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PNL-9098

DATE November 17, 1967
TO R. S. Paul
FROM H. M. Parker
SUBJECT HUMAN SUBJECTS COMMITTEE MEETING
THURSDAY, NOVEMBER 16, 1967

See Item # 3

F. W. Albaugh
W. D. Norwood
W. J. Bair
R. H. Scott
C. E. Newton, Jr.
P. T. Santilli
G. M. Dalen

All members were present with the exception of George Dalen. The Committee met to discuss three topics, which were treated in the following manner.

1. Extension of the Promethium-143 Study to Cover DTPA Injections

This review was made in response to a letter of October 24 from Dr. G. H. Crook, Assistant Medical Director, HEHF, addressed to the chairman of the Committee. We note that the subject letter refers to DPTA throughout instead of DTPA. Although the intention is obvious in this case, it occurred to the Committee that in the future all references to drugs in connection with human subjects application should be spelled out with their full chemical terminology (diethylene triamine pentacetic acid, in this case).

Dr. Norwood advised that considerably higher doses of DTPA than are contemplated in the subject study have been given on several occasions at Hanford and he sees no problem arising from the proposed drug regimens. BNW is judged to be insulated from the involvements of drug utilization approvals by FDA. As far as the radiation aspects are concerned, the doses received by these volunteers should be either equal to or less than those already approved for the main ¹⁴³Pm study.

The only objections to the study arise from the fact that, other things being equal, it would be preferable to perform companion experiments in animals in order to get maximum value from the data. A severe reduction in the overall funds for this project currently makes it impossible to do such experiments as a part of this project. Since the biomedical data is intrinsically more direct and is needed promptly, the Committee, by voice vote, unanimously approved this extension of the promethium study.

From the protocol of the Committee, as established in the memo of October 20, 1967 it appears that this approval, if concurred in by R. S. Paul, should be conveyed to Dr. Crook through Department channels and not in terms of an answer to Dr. Crook from the chairman of the Committee.

COLLECTION
PROMETHIUM
BOX No. 2977
FOLDER HSC 67-2

APPROVAL
PNL

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2. Extension of the Promethium-143 Study to Cover Inhalation of Soluble Aerosol

This review was made in response to a request of November 7, 1967 by H. E. Palmer, who was unable to be present at the meeting. The brief proposal refers to using three additional volunteers to inhale 100 nCi or less of $^{143}\text{PmCl}_3$. The $^{143}\text{PmCl}_3$ would be contained in an aerosol of NaCl particles generated from a solution of ^{143}Pm in saline solution. The brief note from Mr. Palmer provided estimates of the radiation dose to the volunteers under rather stereotyped assumptions. The Committee agrees with the general purpose and intent of the study but would be unable to register approval without additional information. C. E. Newton, Jr. is accumulating a list of additional items from the Committee members for communication to Mr. Palmer. At the present time, these include recalculation of possible radiation doses under the worst credible conditions of distribution of the material, and much more detailed information on the type of aerosol generator, its functioning, and who would actually administer the aerosol.

Mr. Palmer's note indicates a desire to start this experiment during the first week of December. Due to a combination of the financial limitations of this project, as discussed in Item 1, and through the deficiency of information in Mr. Palmer's note, it would appear that he should be advised that very vigorous action on his part would be required in order to clear the proposal with the Human Subjects Committee in calendar year 1967, let alone the first week of December.

3. Neutron Irradiation on Spermatogenesis Project in Collaboration with Dr. C. A. Paulsen of the University of Washington

At the last minute, this review was divided into two parts in response to two letters from Dr. Julian Nielsen to the chairman. The first letter requests release of a report entitled "Fast Neutron Medical Research Facility - Dosimetry, BNWL-589". On the whole, the committee felt that it should not be in the position of approving this document, as such. It is a technical discussion of some aspects of the calibration of the University of Washington's fast neutron medical research facility, as set up for irradiation of human testes. In the opinion of the Committee, every item in this report could be technically correct and yet the actual exposure of human volunteers could be completely botched. It would appear, for example, to be quite foolhardy to conduct these experiments without making

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various measurements of the dose actually received by the volunteers. In discussing this point with the sponsors of the report, it was clear that these steps were intended. They are, however, not included in the document. For this reason, the Committee takes the position that it notes the existence of the document, BNWL-589, but neither approves nor disapproves its publication.

The second portion of this review was in response to the letter from Dr. Nielsen entitled "Support of Dr. C. A. Paulsen on Study of Effects of Neutron Irradiation on Spermatogenesis in Man." The Committee does not feel comfortable with support of the type described in the subject letter. The key issue is who should actually be described as the operator of the neutron generating equipment. The Committee realized that Dr. Paulsen considers himself to be wholly responsible and as a consequence is somewhat disturbed by Battelle's intervention in the case. As seen by us, Dr. Paulsen's ready intention to consider himself the sole responsible person is very fine but potentially meaningless as something could, in fact, go wrong with the experiments, and involve Battelle personnel. We therefore spent considerable time in our session to devise a mechanism that would separate the responsibilities of the University of Washington and ourselves as completely as possible.

Ideally, this separation would involve complete retirement of BNW from the project. The project was begun, in fact, under the former Hanford Laboratories structure when the University was by no means broadly versed in dosimetry. At the present time, the University staff includes experts in radiological physics and experts in radiation protection. For example, a meeting at the University next week on the subject of solid state dosimetry clearly implies an interest and some degree of competence in the most modern methods of dosimetry. The Committee thus intrinsically recommends that the whole matter be placed in the hands of University specialists as soon as possible.

In realistic terms, Dr. Paulsen has been expecting more help from Battelle. In the interest of good relationships, an arrangement should perhaps be found to provide that support in the presently contemplated work only and without compromising the corporate interests of Battelle or the personal interest of our dosimetrists.

To this end, the following format is proposed. The equipment is the property of the University. The tritium

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targets needed for the apparatus are provided under a Materials License by the Atomic Energy Commission. We have no information as to the licensing status of the equipment regarded as a facility for the irradiation of human subjects. In our view, it should be so registered with the State of Washington. In that registration, the University of Washington should establish competence to operate the machine with its own personnel. Our dosimetrists believe that Dr. Paulsen could capably operate the machine, provided that some guidance is provided by us. Such guidance over a 20-session experiment could become a serious drain on our technical staff. We are therefore proposing a graded system in which the first two or three sessions would be covered by K. L. Swinth, accompanied by F. L. Rising. It is our opinion that for the remaining sessions, Mr. Rising would then be adequately qualified to provide the needed guidance to Dr. Paulsen. We recommend going forward on this basis, with one reservation that has yet to be checked by Mr. Santilli. The question as to who is the responsible operator of a machine is not always settled by who physically has his finger on the button. It is still possible that in the event of difficulty, an adverse court could judge the Battelle members to be operators of the machine. The problem that then arises is one of insurance protection for our people. The Committee's understanding of the situation is that named Battelle individuals are fully protected by insurance except for matters affecting fellow employees. There is some uncertainty as to whether a partnership-type relationship could be interpreted to make University of Washington personnel "partners" or essentially "fellow employees" within this insurance meaning. Mr. Santilli will clarify this contractual issue before the experiments are actually performed.

Note to Committee Members

In the interest of trying to speed up the work, I am not circulating these reports of recommendations for your formal approval prior to presenting them to Dr. Paul. If at any time you feel that our discussions have been significantly misrepresented, you are asked to bring the matter to my attention immediately. Thereafter, we will automatically switch to the slower mechanism of circulating our proposed recommendations for committee approval prior to release.

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JM Nielsen
WE Wilson

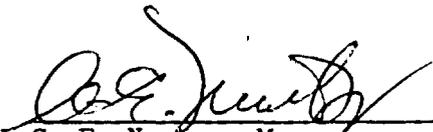
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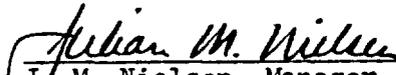
TO H. M. Parker, Chairman
Human Subjects Committee

FROM Julian M. Nielsen, Manager
Radiological Sciences Section

SUBJECT Support of Dr. C. A. Paulsen on Study of
Effects of Neutron Irradiation on Spermatogenesis
In Man

With the issuance of the report "Fast Neutron Medical Research Facility - Dosimetry" the development portion of this project is deemed to be concluded. There remains, however, the matter of furnishing to Dr. C. A. Paulsen operational assistance for the equipment and verification of the absorbed dose administered to the subjects. Carlos Newton, also of this department, has agreed to provide the services of F. L. Rising to operate the equipment for two days per week for approximately 30 weeks and to verify the dosages administered based upon BNW's dosimetry report. In order to implement this portion of the study the Human Subjects Committee's recommendations are solicited for participation as outlined above. The necessary funds in the amount of \$7000 provided for this purpose will be transferred if this arrangement is approved. Should the scope of the work exceed that described above the matter will be again referred to the Committee for its recommendations and to the USAEC for supplemental funding.


C. E. Newton, Manager
BIOPHYSICS SECTION


J. M. Nielsen, Manager
RADIOLOGICAL SCIENCES SECTION

JMN:flb

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DATE November 16, 1967

TO H. M. Parker, Chairman
Human Subjects Committee

FROM *Julian M. Nielsen*
Julian M. Nielsen, Manager
Radiological Sciences Section

SUBJECT Release of Report Entitled "Fast Neutron Medical
Research Facility - Dosimetry"

cc: JM Nielsen
WE Wilson

The subject report "Fast Neutron Medical Research Facility - Dosimetry" by K. L. Swinth and L. A. Braby is submitted to "The Committee on Policy and Procedure in the Use of Human Subjects - Human Subjects Committee" in accordance with Operating Guides 160-1-1 and 160-1-2 for review and recommendations prior to release to Dr. C. A. Paulsen of the University of Washington.

JMN:flb

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DATE November 7, 1967
TO H. M. Parker, Chairman
Human Subjects Committee
FROM H. E. Palmer
H. E. Palmer
SUBJECT ^{143}Pm Study

File
LB

I would like to extend the present ^{143}Pm study to include three volunteers who will inhale 100 nCi or less of $^{143}\text{PmCl}_3$. The $^{143}\text{PmCl}_3$ would be contained in an aerosol of NaCl particles generated from a solution of ^{143}Pm in saline solution. The particles will have a mass median diameter of about 0.5 micron. These particles should be very soluble in the lung and the ^{143}Pm should be readily absorbed into the bloodstream.

The main purpose of this experiment is to establish that the distribution of ^{143}Pm in the body after uptake from the lung is the same (or not the same) as the distribution in the body from intravenous injection of $^{143}\text{PmCl}_3$. Additional information on the rate at which ^{143}Pm leaves the lung and deposits in the liver will also be obtained.

The radiation dose from this experiment will be relatively innocuous. If we assume a case where the ^{143}Pm remains in the lung and is uniformly distributed, the total dose to infinity to the lung would be about 250 mrad. The probability of this happening is very remote with a NaCl aerosol. If 0.1% of the Pm goes to the pulmonary lymph nodes, as it did in the dog experiments, the dose to the lymph nodes would be only 1.2 mrad. If all the ^{143}Pm dissolves, goes into the bloodstream, is absorbed by the body and distributes equally between bone and liver, the dose would be 60 mrad to the liver, as it is in the injection experiments.

If this additional experiment is approved, we hope to start it during the first week of December, 1967.

HEP:tec

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