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June 27, 1945

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Memorandum To: Dr. Dowdy  
From: Dr. Bals  
Re: Metabolism studies

This memorandum is a reply on your note to me of June 5th concerning metabolism studies of radioactive elements. I will discuss these materials in the order of the priority given in that note.

1. POSTUM: Dr. Fink and I believe that our present set-up is adequate for the studies on Postum requested by the District, and providing that the Postum patients may be run consecutively rather than two or more at the same time. This is probably advisable also for the reason that experience with one patient, enables us to carry out a better and more valuable experiment on the next patient.
2. PRODUCT: As you are aware, Product is an alpha emitting element and is biologically a bone seeking material, probably intermediate in characteristics between My and T. In a manner similar to My, excretion rapidly falls to a very low value. Also there is no gaseous daughter substance such as Mz to make isolation of an appropriate radioactive fraction anything but difficult. It has been estimated by the Chicago group that the daily urine excretion with tolerance amount of Product in the body is approximately 1 alpha count per min. Col. Friedell's estimate, I believe, will be five or ten times larger. In patients with short life expectancy we can perhaps increase the dose five or ten fold over Col. Friedell's tolerance estimate.

Even under these conditions such experiments will require extreme precautions to avoid contaminations with other materials used. It will be preferable to have new glassware for each sample taken, and a definite uncontaminated area, preferably in the hospital, for handling samples. It may be desirable to be able to centrifuge and perhaps digest blood samples while fresh. It may also be necessary to digest urine samples before shipment to Dr. H.

Patients from whom bone biopsies or extracted teeth can be obtained, may be very desirable in Product studies.

Due to the very great difficulties and the many, so far unknown, factors involved in work with Product it will be very desirable for someone, probably Dr. Fink, to visit Dr. Hempelman's area to obtain a first hand acquaintance with their experimental technique. An alternative, in my opinion somewhat less desirable, will be for Dr. H. to visit Rochester before too detailed plans are made for this experimental work.

Classification Cancelled

Or Changed To

By Authority of [Signature]  
By [Signature] Date 5/24/45

DEPARTMENT OF ENERGY DECLASSIFICATION REVIEW	DETERMINATION OF [ ] (CIRCLE NUMBER(S))
	1. CLASSIFICATION [ ]
SINGLE REVIEW AUTHORIZED BY:	2. CLASSIFICATION [ ]
0.8/14/45	3. CONTAINS AC DOE UNCLASSIFIED INFO
REVIEWER (ADD):	4. COORDINATOR [ ]
NAME: [ ]	5. CLASSIFICATION [ ]
DATE: 8/16/91	6. CLASSIFIED INFO BRACKETED
	7. OTHER (SPECIFY):

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Assuming that Dr. Fink takes personal charge of this work we need, in addition, somewhere between  $\frac{1}{4}$  to full time of a technician; about  $\frac{1}{2}$  a laboratory apparatus desk and probably a chemical hood in an area isolated from other radioactive work. This work will necessitate an independent supply of chemical glassware, perhaps 400 containers for each sample taken, urine, feces, plasma, erythrocytes etc.

3. LEAD: There are two radioactive isotopes of lead probably suitable for tracer studies of lead metabolism in human subjects. These are 1.) Thorium B, an isotope emitting beta rays with a half life of 10.6 hours, suitable for short time studies. 2.) Radium D, a beta emitter with a 22 year half life, suitable for long term studies. These isotopes have alpha active elements in their degradation chain.

Use of the 10.6 hour half life material probably will necessitate the working up of methods for chemical lead isolation. It can be used in amounts sufficient to give good tracer data over periods of 2 to 3 days without a possibility of harm to any patient.

The 22 year isotope is a mother substance of Postum. By allowing specimens obtained from patients to whom this lead has been administered to remain in the laboratory for a month or two, the amount of lead present can be determined by measuring the amount of Postum with the techniques now in use in our laboratory. The amount of this isotope that can be administered to a patient will be severely limited by its long half life and the toxicity of the Postum produced from it.

Experiments should be carried out with each of these isotopes since they supplement each other in several respects. It is my opinion that the careful use of these isotopes will produce a considerably more quantitative picture of the nature of lead metabolism than will be given by spectroscopic studies. This is not to be interpreted as meaning that we particularly desire to carry out radio lead studies.

To be of substantial use this work should be preceded by a thorough survey of the literature to indicate what blank spots in the present knowledge of lead metabolism need to be filled in. Certain amounts of time will also be needed for the development of standardizing procedures and, perhaps carrying out a few animal experiments before actual work with patients is started. This will probably require 2 to 4 months time by a competent biochemist, preferably someone in addition to our present staff. At least one additional technician will also be required for this work, besides extra laboratory space.

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4. T-METAL: Presumably this will require only office work on our part.
5. ISOTOPE 22: This program will require development and standardization of chemical and biological procedures; also preliminary rat tracer experiments, before human cases are studied. Our estimate of time to complete this preliminary work is one to three months for a competent biochemist. Perhaps Dr. Frenkel will be available for this work.

In the animal experiments planned by Dr. Hodge's group, its not intended that T will be isolated as such. On the other hand, for human tracer studies this isolation will be necessary in order to keep dosage below toxic levels. Therefore, the animal studies cannot serve as pilot studies for our work. Since low dosages must be used in human studies and the chemistry involved is quite extensive this work will require an additional chemical hood and a medium sized chemical laboratory, preferably in an uncontaminated area.

6. RADIUM: We are at present conducting animal tracer studies with radium. Comparatively little development and literature research will be required before expansion to human studies. We shall need additional physical apparatus to measure extremely small amounts of Mz and radon. Part of this equipment is already being developed. We ought to have one additional chemical hood and some additional working space for handling large amounts of urine and feces. The accompanying table summarizes these requirements. This table is compiled on the assumption that all of this work will be under way at approximately the same time. If certain of this work is done consecutively the space and personell requirements will be somewhat reduced, on the other hand the time before which final results will be obtained will be very much extended.

It cannot be too strongly emphasized that whether this work ought to be undertaken at all depends very largely on securing at least some additional competent personnel of professional rank. Of necessity, at the present time so much of this type of work funnels through Dr. Fink and myself for direction and critical evaluation of results that we are in a very real sense the present bottle necks in our experimental program for biological research.

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My budgetary estimates are as follows:

Two chemists, one at \$4,000 and one at \$3,000 per year	\$7,000.00
Three good technicians at \$2400 per year each	7,200.00
Apparatus and glassware	<u>4,000.00</u>
TOTAL	\$18,200.00

This estimate does not include an undetermined item for obtaining the additional laboratory facilities necessary for this proposed work. Our total requirements here are about three laboratory tables with central service supplies plus four medium sized chemical hoods. Some of this space, one hood and one side of one table should be in a hospital area, uncontaminated as concerns radioactivity, to be used only for Product work.

Elimination of radio-lead tracer work will reduce personnel and equipment as indicated in chart. Budget requirements will be reduced by approximately \$6,000.00

William F. Bale

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Personnel, Equipment, and Space Requirements for rapid (1 year) Completion of  
Human Tracer Studies

ELEMENT	CHEMISTS	TECHNICIANS	LAB. BENCH ( $\frac{1}{2}$ table)	HOODS	SUPPLIES & APPARATUS	PRELIMINARY RESEARCH	REMARKS
Postum	0	0	0	0	0	0	0
Product	0 - $\frac{1}{2}$	$\frac{1}{2}$ - 1	$\frac{1}{2}$	0 - 1	considerable glassware and shipping con- tainers	0	(at Rochester)
Lead	1	1	2	1	G-M counter chemical glass- ware	2 - 4 months	
<i>F. Frenkel</i>	0	0	0	0	0	0	(In Div. of Spec. Prob.)
22	1 (probably Frenkel) 6 mo.	1 (6 mo.)	2	1	glassware chemicals		Probably completed 6 months
<u>MY</u>	1 (or physicist)	1	1	1	breath Mx appar- atus, gamma ap- paratus, glass- ware and chem- icals		
Total	2 - 3	3 $\frac{1}{2}$ - 4	5 $\frac{1}{2}$	3 - 4			

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