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DEPARTMENT OF THE NAVY
NAVAL SUBMARINE MEDICAL RESEARCH LABORATORY
NAVAL SUBMARINE BASE NEW LONDON
GROTON, CONNECTICUT 06349-5900

BIOMEDICAL SCIENCES DEPARTMENT

IN REPLY REFER TO

3900
22 DECEMBER 1987

REPOSITORY LLNL B361 Rm 940A
COLLECTION Institutional Review Board
BOX No. IRB Minutes
FOLDER JAN. 26, 1988 Institutional Review Board Mtg

Mr. Paul Meyer
L-280
Lawrence Livermore National Laboratory
P.O. Box 808
Livermore, CA 94550

Dear Paul,

This letter will briefly address the topics raised by your Human Subjects Committee regarding the number of subjects, risks versus benefits, and why the study is done at LLNL. More lengthy presentations are in the enclosed documents and in the references contained therein.

The number of experimental subjects needed is controlled by the precision of experimental data, which is difficult to predict for new biological experiments. We wish to measure differences in uptake kinetics between 2 gases and have chosen to study both gases in the same subject at the same time. Other experimental designs would require more subjects because of the additional uncertainty introduced by comparing across different people or within the same people at different times. The result in a particular subject, for example nitrogen uptake could be 15% faster than argon, still would need to be confirmed in a modest number of other people. We would hope to perform the experiment with 4-6 subjects, then analyze the results. If they are reproducible and convincing, we would stop and publish the study and use the information in designing new decompression tables that use multiple gases. If they are very scattered, we would also stop the study because the resources to conduct a large (say > 20 subjects) study would probably not be available. Only in the intermediate case of borderline reproducibility would we extend to more subjects, with a practical upper bound of 15-20 subjects. Similar considerations would govern the possible $^{13}N_2$ (only) imaging experiment.

The risk-benefit ratio is not zero in these studies. The risks from radiation exposure are explained, adequately I trust, in the Information to Subjects and in the Consent Form. The major pool of test subjects, U.S. Navy divers, are more accustomed to evaluating and accepting risk than are members of the general population. Furthermore, they appreciate the benefit of the experiment as well. The benefit of a successful experiment is replacement of the inadequate gas exchange theory used for the decompression tables of Navy divers. The present tables are known to result in dozens of cases of decompression sickness per year in the Navy and many more among civilian divers. Several percent of the cases leave a permanent disability. Furthermore current decompression procedures are incapable of use in high priority SEAL operations. The diver-subjects have first hand knowledge of the risks of the current decompression tables for which this research is intended to support a more rational replacement.

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When this collaborative research between NMRI and LLNL started (1980), there were very few installations in the world able to produce and measure positron emitting gases. LLNL had a recent successful collaboration with the University of Washington in experiments with many similarities to the present work. Despite numerous technical difficulties over the years, I believe we have made substantial progress. The progress was facilitated by the understanding and patience shown by LLNL and especially you towards the non-technical problems inherent in government research using marginally adequate resources. Today there are a few more institutions possessing the equipment necessary for the research, but still not including Navy Medical laboratories. Changing the collaboration from LLNL to somewhere else would require another lengthy development period with no assurance of technical success. Such a change is very undesirable both for scientific productivity and for prudent use of government research funds.

Should any of the Committee members have further questions, I will be happy to answer by phone or mail.

Sincerely,

Paul

Paul K. Weathersby
Commander, Medical Service Corps, U. S. Navy

encls.

cc: CAPT Flynn, NMRI
Dr. Lillo, NMRI
CDR Kent, NMRDC

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UNIVERSITY OF CALIFORNIA
LAWRENCE LIVERMORE NATIONAL LABORATORY

Consent to Act as a Human Subject

LLNL Human Subjects Committee
Approval Number: 80R-109-02
Approval Date: June 13, 1980, December 15, 1981, October 11, 1984

Subject's Name:_____

Date:_____

1. I hereby consent to act as a test subject in the joint Naval Medical Research and Development Command - Lawrence Livermore National Laboratory study titled Human Subject Experiments With Air Tagged With Radiosotopes ^{13}N and ^{41}Ar.

2. I understand that the procedures for conducting this test will involve:

   Breathing ^{13}N and ^{41}Ar labeled air for up to 120 minutes.

3. I understand that any possible risks and discomfort that may result from the procedures are considered unlikely but include:

   a. The discomfort from breathing through a mouthpiece for up to two hours.

   b. Any exposure to ionizing radiation carries a risk of causing cancer--in this case potentially of the lung or upper air passages where the most significant part of the radiation dose is delivered. The best estimate of the risk of lung cancer from this procedure lies between one chance in 100,000 and one chance in 10,000. The radiation exposure to the lung and air passages in this procedure will be less than 0.4 rem. This amount is slightly below the Federal exposure limit for annual exposure of the general population; is one tenth of the permissible annual exposure of radiation workers; and is approximately three to four times the radiation received by the public in most geographical areas of the United States from natural sources and average usage for medical and dental purposes."

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