

Interdepartmental letterhead

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Biomedical & Environmental Sciences Program

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23 December 1980

TO: A.L. Anderson H.W. Patterson  
J.O. Beatty D.C. Shepherd  
M.W. Biggs  
G.W. Campbell  
S.D. Cole  
P.N. Dean  
R.L. Dobson  
V.L. James  
J.S. Johnson

REPOSITORY LLNL B361 Rm. B940A  
COLLECTION Institutional Review Board  
BOX No. IRB Protocol File  
FOLDER George Campbell 5/12/83  
81P-101-01 IAEA Inhalation  
Experiment

FROM: Fred Hatch

SUBJECT: IAEA <sup>92m</sup>Nb Experiment Update

At the meeting of the Human Subjects Committee on December 8, 1980, this proposal was reviewed and was tentatively approved with two conditions: 1) independent recalculation of the dose commitments to lung and GI tract, and 2) provision to stop the particle inhalation earlier than the plan if the proposed uptake level has already been reached.

Subsequently, further information on the experiment has been provided by Phil Dean, former Principal Investigator on the development and calibration of the LLNL phantom. Upon Phil's recommendation, we have consulted with Dr. J. Thiessen, who is the new chief of the Human Health and Assessments Division of DOE/ASEV. He wishes to review the proposal before it is implemented at LLNL.

The following is the present status of the proposal.

1. LLNL Committee approval is deferred temporarily.
2. Condition (1) above in the first paragraph should be completed, and submitted and condition (2) should be added to the protocol.
3. The data analysis on initial uptake, chest wall thickness measurement, and LLNL body counting data on the first 3 subjects who inhaled <sup>92m</sup>Nb should be completed and compared against the phantom calibration curve. This data analysis should be submitted to the Committee.
4. A statement of the need and justification for doing further human inhalation experiments should be prepared, with detailed comments on the benefits to be expected from obtaining additional data points. This may include input from Dr. Toohy from ANL if desired.



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5. Comment on the experimental protocol, currently available data (No. 3), and supporting arguments (No. 4) by Phil Dean.
6. The assembled proposal and followup materials (Nos. 2-5) will be submitted to Dr. Thiessen for review and determination whether participation of LLNL volunteers is necessary and consistent with DOE policy.
7. At completion of No. 6, the LLNL Committee will take final action on the proposal.

I am sorry to impose this rather extensive series of requirements on this matter. However, this is an important utilization of human subjects in research, and there are substantial differences of opinion about the need and appropriateness of the further experiments.

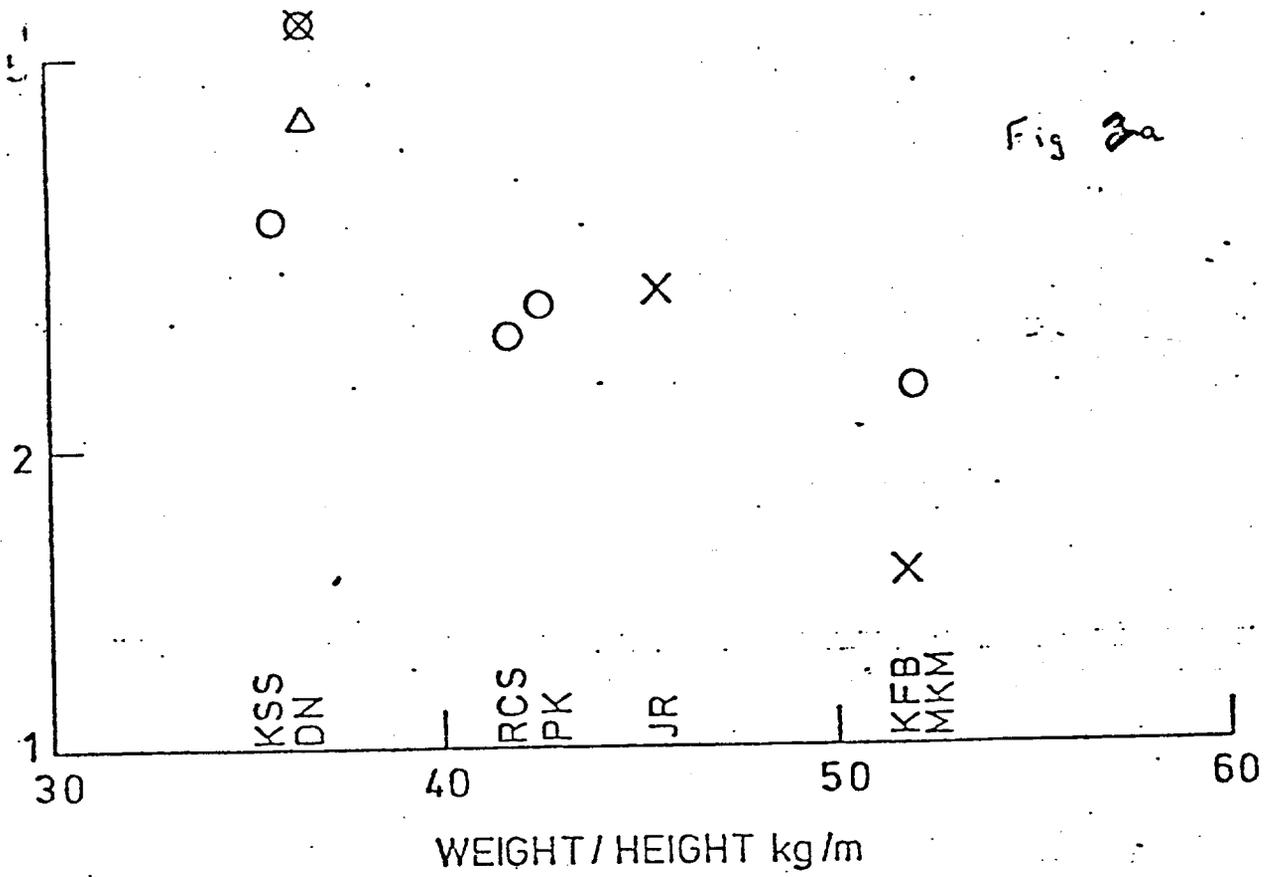
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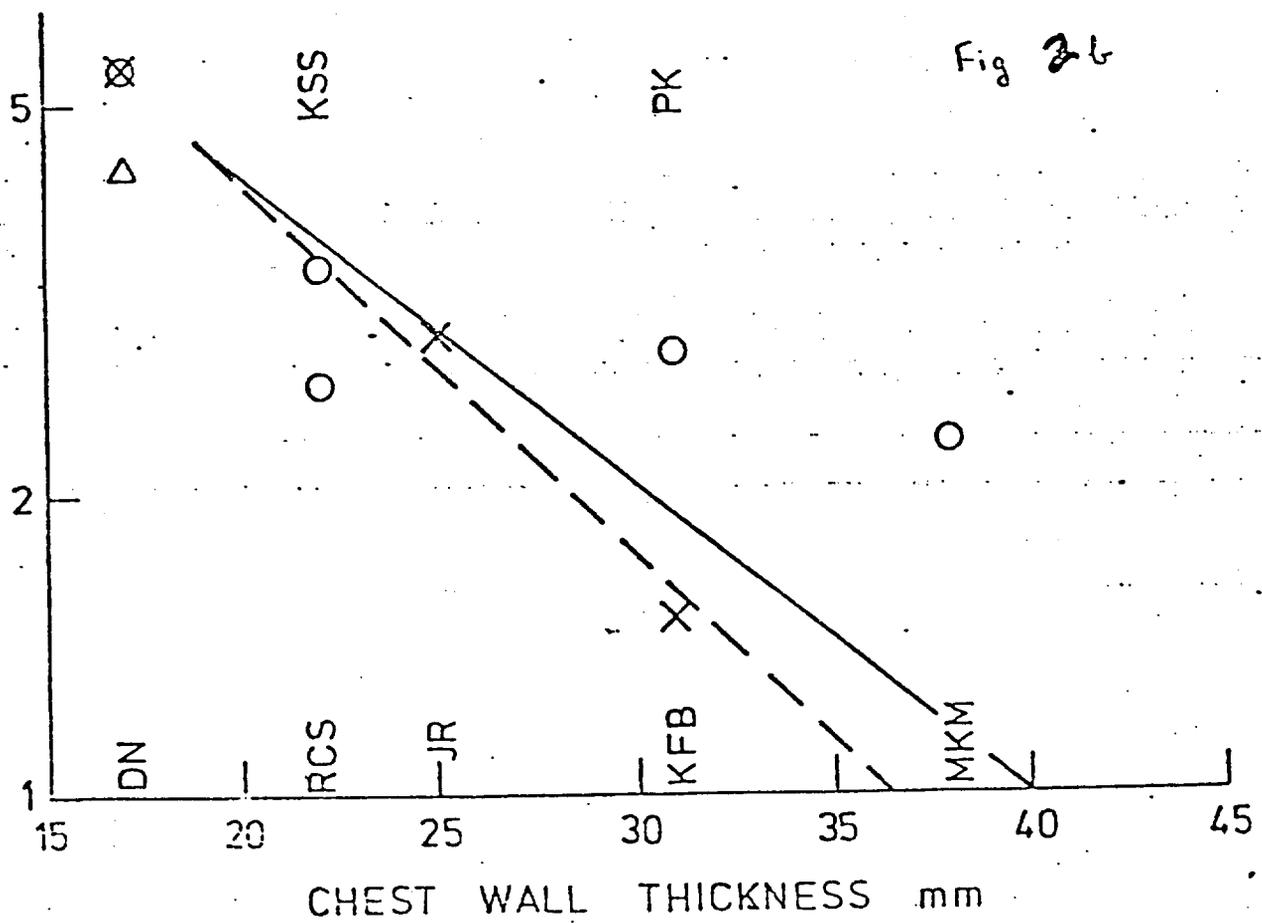
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E<sub>2</sub> (COUNTS PER 1000 X-RAYS)



E<sub>2</sub> (COUNTS PER 1000 X-RAYS)



with the  $\gamma$ -detector geometry at AERE, plotted against weight/height ratio (Fig 3a) and against chest wall thickness (Fig 3b):

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X : Experiment A

O : Experiment B'

$\Delta$  : Experiment C

..... : prediction from Livermore phantom with muscle-equivalent chest wall.

———— : prediction from Livermore phantom with chest wall including adipose-tissue substitute.

recommendations for an ethical committee and report to the COMMITTEE.

Dr. Raison finally drew attention to the "Notes for Guidance..." concerning research projects (paragraphs 48-52) with particular reference to the minimum volunteer age of 18 except under special circumstances, the consent of the subject and the dose commitment. Doses are categorised into <50 mrem, <500 mrem and <5 rem equivalent total body dose, with the individual organ dose equivalents also stated. The Chairman stated that TISAC were empowered to grant approval of up to 50 mrem whole body dose equivalent, with single organ dose equivalent of up to 250 mrem (HMC 76(19)9, TISAC(76)M2). These figures were based on then current views (WHO/RHL/73.1, Br.Inst.Radiol.1(2),4 (1975)) and are within the lowest dose category, equivalent to a level of risk within variations of natural background radiation.

MINUTE II - The COMMITTEE thanked Dr. Raison for his presentation.

## 2. MINUTES OF THE ELEVENTH MEETING OF THE TRACER AND IRRADIATION STUDIES APPROVAL COMMITTEE (TISAC(78)M1)

MINUTE III - The COMMITTEE accepted the minutes

## 3. MATTERS ARISING FROM THE ELEVENTH MEETING

Dr. Chamberlain informed the Committee that the letter to NATURE on the tetra ethyl and tetra methyl lead work was not considered of sufficient general interest and had instead, subsequently appeared in the Proceedings of "Heavy Metals in the Environment" (Imperial College, September 1979).

## 4. PROPOSALS FOR EXPERIMENTS ON THE UPTAKE OF RADIO-CADMIUM FROM THE GUT

The Working Party on the Monitoring of Foodstuffs for Heavy Metals have established that crabs, in particular brown crabmeat, tend to contain high levels of cadmium. Regular consumption of brown crab meat could lead to intakes well in excess of the FAO/WHO standards. The Ministry of Agriculture, Fisheries and Food (MAFF) are seeking to establish the risk to regular consumers and hence wish to ascertain the absorption and retention by humans. Dr. Chamberlain indicated that he had been approached by Dr. J.C. Sherlock of MAFF to perform such a study.

Dr. Chamberlain stated that there were two possible methods of approach to this problem (TISAC(79)2):-

- a) whole body gamma measurement at 5 days and longer after ingestion, measurements of ingested dose and urinary and faecal excretion enabling a balance to be struck
- b) Beta or Gamma measurement of ingested dose, urine and faeces to give retention by difference.

Dr. Chamberlain felt that although method (b) involved lower activity levels, it would require considerable manpower and would have large inherent errors if the retention were small. It was therefore proposed to use method (a) with Cadmium-115m (half-life 43d, 100%  $\beta$ , 1.9%  $\gamma$ ). An initial administration to two subjects of 0.5  $\mu$ Ci would occur with a possible repeat at a dose of 2  $\mu$ Ci if the counting statistics were poor. Dr. Chamberlain pointed out that such an experiment would not only satisfy the requirements of MAFF, but would provide useful additional data on the blood:urinary excretion:faecal excretion ratios, an area where little information is currently available. Due to this, however, uncertainty exists as to the degree of uptake of cadmium in order to estimate the radiation dose to the volunteer. Dr. Newton assisted Dr. Chamberlain by presenting a table of equivalent whole-body doses for a range of uptakes, also indicating the experimental uncertainties.

TRACER AND IRRADIATION STUDIES APPROVAL COMMITTEE

Minutes of the twelfth meeting held on Monday, 8th October, 1979 in Environmental & Medical Sciences Division, AERE, Harwell.

PRESENT

|                                      |  |
|--------------------------------------|--|
| Mr. N.G. Stewart (Chairman)          | Environmental & Medical Sciences Division  |
| Dr. R.H. Mole                        | Medical Research Council Radiobiology Unit |
| Dr. S. Rae                           | National Radiological Protection Board     |
| Dr. J.C.A. Raison                    | " " " "                                    |
| Dr. A.N.B. Stott                     | Environmental & Medical Sciences Division  |
| Dr. A.C. Chamberlain                 | " " "                                      |
| Mr. M. J. Heard                      | " " "                                      |
| Mr. D. Newton                        | " " "                                      |
| Mr. J.N. Pritchard(Acting Secretary) | " " "                                      |

1. LEGISLATION FOR THE ADMINISTRATION OF RADIOACTIVE SUBSTANCES TO HUMANS

In order to comply with a recent direction from the EEC on the use of ionising radiation (Article 5(a) of Directive 76/579/Euratom), the Government has introduced legislation to cover the administration of radioactive substances to humans for purposes of diagnosis, therapy or research. To assist in the implementation of this legislation, the Administration of Radioactive Substances Advisory Committee (ARSAC) has been appointed. The Chairman welcomed Dr. J.C.A. Raison, a member of ARSAC who had been invited to describe the new legislation and the manner in which it would affect proposals put before TISAC.

Dr. Raison began by explaining the definitions used in the regulations, pointing out that a "radioactive medicinal product" covered sealed sources (except nuclear-powered cardiac pacemakers), unsealed sources (including radioactive aerosols in this category) and irradiation induced activity, except where this is a by-product of treatment. However, naturally occurring radioactivity does not require authorisation. Such authorisation takes the form of a certificate issued by a Minister empowering the administration of a specified quantity of radioisotope or isotopes in a stated form to an indicated group of people. Such a certificate may be obtained by completing the attached application form and forwarding it to the Department of Health and Social Security, whence it is circulated to members of ARSAC who then make their recommendations to the Minister. Should a certificate be refused or revoked, a system of appeal exists to the Minister or to the Committee on Radiation from Radioactive Medicinal Products (CRMP). Certificates are only issued to a medical doctor or dentist, although he does not have to be personally involved, work may proceed under his direction. The certificate holder does not even have to be present although "in the case of long absences, or of the appointment being vacated", a new certificate holder must be arranged.

Dr. Raison indicated that ARSAC is not primarily concerned with the ethics of the experiment and that ultimate approval for the work still lies with the local ethical committee, even when a certificate has been granted (see paragraphs 53-55 of the attached "Notes for Guidance..."). However, ARSAC will normally expect the approval of the local committee before making a positive recommendation to the Minister. Guidelines for the performance of an ethical committee are laid down in "Supervision of the Ethics of Clinical Research Investigations and Foetal Research" DHESS, HSC(IS)153, although Dr. Raison was not clear how closely TISAC conformed to these regulations.