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HANFORD ENVIRONMENTAL
HEALTH FOUNDATION

September 12, 1968

William T. Doran, M.D.
Chief, Occupational Health Physician
Division of Operational Safety
U. S. Atomic Energy Commission
Washington, D.C. 20545

SUBJECT: HEHF & BATTELLE ^{143}Pm Study

Dear Dr. Doran:

This is in response to your request for information requested of you by Dr. E. L. Meyers, Director, Division of Oncology and Radiopharmaceuticals, FDA, concerning a clinical investigation involving use of ^{143}Pm.

The purpose of this study and the extremely minute quantities involved may not have been made clear. We have prepared a discussion of the experiment which, hopefully, will clarify its need, the materials used, the place of animal studies, and safeguards for the individual test subjects. We have also included a Battelle monthly report in order to acquaint Dr. Meyers more fully with the extent and type of research being conducted at Battelle.

We feel strongly that research to provide adequate means of diagnosing internal depositions of ^{143}Pm and other radionuclides having poor in vivo measurement characteristics is vitally needed. We hope that we will be able to obtain the necessary approvals to continue this work until we are convinced that the proper bases of internal dosimetry of these radionuclides have been obtained for the radiation worker. Should you desire further clarification on any phases of the studies, please do not hesitate to let us known.

We underwent a State of Washington inspection Tuesday, September 10th, of our Radioactive Materials License. Mr. Gronemyer of the Washington State Department of Health was the inspector and he was accompanied by Ernest P. Resner, Senior Technical Specialist, Division State & Licensee Relations, USAEC. It was Mr. Gronemyer's statement that it is not now necessary to provide information to FDA concerning reactor made material. Could you provide any insight for me as to the validity of this statement?

Very truly yours,

P. A. Fuqua, M.D.
Medical Director

cc: Iral Nelson
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REPOSITORY PNL, ENG BLDG AREA 3000
COLLECTION PROMETHIUM STUDY
BOX No. 0
FOLDER NELSON IC

KADLEC MEDICAL-DENTAL BUILDING / P. O. BOX 100, RICHLAND, WASHINGTON 99352 / PHONE AREA CODE 509 942-1111

ATTACHMENTS

1. Diagnosis of Deposited Promethium - A Case for Human Testing
2. Preparation of Materials for Administration
   a. Letter from Abbott Laboratories
   b. Memo from H. E. Palmer, Principal Investigator
3. Volunteer Consent Form
4. Summary and Reprints of Promethium Research in Animals
5. Selected Internal Dosimetry Parameters from ICRP Committee II Recommendations
6. Monthly Report, PNL to DBM

DIAGNOSIS OF PROMETHIUM DEPOSITION - A CASE FOR CLINICAL INVESTIGATION

P. A. Fuqua, M.D.*
I. C. Nelson, M.A., C.H.P.†

INTRODUCTION

In the Pacific Northwest Laboratory alone there are some 50 workers who could be at risk of exposure to significant quantities of promethium-147. The principal mode of exposure for these individuals is through accidental inhalation of promethium-147 oxide. The radiation from ^{147}Pm consists of low energy beta (0.2 MeV) and bremsstrahlung and is not easily detected from outside the body.(1) Consequently, the ability to quantitatively establish the presence of ^{147}Pm in these workers' bodies through use of such devices as whole body counters is virtually non-existent. In the absence of such techniques, analysis of body excreta must be relied upon to provide a basis for body burden estimates. Prior to commencement of the Pacific Northwest Laboratory studies of the excretion and retention of ^{143}Pm in humans, there were no data upon which to deduce a model for diagnosis of promethium in humans. Without such excretion data, no reliable estimates of internal depositions of promethium in workers could be made, and their protection from radiation exposure due to ^{147}Pm could not be concluded as satisfactory. In some cases suspected of being severe exposures, the chelating agent diethylenetriaminepentaacetic acid may be given to increase excretion of the material from the body. The administration of DTPA

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further complicates efforts to establish the amount of body deposition.

Animal data are inadequate to formulate needed diagnostic procedures. Even if the data were abundant, there are many uncertainties in extrapolating animal excretion data to man and little confidence could be generated in models so developed. The ^{143}Pm studies in volunteer human test subjects were initiated specifically to resolve these problems.

The use of human test subjects poses some additional ethical considerations; however, these studies are for development of diagnostic methods only and do not involve determination of toxicity. The studies are to be performed using amounts considerably below those amounts generally agreed upon by authoritative bodies as unlikely to produce untoward radiological effects and are several orders of magnitude below levels at which chemical toxicological effects might be expected. In the studies involving DTPA, only those amounts which have been demonstrated in earlier situations as being without deleterious effect would be used.

ANIMAL STUDIES

A number of animal studies have been performed here and elsewhere on the metabolism of promethium in animals.[2-17] While these various reports give values for organ content of promethium at sacrifice and discuss histopathological findings of the dosed animals, very few excretion-retention data are presented from which models may be developed. In instances where excretion data have been obtained, its relationship to excretion of promethium by humans is not clear. There are, of course, short term experiments

conducted on animals locally in the Pacific Northwest Laboratory's Biology Laboratory to verify the pyrogen-free qualities of the materials to be administered to humans. These are usually done at about 100 times the dose to be administered in humans and constitute a final short term toxicological safety check.

There are also parallel animal studies which are planned in conjunction with the clinical investigations. These studies are not intended primarily as protective effort for the clinical investigation work and because of this they need not be done prior to the clinical investigations. These studies are intended to satisfy the need to obtain additional knowledge on the similarities or dissimilarities between the metabolism of various radiochemicals in man and animals. Through experimentally established correlation between the uptake, excretion, translocation and retention of radionuclides in both man and laboratory animals, the use of and confidence in animal studies can be maximized and the need for clinical investigations minimized. This knowledge is also needed to improve confidence in the extrapolation to man of the results of experiments carried out at histopathological levels in animals.

RADIOLOGICAL CONSIDERATIONS

The radionuclide of potential exposure interest is ^{147}Pm; however, the use of ^{147}Pm is contraindicated for use in clinical investigations on three counts. One, it would require radiochemical assay of excreta with retention estimates made by the cumbersome material balance technique; two,

no indication would be given as to favored deposition sites or translocation between organs with time; and three, the amount of material necessary for detection would most likely result in excessive radiation dose to the test subject. In searching for a more suitable isotope of promethium to use in clinical investigations, it was found that ^{143}Pm could be prepared at moderate cost, could be measured adequately in vivo by whole body counting techniques, and would result in an extremely small dose to the human volunteer. In the preparation of ^{143}Pm about 10% of the promethium formed was ^{144}Pm. Promethium-143 decays to stable Nd, whereas ^{144}Pm decays to ^{144}Nd, which, however, is an extremely long lived radionuclide and its decay does not alter the dosimetry significantly.

To arrive at a basis for admissable exposure for the test subjects, the recommendations of the International Commission on Radiological Protection were consulted.[18] The Maximum Permissible Doses recommended by the Commission are:

Gonads and red bone marrow (and, in the case of uniform irradiation, the whole body)	5 rems in a year
Skin; thyroid; bone	30 rems in a year
Hands and forearms; feet and ankles	75 rems in a year
All other organs	15 rems in a year

While the minimizing of occupational exposure to radiation is always to be desired, the ICRP concludes that, "However, in the light of present

knowledge, occupational exposure for the working life of an individual at maximum permissible values recommended in this report (ICRP Publication 2) is not expected to entail appreciable risk of damage to the individual or to present a hazard more severe than those commonly accepted in other present day industries."

In the studies of ^{143}Pm in clinical investigations, levels of 0.1 μCi ^{143}Pm for intravenous injection and 10 μCi for ingestion were chosen as a balance between enough activity to follow the body burdens for about one year and the smallest possible dose to the volunteer. The doses using standard man parameters were calculated in the manner appended and are tabulated as follows:

Total Dose to Standard Man
from I.V. Injection of 0.1 μCi ^{143}Pm

Organ	Dose
Whole Body	0.007 rem
Bone	0.012
Liver	0.055

Total Dose to Standard Man
from Ingestion of 10 μCi ^{143}Pm

Organ	Dose
Total Body	< 0.001 rem
Bone	< 0.001
Liver	< 0.001
Lower Large Intestine	0.108
Upper Large Intestine	0.053
Small Intestine	0.013
Stomach	0.006

Comparison of the tabulated doses to the previously presented permissible levels of occupational exposure shows that for the highest exposed organ, the lower large intestine, the one time test subject dose is less than one percent of the maximum permissible annual limit. Doses to other organs are even smaller in comparison to their respective limits, and it is concluded that the dose administered is insignificant in terms of radiological safety.

OTHER TOXICOLOGICAL CONSIDERATIONS

Assurance of the pyrogen-free nature of the material was obtained by injection of about 100 times the amount of $PmCl_3$ to be used in humans into a 70 kg Hanford miniature swine which was observed for about three days before the first human injection. No pyrogenicity, or other sign of toxicity from the injectant, was noted.[2]

Gamma spectrometric measurement of each syringe loaded with $PmCl_3$ was made prior to and after injection of the material by the physician to quantitatively establish the correct content of the syringe and the quantity injected.

The approximate quantities of the injectants in terms of mass were as follows:

Cl	0.6 mg
Na	0.4 mg
Nd	$\sim 1 \times 10^{-3}$ mg
Pm	3×10^{-8} mg

The amounts of Na and Cl were known from amounts added to obtain the desired solution. The amount of Nd was less well known because it was removed from the Pm as much as practical, i.e., until it was not detectable. The maximum Nd injected, had no purification taken place, would have been 0.1 mg. The mass amount of Pm is known quite well from relation to its radioactivity.

Although no data have been found which specifically establish the toxicity levels of the rare earths in humans, the amounts of Nd and Pm introduced are much, much smaller than those amounts found to be toxic among inorganic compounds in general.[19-25]

CONCLUSIONS

The need for data relative to retention and excretion of promethium in humans both in the presence and absence of therapeutic administration of

chelating agents has been established. Past studies of animals by others have provided gross estimates of biological halftimes, permissible body burdens, etc. The pyrogen testing of the materials to be used in clinical investigations by the pharmaceutical house preparing the material, followed by checking of its pyrogenicity in our own laboratories, is considered to be sufficient pre-clinical animal studies. Again this view is taken because the human studies to develop methods of diagnosis of body deposition of promethium are conducted at tracer levels which are orders of magnitude smaller than amounts which chemically or radiologically can be considered toxic to the human body.

APPENDIX

Doses for selected critical organs were calculated using the ICRP[1] parameters and the equation

$$D = \frac{73.8\ f_2' \varepsilon T q}{m} \left(1 - e^{\frac{.693}{T} t}\right) \qquad (1)$$

where

D = dose in rems for time period t days

f_2' = fraction from blood to organ of reference

q = amount in μCi taken into the blood

m = mass of organ in grams

ε = effective absorbed energy per disintegration of the radionuclide

t = time since entry of radionuclide

T = effective half-life of radionuclide in organ of reference.

For photons

$$\varepsilon = \Sigma h\nu_i (f) \left(1 - e^{-\left[\frac{\mu_{en}}{\rho}\right] X\rho}\right) = \Sigma E_{eff} \qquad (2)$$

where

$h\nu_i$ = energy of emitted photon in MeV

f = fraction of disintegrations resulting in photon of $h\nu_i$

$\frac{\mu_{en}}{\rho}$ = mass energy absorption coefficient in $\frac{cm^2}{g}$. Coefficients for muscle are used for all organs except bone. For the latter compact bone coefficients are used.[2]

ρ = 1.00 gm/cm^3 for muscle; 1.85 for bone.[3]

X = effective radius of organ of interest in cm.

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Total Body and Small Intestine

$X = 30$ cm; $\rho = 1.00$ gm/cm^3

^{143}Pm

i	$h\nu_i$ MeV	f	$\frac{\mu_{en}}{\rho}$ cm^2/g	$X\mu_{en}$	$E_{eff/dis}$ MeV
1	0.74	0.46	0.032	0.96	0.209
2	0.038	0.76	0.073	2.19	0.026
3	0.006	0.14	> 10	> 300	∿ 0.001

$\varepsilon = \Sigma E_{eff} = 0.236$ MeV

Liver and Stomach

$X = 10$ cm; $\rho = 1.00$ gm/cm^3

^{143}Pm

i	$h\nu_i$ MeV	f	$\frac{\mu_{en}}{\rho}$ cm^2/g	$X\mu_{en}$	$E_{eff/dis}$ MeV
1	0.74	0.46	0.032	0.32	0.093
2	0.038	0.76	0.073	0.73	0.015
3	0.006	0.14	> 10	> 100	∿ 0.001

$\varepsilon = \Sigma E_{eff} = 0.099$ MeV

Upper Large Intestine and Lower Large Intestine

$X = 5$ cm; $\rho = 1.00$ gm/cm^3

^{143}Pm

i	$h\nu_i$ MeV	f	$\frac{\mu_{en}}{\rho}$ cm^2/g	$X\mu_{en}$	$E_{eff/dis}$ MeV
1	0.74	0.46	0.032	0.160	0.0503
2	0.038	0.76	0.073	0.365	0.009
3	0.006	0.14	> 10	> 50	0.001

$\varepsilon = \Sigma E_{eff} = 0.060$ MeV

Bone

$X = 5$ cm; $\rho = 1.85$ gm/cm^3

^{143}Pm

i	$h\nu_i$ MeV	f	$\frac{\mu_{en}}{\rho}$ cm^2/g	$X\mu_{en}$	$E_{eff/dis}$ MeV
1	0.74	0.46	0.040	0.373	0.106
2	0.038	0.76	0.36	3.330	0.028
3	0.006	0.14	> 10	> 50	0.001

$\varepsilon = \Sigma E_{eff} = 0.135$ MeV

The biological half-lives in the organs of interest together with the computed effective half-lives are as follows:

	T_B (1)	T_p (3)	T_E
Total Body	656	265	189
Bone	1500	265	225
Liver	656	265	189

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Residence times of ingested radioactive material in the G.I. tract are taken to be:[1]

	Days
Stomach	1/24
Small Intestine	4/24
Upper Large Intestine	8/24
Lower Large Intestine	18/24

The values used for f_2', the fraction of the radionuclide going from blood to the organ of reference and the masses of the organs, are as follows:[1]

	f_2'	m
Total Body	1.0	70,000 gram
Bone	0.35	10,000
Liver	0.40*	1,700

* Estimated. The ICRP value is 0.06. In more recent studies with IV injections of ^{147}Pm in miniature swine, the fraction of the injected dose in bone was 0.4 and in the liver was 0.4 at ten days after injection for two animals.[5] In another experiment the fraction of injected dose of ^{143}Pm in bone was 0.58 and in the liver was 0.24 at 100 days after injection for one animal.[6]

Letting time become large compared to the effective half-life in equation (1), the total lifetime dose to the organ of interest is obtained. By setting q equal to one, the dose is defined on a per μCi basis. Equation (1) then

reduces to

$$D = 73.8\ f_2'\ Tm^{-1}\ rem/\mu Ci \qquad (3)$$

Substituting the values of the parameters presented into equation (3), the doses from intravenous injection of 1 μCi $^{143}PmCl_3$ are as follows:

Total Body	$(73.8)(1)(0.236)(189)(7x10^4)^{-1}$	=	47 mrem/μCi
Bone	$(73.8)(0.35)(0.135)(225)(1x10^{-4})$	=	79
Liver	$(73.8)(0.4)(0.099)(189)(1.7x10^3)^{-1}$	=	360

Since the time of residence of the radioactive material in the gastrointestinal compartments is very small compared to the physical half-life of the radionuclide, (1) may be rewritten as

$$D = \frac{51\ \varepsilon q \tau}{2m} \qquad (4)$$

Where τ is the residence time in a given compartment, m is now the mass of the contents of the compartment, q is the amount in μCi ingested, and the factor 1/2 is introduced to account for the fact that the dose to the intestinal walls, is, on the average, only half the dose to the contents of the G.I. tract.

Then substituting parameters into (4) the following G.I. tract doses are obtained.

Stomach	$\frac{(51)(0.099)(1)(1/24)}{(2)(250)}$	=	0.47 mrem/μCi
Small Intestine	$\frac{(51)(0.236)(1)(4/24)}{(2)(1100)}$	=	0.92

Upper Large Intestine $\frac{(51)(0.060)(1)(8/24)}{(2)(135)} = 3.8$ mrem/μCi

Lower Large Intestine $\frac{(51)(0.060)(1)(18/24)}{(2)(150)} = 7.7$

To calculate the amount of dose to the other body organs as a result of ingesting ^{143}Pm, the fraction of material reaching the organ of reference from ingestion is needed. These values are as follows:

Total Body	1×10^{-4}
Bone	3.5×10^{-5}
Liver	6×10^{-6}

Using these values in place of f_2' in equation (3), the following doses are obtained.

Total Body	$(73.8)(1\times10^{-4})(0.236)(189)(7\times10^{4})^{-1}$	= 4.7 μrem/μCi
Bone	$(73.8)(3.5\times10^{-5})(0.135)(225)(1\times10^{-4})$	= 7.9
Liver	$(73.8)(6\times10^{-6})(0.099)(189)(1.7\times10^{3})^{-1}$	= 5.4

The previous calculations are repeated to obtain the organ dose per unit quantity of ^{144}Pm injected or injested.

Total Body and Small Intestine

$X = 30$ cm; $\rho = 1$ gm/cm^3

^{144}Pm

i	$h\nu_i$ MeV	f	$\frac{\mu_{en}}{\rho}$ cm^2/g	$X\mu_{en}$	$E_{eff/dis}$ MeV
1	0.474	0.46	0.032	0.96	0.134
2	0.615	1.0	0.032	0.96	0.379
3	0.695	1.0	0.032	0.96	0.428
4	0.038	0.78	0.073	2.19	0.026
5	0.006	0.14	> 10	> 300	∿ 0.001
Conversion electrons					0.009

$\varepsilon = \Sigma E_{eff} = 0.977$ MeV

Liver and Stomach

$X = 10$ cm; $\rho = 1.00$ gm/cm^3

^{144}Pm

i	$h\nu_i$ MeV	f	$\frac{\mu_{en}}{\rho}$ cm^2/g	$X\mu_{en}$	$E_{eff/dis}$ MeV
1	0.474	0.46	0.032	0.32	0.060
2	0.615	1.0	0.032	0.32	0.169
3	0.695	1.0	0.032	0.32	0.190
4	0.038	0.78	0.073	0.73	0.015
5	0.006	0.14	> 10	> 100	0.001
Conversion electrons					0.009

$\varepsilon = \Sigma E_{eff} = 0.444$ MeV

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Upper and Lower Large Intestine

$X = 5$ cm; $\rho = 1.00$ gm/cm^3

^{144}Pm

i	$h\nu_i$ MeV	f	$\frac{\mu_{en}}{\rho}$ cm^2/g	$X\mu_{en}$	$E_{eff/dis}$ MeV
1	0.474	0.46	0.032	0.16	0.032
2	0.615	1.0	0.032	0.16	0.092
3	0.695	1.0	0.032	0.16	0.104
4	0.038	0.78	0.073	0.365	0.009
5	0.006	0.14	> 10	> 50	0.001
Conversion electrons					0.009

$\varepsilon = \Sigma E_{eff} = 0.247$ MeV

Bone

$X = 5$ cm; $\rho = 1.85$ gm/cm^3

^{144}Pm

i	$h\nu_i$ MeV	f	$\frac{\mu_{en}}{\rho}$ cm^2/g	$X\mu_{en}$	$E_{eff/dis}$ MeV
1	0.474	0.46	0.032	0.296	0.065
2	0.615	1.0	0.032	0.296	0.182
3	0.695	1.0	0.032	0.296	0.206
4	0.038	0.78	0.073	0.675	0.014
5	0.006	0.14	> 10	>90	0.001
Conversion electrons E_{eff} = Ex5					0.045

$\varepsilon = \Sigma E_{eff} = 0.513$ MeV

The biological half-lives of ^{144}Pm in the organs of interest together with the computed effective half-lives are as follows.

	T_B (1)	T_p (3)	T_E
Total Body	656	400	248
Bone	1500	400	316
Liver	656	400	248

Again equation (3) is used to calculate the doses of interest.

$$D = 73.8\ f_2'\ \varepsilon T m^{-1}\ \text{rem}/\mu\text{Ci}$$

Substituting the values of the parameters developed into this equation, the doses from intravenous injection of 1 μCi are as follows.

Total Body	$(73.8)(1)(0.977)(248)(7\text{x}10^4)^{-1}$	=	255 mrem/μCi
Bone	$(73.8)(0.35)(0.513)(316)(1\text{x}10^{-4})$	=	419
Liver	$(73.8)(0.4)(0.444)(248)(1.7\text{x}10^3)^{-1}$	=	1910

Similarly, substituting values into equation (4) the following G.I. tract doses as a result of injesting 1 μCi of ^{144}Pm are obtained.

Stomach	$\frac{(51)(0.444)(1)(1/24)}{(2)(250)}$	=	1.887 mrem/μCi
Small Intestine	$\frac{(51)(0.977)(1)(4/24)}{(2)(1100)}$	=	3.775
Upper Large Intestine	$\frac{(51)(0.247)(1)(8/24)}{(2)(135)}$	=	15.5
Lower Large Intestine	$\frac{(51)(0.247)(1)(18/24)}{(2)(150)}$	=	31.4

Total Body	$(73.8)(1x10^{-4})(0.977)(248)(7x10^{4})^{-1}$	= 25.5 μrem/μCi
Bone	$(73.8)(3.5x10^{-5})(0.513)(316)(1x10^{-4})$	= 41.9
Liver	$(73.8)(6x10^{-6})(0.444)(248)(1.7x10^{3})^{-1}$	= 28.7

Assuming the mixture of ^{143}Pm and ^{144}Pm is such that there exist 1 μCi ^{143}Pm + 0.1 μCi ^{144}Pm in the injectant, then the doses as calculated above combine as follows.

Total Body	72 mrem
Bone	121
Liver	550

In the case of ingestion of 1 μCi ^{143}Pm it is assumed that 0.1 μCi ^{144}Pm is ingested and the resulting doses are:

Stomach	0.66 mrem
Small Intestine	1.3
Upper Large Intestine	5.3
Lower Large Intestine	10.8

Total Body	7.2 μrem
Bone	12.1
Liver	8.3

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ABBOTT

LABORATORIES

RADIO-PHARMACEUTICAL OPERATIONS
Abbott Park
North Chicago, Illinois 60064

MAY 28 1968

May 23, 1968

P. A. Fuqua, M.D.
Hanford Environmental Health Foundation
Medical-Dental Building
1001 Goethals
Richland, Washington 99352

Dear Dr. Fuqua:

This will acknowledge the letter form Dr. Palmer requesting more information on the $^{143}PmCl_3$ we diluted and sterilized for you last October.

We dissolved the residue in 90 ml. of Water for Injection containing 0.9% sodium chloride and 1.0% benzyl alcohol. The pH was adjusted to 3.5 with 1.0M HCl and then diluted to 100 ml. The 100 ml. was divided into nine 10 ml. samples, two 1.0 ml. samples, one 5.0 ml. sample, and one 3 ml. sample. The samples were autoclaved for 20 minutes at 121°C. The two 1.0 ml. samples were used for sterility testing for seven days in thioglycollate media. The 10 ml. samples were held until sterility was assured. Pyrogen tests were also performed as stated in the U.S.P. Three 3 Kg. rabbits were injected with one milliliter each. No temperature rise in any animal was experienced during the three hour test period.

If we can be of further help, please contact us.

Sincerely yours,

B. J. Green, Chemist
Research Service Support Group

BJG:cal

cc: Dr. H. R. Palmer

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PREPARATION OF PROMETHIUM-143 CHLORIDE

H. E. Palmer

The promethium-143 used in our experiment was produced at Oak Ridge National Laboratory using high energy proton irradiation of enriched $^{144}Nd_2O_3$ (94.4%). A small amount (about 10%) of ^{144}Pm was also formed. The ^{143}Pm was separated from the irradiated neodymium at Battelle-Northwest by an ion exchange method using Dowex 5X-4 fine mesh resin and eluting the ^{143}Pm carrier free with 0.25 normal α hydroxybutyric acid at a pH of 4.6. Ten mg of sodium chloride was added to the solution containing the ^{143}Pm and the hydroxybutyric acid and the solution was then evaporated to dryness and the residue shipped to Abbott Radiopharmaceutical Laboratories. The total separated ^{143}Pm activity was about 125 μCi.

Abbott Laboratories dissolved the residue in 100 milliliters of sterile pyrogen free sodium chloride solution containing 900 mg of NaCl per 100 ml of solution. Hydrochloric acid was added to bring the pH of the solution to 3.0 to ensure that the ^{143}Pm remained in solution. The entire solution was autoclaved. One ml aliquots were injected into rabbits and pyrogen reaction was not detected. The solution was sent to HEHF in nine vials of 10 ml each, with each ml containing 1.25 μCi of ^{143}Pm, on October 10, 1967.

May 2, 1968

AGREEMENT

THIS AGREEMENT made this _____ day of _____, 1967, between

_____ of _____,
(City & State)
and Hanford Environmental Health Foundation, Inc., a Washington nonprofit corporation.

In consideration of the sums indicated in the attached schedule of payments, I hereby volunteer and agree to take part in experiments and studies of the effect of radioisotopes in humans. It has been explained to me that these experiments will provide valuable data for use in possible treatment of radiation and contamination victims as well as basic research information. I understand that doses of radioisotopes in the low-level range of 0.1 to 0.15 roentgens will be administered by injection (needle). I also agree to donate blood and excretion samples, including urine and feces as indicated in Appendix A, attached. I also agree to examinations which would include the use of a Whole Body Counter as indicated in Appendix A, attached. All these procedures have been fully explained to me.

I am in sound mental and physical condition and am participating in this experiment of my own volition. I understand that the program and the techniques involved are experimental and are not for purposes of treatment or diagnosis. It is further understood that the said procedures are to be performed at the Kadlec Medical-Dental Building or Kadlec Methodist Hospital, or both, and will be performed under the direction of Dr. P. A. Fuqua. He is authorized to utilize in the performance of these procedures the services of physicians and members of the Foundation, the Kadlec Hospital staff, and other parties as selected by him.

The nature, procedures, and probable effects, possible consequences involved and the fact that unforeseen results may occur have all been fully explained to me. I have had an opportunity to ask questions about the experiment, procedures and risks before signing this agreement.

For the purposes of these experiments and studies it is understood that I am not an employee of the Hanford Environmental Health Foundation, the Atomic Energy Commission, or any of the parties performing services or providing materials or equipment for the conduct of the experiments or studies described herein. I have not been urged or coerced to participate in this program by anyone.

I agree to assume all the direct and indirect risks involved including injuries which I may sustain as a result of this experiment, and hereby absolve the Hanford Environmental Health Foundation, the United States Government (as represented by the Atomic Energy Commission), Kadlec Methodist Hospital, all physicians and staff, and all other parties performing services or providing materials or equipment in the conduct of the experiments or studies described herein, from any liability.

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I certify that I am 21 years of age or older.

Signed: _____
(Volunteer)

Address: _____

Date: _____

The foregoing agreement was read, discussed and signed in my presence and in my opinion the person so signing did so freely and with full knowledge and understanding.

Signed: _____

Address: _____

Date: _____

APPENDIX A

The volunteer agrees to donate excretion samples, allow blood samples to be taken, and allow whole body counting measurements to be made according to the following schedule:

Urine Samples

1. Total 24 hour samples for each day for fourteen (14) days before injection.
2. Total 24 hour samples for each day for fourteen (14) days after injection.
3. Total 24 hour samples for Tuesday, Wednesday and Thursday of the third and fourth weeks after injection.
4. Total 24 hour samples for Tuesday, Wednesday and Thursday of the first week in each of the following eleven months, if requested.

Fecal Samples

1. Total 24 hour samples for each day for seven (7) days after injection.

Blood Samples

1. cc blood samples at minutes, minutes, hour, hours, hours, and daily for days.

Whole Body Counting

1. Whole Body Counts at one (1) hour, six (6) hours, 24 hours, and daily for five (5) days after injection.
2. Whole Body Counts three (3) times during the second week, one (1) time per week during the third and fourth week after injection.
3. Whole Body Counts one (1) time per month during the next eleven (11) months, if requested.

Whole Body Counts will require one to one and one-half hours each.

Signed: _____
(Volunteer)

_____
Witness

PACIFIC NORTHWEST LABORATORY

MONTHLY ACTIVITIES REPORT

August, 1968

AEC DIVISION OF BIOLOGY AND MEDICINE PROGRAMS

INTERNAL DEPOSITIONS OF RADIONUCLIDES IN MAN - A. J. Haverfield/W. J. Bair

The test subjects participating in the promethium-143 study were examined with the whole-body counter for translocation of promethium since injection. Analysis of the data continues. Several grams of 99 plus percent enriched $^{235}U_3O_8$ were requested from the Oak Ridge National Laboratories for use in preparing more pure ^{237}Pu for clinical studies. A brief study of creatinine in urine as a function of time after leaving the body was made to determine if analysis delays would produce significant variation in creatinine content. Slight loss of creatinine was observed in non-refrigerated samples after one week. Refrigerated samples showed no loss. Study of creatinine as an indication of metabolic time periods in humans continued.

Preparatory work necessary to perform inhalation experiments with promethium continued. Additional measurements of the particle size distribution from the prototype aerosol generator were completed. A new SAI cascade impactor having a 0.25μ cutoff particle size in the final stage was used for the measurements. As in previous measurements, the aerosol was generated from a Na_2CO_3 solution. The MMD varied from 0.3 to 0.4μ and seemed to be independent of sodium concentration in the range of 0.01% to 0.1% Na.

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