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March 21, 1989

TO: Bart Gledhill
FROM: A. Larry Anderson/Deborah A. Kruchten
SUBJECT: Information to be Included With the Project Entitled, "Counting of Human Subjects Containing Nb-92m, Ba-133, and Sr-85 at the LLNL Whole Body Counter."

Attached please find copies of the British approval for the Ba-133 injections and answers to Jack Shearer's questions for the Ba-133 and Sr-85 measurements.



A. Larry Anderson
Whole Body Counter
Hazards Control Department



Deborah A. Kruchten
Whole Body Counters
Hazards Control Department

ALA/DAK:beb

attachment:

22-03/87

Orig to IRB file
XC to all IRB members
FYI, only

B

REPOSITORY LLNL B361 Rm. B940A

COLLECTION Institutional Review Board

BOX No. IRB Protocol File
Anderson IRB 88-101

FOLDER Counting of Human Subjects Containing
Nb-92m, Ba-133 and Sr-85 at the LLNL
Whole Body Counter (title change at
3/8/89 mtg)

University of California

 **Lawrence Livermore**
National Laboratory

1121971

**Counting of Human Subjects Containing Nb-92m, Ba-133, and Sr-85
at the LLNL Whole Body Counter**

March 21, 1989

Answers to questions by Jack Shearer regarding Ba-133 and Sr-85 measurements.

1. What problem does the proposed experiment address?

Problems can arise in the interpretation of lung counting data from plutonium, americium, and other bone-seeking radionuclides if these materials have partially translocated to bone in the body following an initial deposition in the lung. This is because some fraction of the counts received during the lung count will actually be from the ribs overlying the lungs, rather than from the lungs themselves. Because the ribs are viewed more efficiently by the counters than the lung (due to geometry effects), considerable error in the assessment of true lung activity is possible in situations where part of the radioactivity being measured is located in bone.

In order to compensate for this effect, it is necessary to determine the ratio of activity in the ribs compared with some other part of the body not being counted, so that the rib contribution can be subtracted from the lung measurement. This can be done by using pre-obtained skull/chest count ratios from a "bone only" labeled subject containing these or other radionuclides.

2. Is the problem sufficiently important to warrant the use of human subjects?

Yes. The same rationale is applicable here as it is for using human subjects containing Nb-92m in the lung to simulate plutonium.

We are unable to meet current guidelines required by DOE Order 5480.11 specifying reporting levels for internally deposited plutonium, and our calibration errors are presently above those allowed by the proposed DOE ANSI N 13.30 Trial Use Standard. Our problem is that we are not able to properly subtract bone contributions, due to the lack of accurate calibration data.

3. Is the protocol designed to provide the desired information?

Yes. Short half-life Sr-85 provides calibration data at 13 and 15 keV X ray energies, which are very close in energy to the X rays associated with uranium, thorium, americium, and plutonium. There is also a useful gamma ray at 514 keV in energy. Ba-133 provides additional data at 32, 79, 276, 302, and 356 keV, allowing us to infer additional calibration data for the 59 keV gamma-ray from americium and the 63, 93, and 185 keV gamma-rays associated with U-238 and U-235.

4. What is the worst thing that can happen to a human as a result of being a subject?

Death. The radiation dose to the subjects for Sr-85 and Ba-133 is not expected to exceed a 50 year committed effective dose equivalent of 12.5 mrem and 23.3 mrem, respectively. For reference, the dose an air traveler would receive from a round trip flight to Europe over the polar route is approximately 10 mrem. It is, however, statistically possible that this small exposure could produce a future cancer.

1121972

5. What is the probability that one of the subjects will experience this worst-case threat?

The risk of contracting a fatal cancer from the Sr-85 dose of 12.5 mrem or the Ba-133 dose of 23.3 mrem is from 0 to 2 persons-per-million. In contrast, the risk of contracting a fatal cancer from a cosmic ray dose of 10 mrem is 0 to 1 persons-per-million.

6. Can some or all of the needed information be obtained by some alternate procedure that reduces or eliminates the need for using human subjects?

No. Accepted scientific practice is to verify a model with what is being modeled. This means that current bone-labeled phantoms must be checked for validity using humans.

To date, two subjects have been measured at LLNL. Varying skull measurements between these individuals and the phantom illustrate the need for further human measurements.

7. In the case where some or all of the subjects are not LLNL employees; would I approve the protocol if they were? (e.g., all LLNL employees)?

Yes, the experiment should be approved.

Although not specifically involving bone-seeking radionuclides, LLNL employees and one Argonne National Laboratory (ANL) employee have participated in these types of programs in the past. The ANL employee has been also approved for participation in the 1988-89 study involving inhalation of Nb-92m labeled particles.

Tracer and Irradiation Studies Approval Committee

Minutes of the eighteenth meeting held on Tuesday, 20th August, 1985 in the Environmental and Medical Sciences Division; AERE Harwell.

Present

Dr. J. Vennart	(Chairman)	External member
Dr. K. Duncan		National Radiological Protection I
Dr. J.C. Evans		Head of Medical Services, AERE
Dr. R.H. Mole		External member
Dr. A. Morgan		Environmental & Medical Sciences I
Dr. D. Newton		Environmental & Medical Sciences I
Mr. J.N. Pritchard	(Secretary)	Environmental & Medical Sciences I

Apologies for absence were received from Dr. A.C. Chamberlain and Dr. S. Rae.

1. CHANGES IN THE COMPOSITION OF THE COMMITTEE.

The Secretary opened by reading a communication from the outgoing Chairman, Dr. Stott, who thanked the COMMITTEE for their support and introduce Dr. Vennart, who had been invited by the Director of AERE to take the Chair. Dr. Rae had also tendered his resignation from the COMMITTEE following his retirement from the N.R.P.B. However, Dr. Duncan proposed that Dr. Rae be asked to reconsider this decision. Dr. Evans agreed to contact Dr. Rae and ask him to reconsider.

JCE

2. MINUTES OF THE SEVENTEENTH MEETING OF THE COMMITTEE (TISAC (85) M1).

Dr. Newton felt that the description of investigations concerning the ICRP's model for alkaline earth metabolism (section 2.4) required clarification. The following amendments were adopted:-

Section 2.4	1st paragraph line 3	insert "under certain assumptions" after "
Section 2.4	1st paragraph line 7	insert "short-term" before "retention pat
Section 2.4	1st paragraph line 9	replace "osteoporosis" by "bone turnover"
Section 2.4	2nd paragraph line 1	insert "concerning ¹³³ Ba" after "findings"

MINUTE I - Subject to the above alterations, the COMMITTEE accepted the Minutes

3. MATTERS ARISING.

It had been agreed that a publication detailing the workings of the COMMITTEE, together with information on investigations conducted with the resulting doses should appear through the offices of the Chairman (TISAC (85)M Minute II). Dr. Morgan suggested that, as the new Chairman did not work at AEI it would be appropriate for another member of the COMMITTEE to prepare this publication. The Chairman thanked Dr. Evans for agreeing to undertake this task, with the assistance of Dr. Morgan.

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AM

4. PROGRESS REPORTS ON APPROVED PROPOSALS

1121974

MINUTE III - The COMMITTEE suggest that the terms of reference be reviewed as soon as possible

One or two comments were directed to the protocol for carrying out volunteer experiments. In particular, the question of independently checking dose estimates was raised. It was pointed out that it was not a responsibility of A.R.S.A.C. to check the validity of such estimates. Mr. Pritchard indicated that A.E.R.E. would review their current practices in the light of the N.R.P.B. document at the same time as discussing the terms of reference of the COMMITTEE.

The Chairman concluded the discussion by thanking the COMMITTEE members for helping to air several important issues.

7. PROPOSED ADMINISTRATION OF ^{133}Ba BY INTRAVENOUS INJECTION (TISAC (85) 8).

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figures
1*

Dr. Newton introduced this proposal by summarising its background. By interpreting the available data, there is some support for the underlying postulates in the ICRP's model for alkaline earth metabolism although long-term experiments in one subject suggests that the rate constants may be inappropriate. However, other postulates in this model have not yet been tested. One of the objects of the proposed study is to check that the distribution is not dependent on the age at intake. Dr. Newton pointed out that "it" in paragraph 8 refers to the dose estimate of 233 μSv . He stressed that this is based on one subject who could have a higher than average bone turnover. The actual dose could exceed this by a factor of 2 but would still remain within category I. Dr. Mole stated that this factor of 2 was based on a high bone resorption in this one subject, but turnover also takes place by diffusion, so that the actual dose may exceed the estimate by less than a factor of 2. After some minor clarification of Dr. Newton's paper, this proposal was approved.

MINUTE IV - The COMMITTEE approved the administration by intravenous injection of 75 kBq ^{133}Ba to 5 subjects with a resulting whole-body weight ^{sa} dose commitment of 233 μSv

Discussion then turned to possible modifications to the experimental protocol. In particular, it was felt that information should be obtained on the short-term bone turnover; if a short-term variation with age was observed this could be an important cause of any long-term difference observed in the main study. Such information could better be obtained by performing both experiments in the same subject rather than by attempting a correlation in different groups of subjects. It was suggested that this information could be obtained either by injection of ^{47}Ca or ^{223}Ra . Dr. Newton agreed with the scientific merit of these proposals, but feared that the extra time requirements placed on the volunteers might prove unacceptable to them. Also, he felt that the extra dose commitment may make it a category II experiment. Despite this the COMMITTEE felt it was a worthwhile additional experiment and approved it, subject to being informed of the dose commitment by memo.

MINUTE V - The COMMITTEE approved in principle an additional experiment on these 5 volunteers to measure short-term bone turnover rates

.. Dr. Newton said that he would carefully consider this recommendation and reply to the COMMITTEE in due course (see attached memo).

8. PROPOSED STUDY OF THE FACTORS AFFECTING MAINSTREAM TAR DEPOSITION (TISAC(85)9).

Mr. Pritchard began by reviewing the data on tar deposition obtained in a previous study. Modelling of this data suggests that the tar particles grow hygroscopically whilst in the lung and deposit in the tracheobronchial region during exhalation. There is experimental evidence that significant deposition can occur during exhalation. Models would suggest a substantial variation in the pattern of deposition between inert and hygroscopic materials, although there is no experimental data on the regional deposition of hygroscopic aerosols. It is proposed to use cigarette smoke to investigate the regional deposition of a hygroscopic material as a function of breathing pattern. It will also provide information on the way to inhale cigarette smoke in order to minimise tar deposition. It is proposed to administer 55 kBq of ^{123}I on seven occasions with a resulting maximum dose commitment of 16.8 μSv to the lung, 105 μSv to the upper large intestine and 155 μSv to the lower large intestine, the whole-body equivalent dose being 18.2 μSv .

After some discussion of the mechanism of deposition during exhalation and the use of human lung casts in deposition studies, the study was approved.

MINUTE VI - The COMMITTEE approved the administration of 55 kBq of ^{123}I as 1-iodohexadecane in mainstream cigarette smoke on a maximum of 7 occasions to 6 subjects with a resulting whole-body equivalent dose of 18.2 μSv

9. ANY OTHER BUSINESS.

There being no further business, the Chairman closed the meeting.

J.N. Pritchard

18 November 1985

AERE (85) 22

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1121977

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One or two comments were directed to the protocol for carrying out volunteer experiments. In particular, the question of independently checking dose estimates was raised. It was pointed out that it was not a responsibility of A.R.S.A.C. to check the validity of such estimates. Mr. Pritchard indicated that A.E.R.E. would review their current practices in the light of the N.R.P.B. document at the same time as discussing the terms of reference of the COMMITTEE.

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