may expose individuals to radiation in excess of the limits prescribed in Title 10, Part 20, Code of Federal Regulations, Chapter 1, "Standards for Protection Against Radiation", as provided in the application.
- 12. Byproduct material shall be used by, or under the supervision of, C. Alvin Paulsen, M.D., and Kenneth Swinth.
- 13. The use of byproduct material for human irradiation studies, on individuals who have voluntarily consented in writing, shall be contingent upon review and approval of the University of Washington Radiation Safety and Radioisotope Committee, Robert Vanderbosch, Ph.D., Chairman.

(See Page 2)

U. S. ATOMIC ENERGY COMMISSION
BYPRODUCT MATERIAL LICENSE

Supplementary Sheet

License Number 46-01662-05

Continued from Page 1:

CONDITIONS

14. Except as specifically provided otherwise by this license, the licensee shall possess and use byproduct material described in Items 6, 7, and 8 of this license in accordance with statements, representations, and procedures contained in the application dated April 13, 1966, including the attachments thereto, particularly the letters from Dr. Joseph L. McCarthy and Ralph M. Baltzo, both dated April 7, 1966; teletype dated June 23, 1966, from Ralph M. Baltzo; and "SUPPLEMENTAL INFORMATION ON HUMAN USES" and University of Washington Radiation Safety Manual (1964) submitted as Appendices IV and VI respectively to the application dated April 23, 1965, for renewal of Byproduct Material License No. 46-1662-1.
15. Preliminary neutron exposure studies shall be conducted on manikins to assure that doses to body areas of volunteers, other than the gonads, shall be kept at the minimum consistent with attaining the objectives of the program as proposed in the application.

Date JUL -1 1966

For the U. S. Atomic Energy Commission

Cecil R. Buchanan
by _____
Isotopes BranchDivision of Materials Licensing
Washington, D. C. 20545

0009032