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PNL-9321

November 21, 1966

TO: H. M. Parker and Members of the Committee for Review of Human Experiments
FROM: H. E. Palmer

At the first committee meeting on the ¹⁴³Pm metabolism study three items of information were requested. I have provided this information below:

I. Are there any other promethium isotopes that would be better than the ¹⁴³Pm and ¹⁴⁴Pm mixture?

<u>Mass No.</u>	<u>Half-Life</u>	<u>Usefulness</u>
141	22 min.	half-life too short
142	34 sec.	
143	265 days	good
144	400 days	good
145	18 years	half-life too long - gamma energies too low
146	710 days	cannot be made without contaminates with ¹⁴⁵ Pm or ¹⁴⁷ Pm
147	2.5 years	Beta emitter - no gamma - half-life too long
148	41 days	could be used but half-life is a little short - beta emitter
149	53 hrs.	
150	2.7 hrs.	
151	28 hrs.	half-life too short
152	6 min.	
153	5.5 min.	
154	2.5 min.	

The only adequate isotopes seem to be ¹⁴³Pm or ¹⁴⁴Pm. Pm-148 could possibly be used but it offers no advantage over the other two.

II. Literature Review of the Metabolism of Pm

The only literature cited in the I.C.R.P. for the metabolic parameters of Pm and all other rare earths is an article by Hamilton et.al. on the metabolism of the lanthanons in the rat (1955)⁽¹⁾ and a personal communication from J. G. Hamilton to K. Z. Morgan (1956). The animals used in past metabolic studies of Pm have been rats except for the miniture swine⁽²⁾ and dog⁽³⁾ experiments at Hanford.

Ekman et.al. (1961)⁽⁴⁾ found that Pm administered as chloride both intravenously and to rat serum in-vitro was absorbed by the blood proteins (albumine) within five minutes. Graca⁽⁵⁾ agrees and says that rare earths injected as the chloride will

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hydrolyze at the pH level of blood and be chelated by the blood proteins. Gensicke (1962)⁽⁶⁾ found that Pm injected intravenously as the citrate did not combine with blood proteins but was transported as metal citrate complexes in the serum. Several investigators report values for uptake by ingestion that are all less than 0.5%. Considering all the available data it appears that once the Pm is absorbed most of it (~80%) goes to the liver and skeleton regardless of whether it was given by injection, inhalation, or ingestion and regardless of whether it is in the chloride, citrate, or perchlorate form. The Hanford swine and dog results show no significant difference in the percentage of Pm in the liver and bone at 10, 30, and 55 days after administration. Injections of Pm citrate or a mixture of chloride and citrate give less trouble with deposition at the site of injection than do injections of the chloride only.

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2. R. O. McClellan, Metabolism of Pm¹⁴⁷ and Ce¹⁴⁴ in Minature Swine, HW-76000, page 39.
3. B. O. Stuart, Preliminary Studies of Inhaled Pm¹⁴⁷ Perchlorate, HW-80500, page 59.
4. L. Ekman, F. Valmet, Baberg, "Behavior of Y⁹¹ and Some Lanthanons Towards Serum Proteins in Paper Electrophoresis", Intern. J. Appl. Rad. and Isotopes 12, 32-41, November, 1961.
5. Personal Communication from J. G. Graca to H. E. Palmer, February 1, 1966.
6. F. Gensicke, "The Transport of Ce¹⁴⁴, Pm¹⁴⁷, and Y^{90,91} in the Mouse Serum", Strahlentherapie, 118, 369-74, July, 1962.

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G. Magnussen, "The Behavior of Certain Lanthanons in Rats", Acta. Pharmacol. Toxicol. 20, Suppl. 2, 95p (1963)

Y. I. Moskalev, Med. Radiol. 4, No. 6.73-5 (1959) June (In Russian) NSA#13: 16707.

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III. Detailed Procedure

Note: Pm-143 as used here includes the ^{143}Pm and ^{144}Pm mixture that we have.

Ingestion Experiment

1. Two volunteers obtained by HOHF will orally consume a known quantity (about $1\ \mu\text{Ci}$) of ^{143}Pm under the direction of HOHF physicians.
2. During the passage through the G.I. tract the subject will be measured with a whole body counter.
3. Blood samples will be taken and analyzed at various intervals after ingestion. The number of samples taken will depend on the concentration in the first few.
4. All urine and fecal samples will be collected and analyzed until ^{143}Pm is no longer detectable.
5. After the G.I. tract has been cleared attempts will be made to measure the absorbed ^{143}Pm especially in the liver.
6. Depending on the information obtained from the above steps additional volunteers may be studied in similar experiments. If the uptake is very low as is expected, it may be desirable to administer a larger quantity of ^{143}Pm with the additional approval of the committee. A request for any such action would be submitted to the review committee.

Injection Experiment

1. Six volunteers obtained by HOHF will be injected by physicians of HOHF with not more than $0.1\ \mu\text{Ci}$ of $^{143}\text{Pm Cl}_3$ in a sterile saline solution at a pH of $3 \pm .5$ prepared and analyzed by the Abbott Radiopharmaceutical Company, North Chicago, Illinois. A further check of the radiochemical concentration and purity will be made by Battelle-Northwest.
2. Blood samples will be taken by HOHF and analyzed by PNL at various intervals after injection.
3. All urine and fecal excretion will be collected and analyzed for a 1 week period after injection and then for 24 hour periods at various intervals for one year after injection.
4. Periodic whole body counts, whole body scans, and counts on specific organs will be made at varying intervals for about one year after injection.

HOHF personnel will recruit and hire volunteers, administer the isotopes, draw blood samples, obtain the urine and fecal samples and schedule the volunteers for in vivo counting. Battelle-Northwest personnel will analyze the blood and excretion samples and perform the in vivo counting at facilities located in the 300 and 700 areas

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Inhalation Experiment

Since this experiment is more difficult and will be done after the ingestion and injection experiments, and since the results of these first two will influence the procedure of the inhalation study, I suggest we delay the approval for this part of the experiment until a later date.

H. E. Palmer / H. A. L.

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cc: R. S. Paul
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