

717910

RECEIVED

MAR 08 1989

**INSTITUTIONAL
REVIEW BOARD** *special
meeting*

**CURRENT WHOLE BODY COUNTER
EXPERIMENTS INVOLVING HUMAN
SUBJECTS -- MARCH 6, 1989**

APPENDIX

A.L. Anderson

D.A. Kruchten

REPOSITORY LLNL B361 Rm. B940A

COLLECTION Institutional Review Board

BOX No. IRB Protocol File

FOLDER Anderson IRB 88-101

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)

1122046

I. Ba-133

1122047

PROPOSED ADMINISTRATION OF BARIUM-133 BY INTRAVENOUS INJECTION

Background

1. The ICRP's model of alkaline earth metabolism⁽¹⁾ provides the metabolic basis for the control of exposure to radionuclides of the elements calcium, strontium, barium and radium. Central to this model is a function intended to describe the whole-body retention of a single systemic input, up to times several decades later. Important parameters in this function relate (i) to the skeletal depletion of activity following diffusion through the calcified matrix, (ii) to the initial partition of long-term skeletal deposition between compact and trabecular bone and (iii) to the rates at which activity is lost from compact and trabecular bone through the process of skeletal resorption. Thus, the parameters determine not merely the whole-body retention, but also the retention in the two categories of bone individually. This is important in the dosimetry of radium⁽²⁾, because an α -particle emitted by ^{226}Ra within trabecular bone is assumed to be four times more detrimental compared with one from ^{226}Ra deposited in compact bone. Moreover, an improved knowledge of the local retention functions would assist in the evaluation of data on the incidence of bone cancers in people who had acquired large burdens of radium.
2. To estimate the value of each parameter, the ICRP Task Group which developed the model reviewed evidence from the histological examination of bone and from human metabolic data, including data on the whole-body retention of radium in those relatively few instances where the intake was known. These data (Fig 1) were scattered and fragmentary, and non-existent between 1 and 20 years after intake. The retention function, with the chosen values of its parameters, provides a visually acceptable fit (Fig 1), but the scatter is such that the data can offer only limited support either for that choice of values or for the postulates underlying the model. It would be more convincing if a systematic study of the retention could be undertaken, following a controlled administration of radium; the test would then be whether a function of the general form postulated in the model, embodying metabolically sensible values for its parameters, was found to provide a close fit to such data.

3. In the case of radium, the radiation dose to volunteers in such an experiment would be prohibitive. However, in certain respects, barium appears to be a satisfactory tracer for radium. The excretory plasma clearance for both elements is high⁽¹⁾, so that ions released from bone have little chance of being re-incorporated; consequently, the extent of skeletal re-modelling will be reflected to the same degree in the pattern of whole-body retention of both elements. The losses through diffusion will differ for the two elements, and this will affect the retention pattern, but if the retention of a barium isotope is studied over a long enough period, the effects of diffusion, resorption of compact bone, and resorption of trabecular bone can in principle be separated.

4. Data exist to illustrate these possibilities. Fig 2 shows the percentage retention of an initial 2 μCi ^{133}Ba (half-life 10.7 years), over a 10-year period following its injection into a healthy 60-year-old male volunteer, Subject GH. The purpose of this experiment, which was in the first instance conducted jointly with the RAC Unit at Harwell, was primarily to compare the short-term metabolism of barium with that of other alkaline earth elements in the same subject⁽²⁾; Harwell contributed data from body radioactivity measurements. In fact, we continued to measure the ^{133}Ba for 19 years, making this by far the longest continuous survey of a known dose of a bone-seeker in man. The continuous curve in Fig 2 was derived by rigorous fitting of a function of the general form proposed in the model, and it provides a remarkably close fit over most of the 10-year period of the plotted data. The rate constants necessary to achieve this fit were $8.1 \pm 0.8 \text{ yr}^{-1}$ for resorption of compact bone and $21.9 \pm 1.8 \text{ yr}^{-1}$ for resorption of trabecular bone. These are somewhat larger than the values assumed by the Task Group (2.8 and 10 yr^{-1} respectively). The ratio of these two constants (4.3 ± 0.8) is, however, consistent with the ratio of 4 predicted from the relative surface area: volume ratios in the two categories of bone, which is a fundamental postulate in the model. Other evidence emerging from this study, and supporting both the basis of the model and the validity of ^{133}Ba as a tracer for radium, is given elsewhere⁽⁴⁾.

Proposal and justification

5. The data for ^{133}Ba are confined to those for Subject GE, and they need to be supplemented by studies in other subjects, to indicate the variability between subjects of values for the important parameters. We propose to inject five additional male volunteers with 75 kBq (2 μCi) ^{133}Ba , and also to re-inject Subject GE with the same quantity, in order to compare his retention pattern with that (Fig 2) found 20 years ago. Measurements of whole-body retention would be supplemented in the early stages by assessment of ^{133}Ba in samples of blood and excreta.
6. If the data from these studies, like those already obtained from Subject GE, were found to follow functions of the form predicted by the model, these data would provide valuable additional support for the basis of dosimetry for an important group of radionuclides. If they failed to show such behaviour, implying that the consistency found in our studies with GE was perhaps fortuitous, then this would be an equally important outcome, demonstrating deficiencies in the model. In that case the data, together with those at present available for Subject GE, would provide information, unique in its detail and reliability, on the long-term behaviour of an alkaline earth element in man, which would be invaluable in the formulation of any revised model.

Dose estimates

7. The weighted committed dose equivalents for the organs listed in ICRP Publication 30(8), over a period of 80 years following injection of 75 kBq ^{133}Ba , are as follows:

| Organ | WCDE (μSv) |
|---------------|----------------------------|
| Red marrow | 120 |
| Bone surfaces | 42 |
| Gonads | 38 |
| Lungs | 19 |
| Adrenals | 13 |
| TOTAL | 232 |

REFERENCES

1. ICRP Publication 20 (1972). Alkaline earth metabolism in adult man.
2. ICRP Publication 30, Part 1 Supplement, p 286 (1979).
3. HARRISON et al, Int J Radiat Biol. 11, 235-247 (1967).
4. Newton et al, AERE-R 11407, (1988).
5. ICRP Publication 30, Part 2 Supplement, p 384 (1981).

D Newton

EMS Division
Bldg 364
AERE, Harwell

1st July 1988

1122051

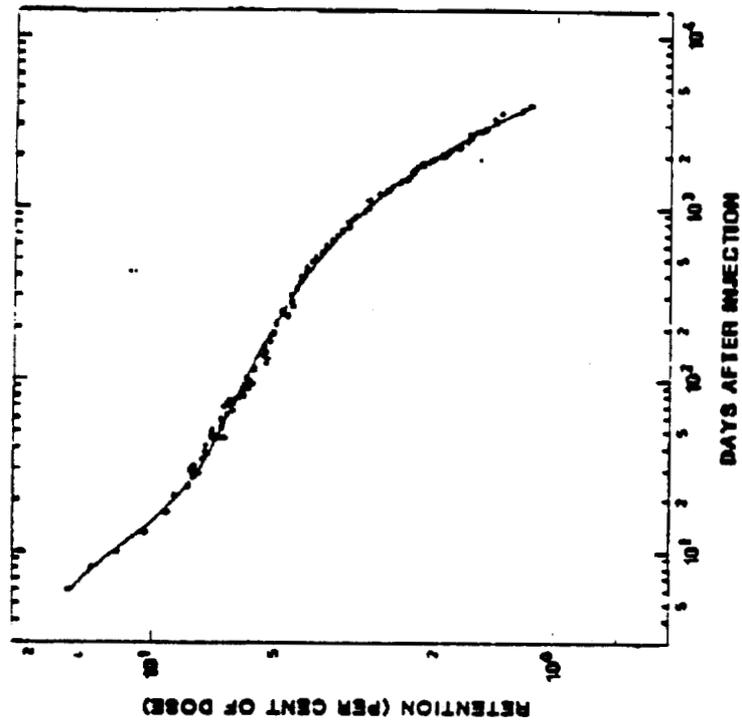


Fig 2 Plotted points : observed whole-body retention in Subject GH, up to 10 years after injection of ¹³³Ba

Curve : function of the form postulated in the ICR model, fitted to the data for Subject GH

1122052

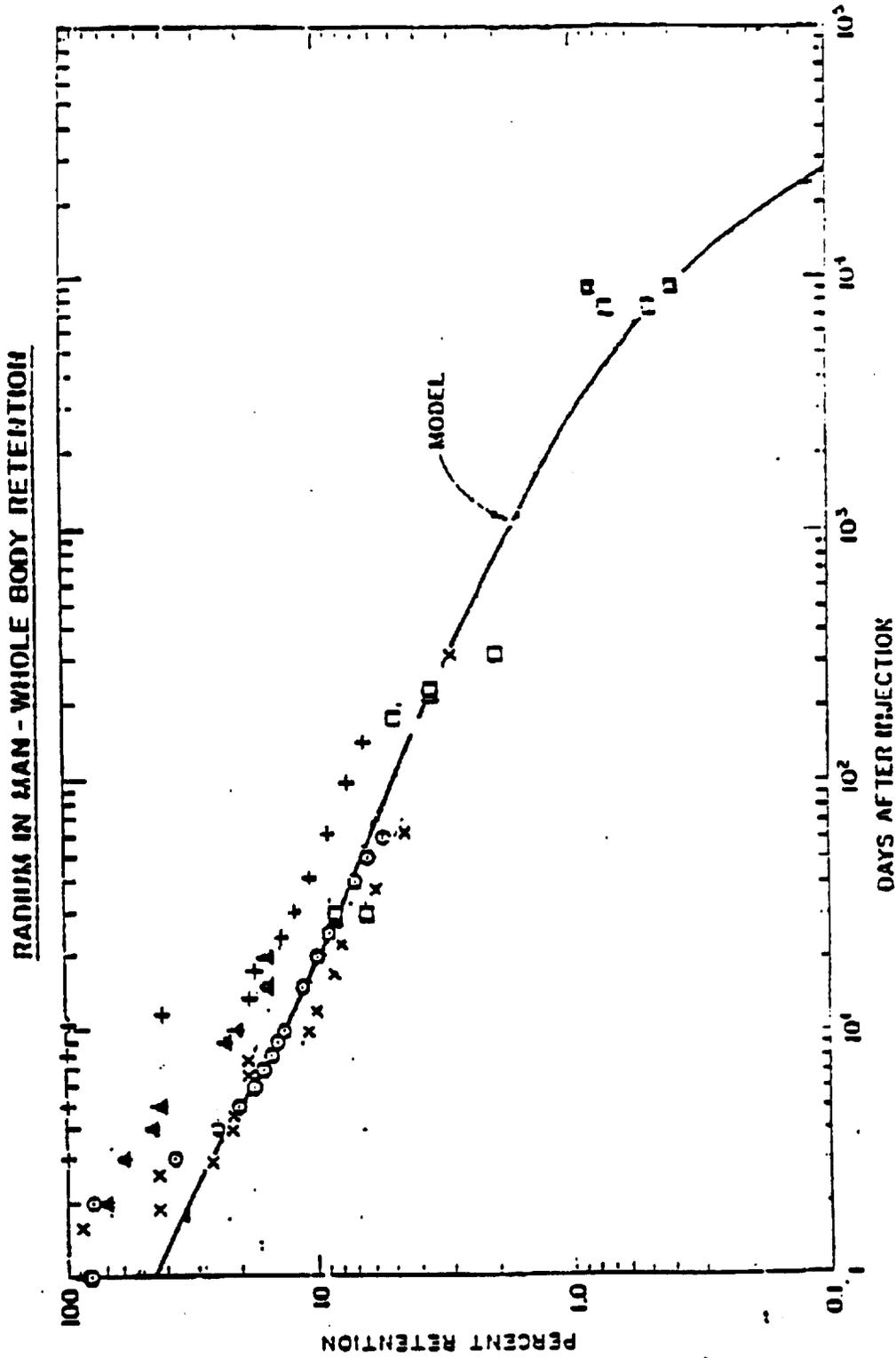


Fig 3 Data on the whole body retention of radium in man, reviewed by the ICRP Task Group in formulating the model of alkaline earth metabolism.

1122053

1985-02-05

Dr. D. Newton
Environmental and Medical Sciences Division
AERE Harwell
Oxon OX11 0RA

Dear Dr. Newton,

I am replying to your letter of 24 January concerning a proposed study for long term retention of barium in man.

Technically, your proposal seems well-considered, although I think you have underestimated the dose to be received, since you apparently forgot about the f_1 of 0.1. From ICRP Publication 30, Supplement to Part 2, page 396, I reckon that the effective dose equivalent from 1 Bq given orally is 4.35×10^{-10} Sv. (I have omitted the dose components from breast and gut).

With an injection of 1 Bq the dose is 10 times higher (1/0.1); so 75 kBq injected will give $75 \times 10^3 \times 4.35 \times 10^{-10} \times 10 = 330 \mu\text{Sv}$ (not 50 μSv). I'm not sure how this will affect the deliberations of your ethical committee.

Yours sincerely,

F.Sowby

F.D. Sowby

NO - this approach includes also dose received by target organs from activity passing through the gut. My 230 μSv is correct for injected activity. SW

II. Sr-85

1122055

Background

1 This proposed study is intended to supplement existing data on alkaline earth metabolism in a single, healthy male volunteer, Subject GH, and in particular to establish whether changes occur in the pattern of clearance of strontium from the skeleton during late adult life. On four previous occasions, Subject GH was injected with nuclides of calcium or strontium of sufficient half-life to allow their retention in the body to be studied for 300 - 400 days (Table 1).

TABLE 1 DATA FROM PREVIOUS STUDIES WITH ^{45}Ca OR ^{85}Sr ADMINISTERED TO SUBJECT GH

| Age | Nuclide | Duration of study (days) | C |
|-----|------------------|--------------------------|-----------------|
| 53 | ^{85}Sr | 336 | 0.16 ± 0.06 |
| 57 | ^{85}Sr | 399 | 0.23 ± 0.02 |
| 60 | ^{85}Sr | 388 | 0.17 ± 0.01 |
| 66 | ^{45}Ca | 388 | 0.15 ± 0.01 |

2 In Table 1, the parameter C is the exponent in the power function

$$R = Bt^{-C}$$

where R represents the retention at time t after intake; the parameters B and C were derived by analysis of the retention data obtained after the early clearance of activity from labile pools was judged to be complete. C is presumed to reflect, empirically, the rate at which tracer in a series of pools associated with bone is depleted; more details of these analyses are given elsewhere*.

3 Although C has no more specific metabolic significance, the trend of C with age may reasonably be used to indicate any age-related changes in the efficiency with which the tracer is removed from the skeleton. Unfortunately, the value (0.15) listed in Table 1 for age 66 does not bear legitimate comparison with the others, since it alone was derived following injection of radiocalcium, whereas the remainder emerged following intakes of strontium activity. Indications⁽¹⁾ are that the long-term treatment of the two elements by the skeleton is similar, but that calcium is less rapidly removed from the body because of the greater efficiency with which it is re-cycled into bone. Consequently, if the experiment at age 66 had involved strontium rather than calcium, it is likely that the value of C derived would have been > 0.15 .

4 Overall therefore, the results in Table 1 suggest no important trend in the clearance pattern in this subject between ages 53 and 66, and this conclusion extends to the efficiency with which the tracer is initially deposited in the skeleton*. The study now proposed would indicate what, if any, differences are to be found at age 82.

* AERE-R 12227

5 The subject will receive an intravenous injection of 150 kBq ^{85}Sr in isotonic saline. Assessments of whole body retention will be made at intervals for as long as feasible - probably 500 days. Complete collections of excreta are envisaged during the first 3 - 4 weeks with probably about 12 blood samples (20 ml) analysed during this period.

Dosimetry

6 Weighted committed dose equivalents for each of the relevant organs listed in ICRP Publication 30 are given in Table 2, and are based on the metabolic model for strontium proposed in that document.

TABLE 2 WEIGHTED COMMITTED DOSE EQUIVALENTS (μSv) FOLLOWING INTRAVENOUS INJECTION OF 150 kBq ^{85}Sr

| Organ | μSv |
|---------------|----------------|
| Red marrow | 32 |
| G I tract | 30 |
| Gonads | 27 |
| Lungs | 11 |
| Adrenals | 10 |
| Bone surfaces | 9 |
| Pancreas | 6 |
| Total | 125 |

Summary

7 Approval is sought for the administration, by intravenous injection, of up to 150 kBq ^{85}Sr to a single, healthy male volunteer aged 82, in an investigation of age-related trends in strontium metabolism.

D Newton
EMSc Division
Building 364

23 September 1986

Reference

(1) J Reeve et al. Calcif. Tissue Int. 35, 9-15 (1983).

1986 1007 82 

Tracer and Irradiation Studies Approval Committee

Minutes of the twentieth meeting held on Thursday, 2 October, 1986 in the Environmental and Medical Sciences Division, AERE Harwell.

Present:

| | |
|------------------------------|--------------------------------------|
| Dr J Vennart (Chairman) | External member |
| Dr A C Chamberlain | External member |
| Dr J C Evans | Head of Medical Section, AERE |
| Dr A Morgan | Environmental & Medical Sciences Div |
| Dr D Newton | Environmental & Medical Sciences Div |
| Dr S Rae | External member |
| Mr J N Pritchard (Secretary) | Environmental & Medical Sciences Div |

Mr R M Brown (Environmental & Medical Sciences Div) also attended.

Apologies for absence were received from Dr K Duncan and Dr R H Mole.

1. MINUTES OF THE NINETEENTH MEETING (TISAC (86) M1)

Dr Evans was erroneously omitted from the list of those present.

Minute I. Subject to this alteration, the COMMITTEE accepted the minutes

2. MATTERS ARISING

2.1 Publication on working practices

JCE/AM Drs Morgan and Evans apologised for the slow progress on the publication dealing with the workings of the COMMITTEE. A combination of factors have impeded its progress and so a draft is unlikely to be available before the end of this year. Mr Pritchard drew the attention of the authors to a paper on a similar theme presented at the 10th Annual Conference of the Australian Radiation Protection Society (R Rosen, Radiation Protection in Australia, 3 (4), 156-159).

2.2 Revised code of practice

The final draft of the revised code of practice was circulated by the COMMITTEE for information. However, prior to the meeting, Dr Mole had drawn the authors' attention to several points requiring clarification, including the omission of a discussion of the confidential nature of some projects. Thus, comments were invited from the remainder of the COMMITTEE. Dr Vennart suggested that doses should now be referred to as 'committed effective' dose equivalents, although Dr Newton pointed out the difficulty of quoting committed doses before the end of long-term metabolic studies. Dr Rae was assured that volunteer dose records are incorporated into medical records and will form part of the annual statement of dose issued to employees. Dr Evans indicated that a framework for compensation may be agreed along lines similar to the BNP plc scheme.

JCE Dr Evans reported that the code of practice is currently being discussed by a sub committee of the Authority Joint Committee on Health and Safety before going to the Establishment's Directors Committee for final approval. In particular, the sub committee of the AJCHS is considering the role of the employees' representative in the newly constituted COMMITTEE. Dr Evans, who is a member of this sub committee, received a strong recommendation that such a representative should not belong to an organisation with a stated policy against volunteer

experiments. It was pointed out that the mechanism for obtaining a deputy for this representative, should he be unable to attend a meeting, needs to be decided, else the COMMITTEE will be inquorate.

2.3 Dealings with ARSAC

JCE

Dr Evans reported that he had been unable to contact Dr Williams by telephone despite numerous attempts. He agreed to write to ARSAC, questioning whether ethical approval was required prior to an application for a licence. However, the response time for research licence applications has improved markedly now that the applications for renewal of the 5-yearly licences for diagnosis and therapy have been processed.

The Chairman then requested an update on the proposal for investigating the effects of certain drugs taken on a prophylactic basis (TISAC (86) 3). Dr Evans replied that the results of an extensive literature search for relevant data were being assessed, prior to formulating a proposal to be put before a hospital Ethics Committee. Mr Pritchard added that preliminary results indicated that the lung could be dilated beyond the normal range in healthy subjects, even with prolonged treatment. This had been shown to affect deposition in the only published study found to date. Effects on mucociliary clearance appear to be drug specific with a range of responses.

3. PROGRESS REPORTS on APPROVED PROPOSALS

3.6 Metabolism of alkaline earths

Dr Newton reported that the first administration of ¹³³Ba had successfully taken place and that the next was anticipated in early November. The data arising from the first injection were presented under item 5.

5. PROPOSED ADMINISTRATION OF ^{85}Sr BY INTRAVENOUS INJECTION (TISAC (86) 7)

Dr Newton reported that the first subject to participate in the study of Ba metabolism (TISAC (85) 6), now aged 82, has taken part in a variety of studies of alkaline earth metabolism over the last 30 years. The Ba data suggest that renal clearance has reduced with age, with faecal clearance remaining similar, resulting in the proportion retained for long periods increasing from an estimated 6% twenty years ago to 8% in this experiment. Most of the early experiments had been conducted with Sr, so it is proposed to investigate whether the changes in Ba retention are mirrored by those in Sr.

In discussion, it was pointed out that the subject in question was a particularly active 82 year-old so that the data may not be typical for his age-group. However, this experiment would demonstrate differences in the behaviour of Sr and Ba, whilst the remaining subjects in the Ba experiment will give a range for inter-subject variability. If differences between Sr and Ba are observed, there is unlikely to be sufficient additional information to propose mechanisms for such a discrepancy; in particular, there is no baseline information on renal function for this subject. The Chairman asked about the total dose accrued by this volunteer. Dr Newton replied that the dose levels were low in comparison to that arising from a pre-existing ^{226}Ra burden. He added that there was no problem in obtaining informed consent; indeed, some of the impetus for this experiment came from the volunteer.

Minute II. The COMMITTEE approved the administration by intravenous injection of 150 kBq ^{85}Sr to a single volunteer, aged 82, with a total committed effective dose equivalent of 125 μSv

6. PROPOSED FURTHER STUDIES WITH $^{92\text{m}}\text{Nb}$ -LABELLED MICROSPHERES INHALED BY MEN (TISAC (86) 8)

Dr Newton began by summarising previous work that had taken place using 5 μm particles. Strictly speaking, the calibration derived from this work applies only for particles of this size, since it relies on the detection of particles within a few centimetres of the surface of the chest; it is conceivable that particles of smaller size could penetrate to this region to a greater extent, thereby altering the calibration factor. Existing evidence tends not to support this hypothesis, but such data are severely limited. Hence, it is proposed to repeat the original calibration exercise with 8 volunteers, using as many of the subjects from the original study as possible.

In the discussion that followed, Dr Newton indicated that, if a particle-size effect is found, it may be possible to use particle size information from concurrent air samples to assist in deriving the correct calibration for in vivo measurements. The administration will take place in stages, so that the desired lung content may be approached gradually. Self-absorption effects within particles are unlikely to be significant at respirable particle sizes. Animal experiments have indicated a long-term clearance pathway to the pleural surface, which might affect detector response. However, no such effect has been observed in contaminees.

Minute III. The COMMITTEE approved the administration by inhalation of approximately 80 kBq ^{92m}Nb, with an estimated committed effective dose equivalent of 53 μSv from lung, 11 μSv from gut and 6 μSv from thymus to a total of 8 volunteers

III. NB-9cm

1122062

A PROPOSAL FOR FURTHER STUDIES WITH ^{92m}Nb - LABELLED POLYSTYRENE PARTICLES INHALED BY MALE VOLUNTEERS

Background

In previous work sanctioned by the Committee (TISAC 79M1), male volunteers inhaled 5- μm monodisperse polystyrene particles incorporating ^{92m}Nb (half-life 10.1 days). That experiment was conceived originally as a study of the energy dependence of counting efficiency for X-ray detectors employed in the assessment of plutonium in lungs: the detection efficiencies for ^{92m}Nb (mean X-ray energy 16 keV) were compared with those previously determined in studies with inhaled ^{103}Pd (mean energy 21 keV), and the relative counting efficiencies were found to accord with predictions based on a computer model of the thorax⁽¹⁾. However, the data obtained from these subjects, which included detection efficiencies measured with a variety of equipment at five laboratories in the UK and USA, became of more direct relevance with the marketing of a realistic phantom thorax⁽²⁾ designed by the Lawrence Livermore National Laboratory and its purchase by some twenty laboratories, mainly in the USA and UK. The detection efficiencies recorded for our subjects were in general agreement with those indicated by the phantom when its lungs were loaded with ^{92m}Nb ⁽¹⁾. These developments led to the implicit endorsement of this design of phantom by the IAEA, as an acceptable calibration standard in this context, to the extent that the Agency purchased two of them for loan to member states lacking such equipment.

However, the direct validation of the phantom rests on experiments with inhaled particles of one size (5 μm) only. Experiments conducted jointly with AWRE suggest that in females lung deposits of ^{92m}Nb present in 3.5- μm polystyrene particles are detected with similar efficiency to those inhaled in 5- μm particles⁽³⁾. Beyond this however, only fragmentary evidence exists. One male subject showed similar detection efficiencies for ^{103}Pd inhaled as 2.3- μm and 5- μm aerosols, but an efficiency reduced by 15-20 per cent when submicron particles were substituted⁽⁴⁾; in that case it should be noted that ^{103}Pd is not the most appropriate simulator for plutonium because of its X-ray spectrum, and that the differential efficiency would almost certainly have been much greater if ^{92m}Nb (or plutonium) had been inhaled.

Proposal

It is proposed that monodisperse aerosols of 1- μm polystyrene particles, labelled with ^{92m}Nb , be prepared and administered to eight male volunteers, chosen preferentially from the group which previously inhaled the 5- μm aerosol. Inhalation would be by mouth, with the same tidal volume (typically 550 ml) as before. Investigations of the X-ray flux from the chest would be made at Harwell, and probably at other laboratories, with the same equipment and techniques as had been employed previously⁽¹⁾. A comparison of data from the two experiments would indicate the relevance of particle size as a determinant of X-ray detection efficiency.

Dose commitment

The proposed alveolar deposit is 40 kBq. To achieve this it may be necessary to deposit a total of 80 kBq (but almost certainly not more) in

the respiratory tract as a whole, and this has been assumed in compiling the table below. An effective half-life of 10 days for the alveolar deposit (cf mean 9.7 days found with 5- μ m particles⁽¹⁾) has been adopted, i.e. it is assumed that no significant reduction occurs other than by radioactive decay.

WEIGHTED COMMITTED DOSE-EQUIVALENTS FROM ALVEOLAR DEPOSITION OF
40 kBq ^{92m}Nb*

| Organ | WCDE (μ SV) |
|--------|------------------|
| Lungs | 53 |
| Gut | 11 |
| Thymus | 6 |
| TOTAL | 70 |

* A further 40 kBq is assumed to be deposited elsewhere in the respiratory tract, and to be subject to rapid clearance via the gut.

Summary

It is proposed to administer up to 80 kBq ^{92m}Nb, incorporated in 1 μ m polystyrene particles, to each of eight male subjects, with an estimated weighted committed dose equivalent of 70 μ SV.

D Newton
EMSc Division
Building 364

22 September 1986

References

- 1 D Newton et al. AERE-R 11210 (1984).
- 2 R V Griffith et al. In: Advances in Radiation Protection Monitoring, pp 493-504, IAEA, Vienna (1979).
- 3 K J Gunston and S J Jefferies - AWRE-0 7/86 (1986).
- 4 S Somasundaram et al. Health Physics 41, 619-628 (1981).



Environmental and Medical Sciences Division
B551 Harwell Laboratory
United Kingdom Atomic Energy Authority
Oxfordshire OX11 0RA

Telex: 83135
Telephone: Abingdon (0235) 24141
Extension 4157

18 November 1987

Mr A L Anderson
Hazards Control
Lawrence Livermore National Laboratory
California 94550
USA

PRIVACY ACT MATERIAL REMOVED

Dear Larry

You asked for the total doses to date attributed to each of the prospective subjects in our proposed studies with ^{91}Nb -labelled particles. These are set out below. Five likely volunteers are known to us at present; we expect to find a further three at a later stage but have not so far advertised for them. Except from one of the five, I have not yet had a chance to obtain the required consent for the release of their dose information, and so I cannot identify the other four people for whom the figures are given.

The occupational doses relate exclusively to external irradiation, monitored by personal films or other devices, and it is assumed that these indicate whole-body exposure. The "experimental" doses in most cases arise from internal irradiation, and refer to committed effective dose equivalent.

| Subject | mSv occupational | mSv experimental | mSv total |
|---------|---------------------|---------------------|--------------|
| | 0 | 14.9 | 14.9 |
| 2 | 69.2 | 0.21 | 69.4 |
| 3 | 81.9 | 0.04 | 81.9 |
| 4 | 0 | 0.43 | 0.43 |
| 5 | 11.1 | 0.14 | 11.2 |

Several points need to be made. work is deemed to entail no occupational exposure and he is not subject to monitoring. Subject 4, as a member of the administrative staff, is in the same category. dose arose largely from one study in 1971 in which he received a controlled exposure to partially moderated 14 MeV neutrons [Reference: J Anderson et al, in: Nuclear Activation Techniques in the Life Sciences, pp 571-588, IAEA, Vienna, 1972].

Only in these two cases (and Subject 4) can the total dose estimates in my table be regarded as realistic. The doses recorded against Subjects 2, 3 and 5 largely arise from an administrative procedure designed to aid control of occupational exposure within prescribed limits. Because dose meters have a detection threshold (currently 0.05 mSv), the practice is to record fortnightly or monthly external doses of this threshold quantity against any radiation worker whose monitor fails to show a response. The bulk of the occupational "dose" recorded for these three people arises from numerous such entries, at intervals of two or four weeks, over the years. With Subject 5 there is an additional aberration. His 11.1 mSv from occupational "exposure" also includes a pessimistic notional dose of 4 mSv deemed, for the record, to have been incurred in one particular month when he lost his film badge.

Consequently, we may regard the total doses recorded for Subjects 2, 3 and 5 as upper limits of their actual exposure, and in all probability they represent gross overestimates.

With kind regards

Yours sincerely

PRIVACY ACT MATERIAL REMOVED



D Newton

COMPARISON OF DOSE DATA WITH U.S. STANDARDS

The current dose standards for the United States are as follows:

1. The annual dose limit to the general public (ie. those individuals who are not radiation workers) is not to exceed 500 mrem (5 mSv) per year.
2. The annual occupational dose limit (ie. to those people who are radiation workers) is not to exceed 5 rem (50 mSv) per year to the lungs.

It should be noted that the annual dose limit to the general public is 10 times more conservative than the annual occupational dose limit.

The dose that the volunteers participating in this subject are expected to receive will be 7 mrem (70 uSv) to the lungs. This dose is over 700 times less than the annual occupational dose limit to the lungs and is over 70 times less than the annual dose limit to the general public.

Experimental doses to date for the individuals participating in this study are included in Newton's letter dated November 18, 1987. All subjects except received experimental doses less than the annual dose limit to the general public. Although experimental dose was above the annual dose limit to the general public, his dose was lower than the annual occupational dose limit for either the whole body or the lungs.

Occupational doses to date are not true dose estimates, but in part were fabricated numbers required by administrative procedures in effect at that time. Newton has indicated that the bulk of the occupational dose record for subjects 2, 3, and 5 arises from numerous such entries at intervals of 2 to 4 weeks over the years. In addition, subject 5 had a notional dose of over 1/3 of his total occupational dose assigned due to a lost film badge. Consequently, the occupational doses assigned to subjects 2, 3, and 5 can be considered high and are probably within the annual occupational dose limits and possibly within the annual dose limits to the general public.

1

Tracer and Irradiation Studies Approval Committee

Minutes of the twentieth meeting held on Thursday, 2 October, 1986 in the Environmental and Medical Sciences Division, AERE Harwell.

Present:

| | |
|------------------------------|--------------------------------------|
| Dr J Vennart (Chairman) | External member |
| Dr A C Chamberlain | External member |
| Dr J C Evans | Head of Medical Section, AERE |
| Dr A Morgan | Environmental & Medical Sciences Div |
| Dr D Newton | Environmental & Medical Sciences Div |
| Dr S Rae | External member |
| Mr J N Pritchard (Secretary) | Environmental & Medical Sciences Div |

Mr R M Brown (Environmental & Medical Sciences Div) also attended.

Apologies for absence were received from Dr K Duncan and Dr R H Mole.

1. MINUTES OF THE NINETEENTH MEETING (TISAC (86) M1)

Dr Evans was erroneously omitted from the list of those present.

Minute 1. Subject to this alteration, the COMMITTEE accepted the minutes

2. MATTERS ARISING

2.1 Publication on working practices

JCE/AM
Drs Morgan and Evans apologised for the slow progress on the publication dealing with the workings of the COMMITTEE. A combination of factors have impeded its progress and so a draft is unlikely to be available before the end of this year. Mr Pritchard drew the attention of the authors to a paper on a similar theme presented at the 10th Annual Conference of the Australian Radiation Protection Society (R Rosen, Radiation Protection in Australia, 3 (4), 156-159).

2.2 Revised code of practice

The final draft of the revised code of practice was circulated by the COMMITTEE for information. However, prior to the meeting, Dr Mole had drawn the authors' attention to several points requiring clarification, including the omission of a discussion of the confidential nature of some projects. Thus, comments were invited from the remainder of the COMMITTEE. Dr Vennart suggested that doses should now be referred to as 'committed effective' dose equivalents, although Dr Newton pointed out the difficulty of quoting committed doses before the end of long-term metabolic studies. Dr Rae was assured that volunteer dose records are incorporated into medical records and will form part of the annual statement of dose issued to employees. Dr Evans indicated that a framework for compensation may be agreed along lines similar to the BNF plc scheme.

JCE
Dr Evans reported that the code of practice is currently being discussed by a sub committee of the Authority Joint Committee on Health and Safety before going to the Establishment's Directors Committee for final approval. In particular, the sub committee of the AJCHS is considering the role of the employees' representative in the newly constituted COMMITTEE. Dr Evans, who is a member of this sub committee, received a strong recommendation that such a representative should not belong to an organisation with a stated policy against volunteer

1122068

experiments. It was pointed out that the mechanism for obtaining a deputy for this representative, should he be unable to attend a meeting, needs to be decided, else the COMMITTEE will be inquorate.

2.3 Dealings with ARSAC

JCE

Dr Evans reported that he had been unable to contact Dr Williams by telephone despite numerous attempts. He agreed to write to ARSAC, questioning whether ethical approval was required prior to an application for a licence. However, the response time for research licence applications has improved markedly now that the applications for renewal of the 5-yearly licences for diagnosis and therapy have been processed.

The Chairman then requested an update on the proposal for investigating the effects of certain drugs taken on a prophylactic basis (TISAC (86) 3). Dr Evans replied that the results of an extensive literature search for relevant data were being assessed, prior to formulating a proposal to be put before a hospital Ethics Committee. Mr Pritchard added that preliminary results indicated that the lung could be dilated beyond the normal range in healthy subjects, even with prolonged treatment. This had been shown to affect deposition in the only published study found to date. Effects on mucociliary clearance appear to be drug specific with a range of responses.

3. PROGRESS REPORTS on APPROVED PROPOSALS

3.6 Metabolism of alkaline earths

Dr Newton reported that the first administration of ¹³³Ba had successfully taken place and that the next was anticipated in early November. The data arising from the first injection were presented under item 5.

5. PROPOSED ADMINISTRATION OF ^{85}Sr BY INTRAVENOUS INJECTION (TISAC (86) 7)

Dr Newton reported that the first subject to participate in the study of Ba metabolism (TISAC (85) 8), now aged 82, has taken part in a variety of studies of alkaline earth metabolism over the last 30 years. The Ba data suggest that renal clearance has reduced with age, with faecal clearance remaining similar, resulting in the proportion retained for long periods increasing from an estimated 6% twenty years ago to 8% in this experiment. Most of the early experiments had been conducted with Sr, so it is proposed to investigate whether the changes in Ba retention are mirrored by those in Sr.

In discussion, it was pointed out that the subject in question was a particularly active year-old so that the data may not be typical for his age-group. However, this experiment would demonstrate differences in the behaviour of Sr and Ba, whilst the remaining subjects in the Ba experiment will give a range for inter-subject variability. If differences between Sr and Ba are observed, there is unlikely to be sufficient additional information to propose mechanisms for such a discrepancy; in particular, there is no baseline information on renal function for this subject. The Chairman asked about the total dose accrued by this volunteer. Dr Newton replied that the dose levels were low in comparison to that arising from a pre-existing ^{226}Ra burden. He added that there was no problem in obtaining informed consent; indeed, some of the impetus for this experiment came from the volunteer.

Minute II. The COMMITTEE approved the administration by intravenous injection of 150 kBq ^{85}Sr to a single volunteer, aged 82, with a total committed effective dose equivalent of 125 μSv

6. PROPOSED FURTHER STUDIES WITH $^{92\text{m}}\text{Nb}$ -LABELLED MICROSPHERES INHALED BY MEN (TISAC (86) 8)

Dr Newton began by summarising previous work that had taken place using 5 μm particles. Strictly speaking, the calibration derived from this work applies only for particles of this size, since it relies on the detection of particles within a few centimetres of the surface of the chest; it is conceivable that particles of smaller size could penetrate to this region to a greater extent, thereby altering the calibration factor. Existing evidence tends not to support this hypothesis, but such data are severely limited. Hence, it is proposed to repeat the original calibration exercise with 8 volunteers, using as many of the subjects from the original study as possible.

In the discussion that followed, Dr Newton indicated that, if a particle-size effect is found, it may be possible to use particle size information from concurrent air samples to assist in deriving the correct calibration for in vivo measurements. The administration will take place in stages, so that the desired lung content may be approached gradually. Self-absorption effects within particles are unlikely to be significant at respirable particle sizes. Animal experiments have indicated a long-term clearance pathway to the pleural surface, which might affect detector response. However, no such effect has been observed in contaminees.

Minute III. The COMMITTEE approved the administration by inhalation of approximately 80 kBq ^{92m}Nb, with an estimated committed effective dose equivalent of 53 μSv from lung, 11 μSv from gut and 6 μSv from thymus to a total of 8 volunteers

IV. UKAEA CODE

1122072