

APPROVED	
PREPARED BY	<i>Weg</i>
APPROVED	<i>[Signature]</i>

REPOSITORY Dak Ridge Operations OfficeCOLLECTION Contract Files
→ AT-(40-1)-288BOX No. Drawer H-578-2FOLDER Bowman Gray School of Medicine
of Wake Forest CollegeContract No. AT-(40-1)-288
(Bowman Gray School of Medicine
of Wake Forest College)
Modification No. 3SUPPLEMENTAL AGREEMENT

THIS SUPPLEMENTAL AGREEMENT, entered into this 26th day of June, 1952, by and between the UNITED STATES OF AMERICA (hereinafter called the "Government"), represented herein by the UNITED STATES ATOMIC ENERGY COMMISSION (hereinafter called the "Commission"), and the BOWMAN GRAY SCHOOL OF MEDICINE OF WAKE FOREST COLLEGE (hereinafter called the "Contractor");

WITNESSETH THAT:

WHEREAS, the Government and the Contractor entered into Contract No. AT-(40-1)-288, dated June 22, 1949, for the performance by the Contractor, commencing on July 1, 1949, of three separate research projects on (1) the distribution and turnover of sodium and potassium in acute infections, (2) the formation of phospholipides in tissues, and (3) the toxicity of P³² as related to the diet and to the chemical nature of the compound; and

WHEREAS, the Contract has been modified heretofore by Modifications Nos. 1 and 2; and

WHEREAS, the parties desire to extend the term of the contract in order to continue and extend the research activities previously undertaken, as such extended program is described in Supplement No. 3 to Appendix "A"; and

WHEREAS, this Supplemental Agreement is authorized by and executed under the Atomic Energy Act of 1946;

NOW, THEREFORE, the parties hereto do mutually agree that Contract No. AT-(40-1)-288 is modified in the following particulars, but in no others:

1. Add the following new section 3 to Article II - TERM OF CONTRACT:

"3. The fourth period of performance for the project covered by this contract will commence on July 1, 1952, and will end on June 30, 1953."

2. Add the following new subsection c. to section 1 of Article III:

"c. In consideration of the performance of the work described in Supplement No. 3 to Appendix 'A', the Government will pay to the Contractor the sum of Twenty-Nine Thousand One

BEST COPY AVAILABLE

1090429

Hundred Eighty Dollars and Seventy-Four Cents (\$29,180.74) for the fourth period of performance, the funds to be applied to the three Titles according to the budget provisions of Supplement No. 3 to Appendix "A".

3. Add the following new Supplement No. 3 to Appendix "A":

"SUPPLEMENT NO. 3

"July 1, 1952 - June 30, 1953

This Supplement No. 3 describes the research projects and budgets agreed upon between the Commission and the Contractor for the fourth period of performance.

"TITLE I

"1. PROJECT

"a. Scope and Plan of Approach

During this period the Contractor will continue its investigations into the distribution and turnover of sodium and potassium in acute infections by proceeding along the following lines of endeavor:

(1) Standardization of Methods

Should it become necessary to utilize guinea pigs for the study of intracellular infections because of the difficulty of establishing a fatal or severe rickettsial infection in rabbits, the Contractor will develop and standardize micromethods for blood volume, Na^{24} , K^{42} spaces and Na and K content of tissue in guinea pigs.

Serial determinations of the K^{42} space in normal young women will be done in order to determine the reliability and reproducibility of results. Similar serial data will be obtained in normal young men. The data obtained is expected to give information of normal physiologic variations and of the stability of the K^{42} space as a basis for interpretation of experimental data to be obtained in diseased states.

Experiments will be undertaken to determine the effect on the K^{42} space and potassium balance of bed rest alone and of starvation without immobilization on normal human beings.

Further studies on normal values in rabbits, guinea pigs and human beings for blood volume and total available protein content will be continued with serial species specific protein fractions labeled with I^{131} .

In order to determine the effect of the normal secretion of the thyroid gland on the distribution of sodium and potassium, rabbits will be made myxedematous by the injection of I^{131} . After myxedema is established, the Na^{24} , K^{42} and I^{131} tagged protein spaces and Na^{24} , K^{42} tissue contents will be determined.

(2) Intracellular Infections

The studies on experimentally-induced Rocky Mountain spotted fever in rabbits and guinea pigs will be continued.

Further attempts will be made to increase the virulence of the rickettsias for rabbits and to induce greater physiologic changes.

Autoradiographic studies by the technique previously developed will be done on representative animals as a check on the physiologic method by an anatomic one.

(3) Extracellular Infections

The experiments previously reported on fluid changes in trichinosis, an extracellular infection, studied by non-isotopic techniques will be repeated with the application of the tracer methods previously developed.

Time permitting, further attempts will be made to standardize an extracellular interstitial infection with virulent type I pneumococci in the skin and subcutaneous tissue of rabbits.

(4) Immune Reactions Without Infection

Further attempts will be made to induce quantitatively greater physiologic changes through the sensitization of rabbits by repeated injections of a single pool of human plasma.

(5) Clinical Studies

Clinical studies will be conducted in human beings with any type of infection when at all feasible.

Between suitable cases of infection, the techniques developed and standardized will be applied to various pathologic states which are known to induce alteration.

The preliminary observations on the K^{24} space in rheumatic fever will be extended and data on K^{42} space will be obtained.

Other types of diseases which are amenable to specific therapy - such as myxedema, hyperthyroidism, diabetes, congestive heart failure, and syphilis - will be studied before and after the institution of specific therapy.

"2. BUDGET - Fourth Period: July 1, 1952 - June 30, 1953

"a. The Contractor will furnish as its contribution to the Title I project:

- (1) Salaries of staff members, including the Project Leader, and other personnel engaged in the work in excess of the Government's payment under b.(1) below.
- (2) Use of laboratory work space; and equipment, materials and facilities required for the work in excess of the Government's contribution under b. below.
- (3) Clerical, administrative and overhead costs in excess of the Government's payment under b. below.

"b. Under this Title I the Government will pay to the Contractor the sum of Sixteen Thousand Nine Hundred Eight Dollars and Twelve Cents (\$16,908.12) which, together with the sum of Eighty-Five Dollars and Sixty-Eight Cents

(\$85.68) (which amount the parties hereby agree shall be deemed to represent the amount by which the total of payments made by the Government under this Title I for the previous periods of performance exceeds total expenditures for the same periods) is to cover generally the following operating estimates:

(1) Salaries

J. K. Aikawa		
Technician (Rhoades)		
Technician (Brooks)		
House officers for clinical studies	500.00	
Electronic Engineer	300.00	
	<u> </u>	
Total Salaries		\$ 8,450.00

(2) Permanent Equipment

Beta-gamma survey meter	275.00	
Sample storage unit	30.00	
Steel bricks	<u>200.00</u>	
Total Equipment		505.00

(3) Isotopes

Na ²⁴ and K ⁴² , handling charge and transportation	3,120.00	
Iodinated Albumin	<u>260.00</u>	
		3,380.00

(4) Animals

1,200.00

(5) Supplies

Geiger-Mueller tubes	400.00	
Glassware	500.00	
Chemicals, etc.	<u>400.00</u>	
Total Supplies		1,300.00

(6) Travel

500.00
 \$15,735.00

(7) <u>Overhead @ 8%</u>	<u>1,258.80</u>
Subtotal	\$16,993.80
Balance from previous payments	<u>85.68</u>
TOTAL	\$16,908.12

"c. Items of property procured or manufactured by the Contractor, title to which will vest in the Government (see Article VI): None.

"TITLE II

"1. PROJECT

"a. Scope and Plan of Approach

During this period the Contractor will continue and extend its studies on the formation of phospholipides in tissues, proceeding along the following lines of endeavor:

(1) Intermediate Stages in the Synthesis of the Phospholipide Molecule

The following described experiment will be undertaken, to investigate whether or not phosphorylcholine is an intermediate stage in the incorporation of choline into the phospholipides. Liver homogenates will be incubated with C^{14} labeled choline in the presence or in absence of non-labeled phosphorylcholine. Other experiments similar in nature will be conducted.

(2) Incorporation of Nitrogenous Constituents (Other than Choline) in the Phospholipides

The Contractor will attempt to synthesize (or obtain from other sources) a preparation of ethylanolamine labeled with C^{14} . The incorporation of this compound into the phospholipides will be studied.

(3) Metabolic Pathways of Choline in Isolated Liver

The Contractor will attempt to improve the procedures for the separation and characterization of the probable products of choline metabolism. If this attempt is successful, the Contractor will try to

identify certain products of choline metabolism which appear to be quantitatively important.

(4) Oxidation of Fatty Acids in the Liver of Choline-Deficient Animals

The Contractor will conduct experiments testing the hypothesis that choline acts by enhancing the degradation of fatty acids in the liver itself. This will be done by studying the oxidation of isotopic fatty acids in the isolated liver from animals in choline deficiency.

(5) Other Investigations

Limitations in time and personnel permitting, the Contractor will continue certain collateral investigations, such as that on the enzymatic condensation of formaldehyde with pyruvate.

"2. BUDGET - Fourth Period: July 1, 1952 - June 30, 1953

"a. The Contractor will furnish as its contribution to the Title II project:

- (1) Salaries of staff members, including the Project Leader, and other personnel engaged in the work in excess of the Government's payment under b.(1) below.
- (2) Use of laboratory work space; and materials, equipment and facilities required for the work in excess of the Government's contribution under b. below.
- (3) Clerical, administrative and overhead costs in excess of the Government's payment under b. below.

"b. Under this Title II the Government will pay to the Contractor the sum of Seven Thousand Eight Hundred Twelve Dollars and Sixty-Seven Cents (\$7,812.67) which, together with the sum of Three Thousand Seven Hundred Ninety-Seven Dollars and Thirty-Three Cents (\$3,797.33) (which amount the parties hereby agree shall be deemed to represent the amount by which the total of payments made by the Government under this Title II for the previous periods of performance exceeds total expenditures for the same periods) is to cover generally the following operating estimates:

1090435

(1) <u>Salaries</u>		
Research Associate	\$1,500.00	
Graduate Student (Pollard)	1,500.00	
Technician (full-time)	2,400.00	
Technician (part-time)	1,200.00	
	<hr/>	
Total Salaries		\$ 6,600.00
(2) <u>Permanent Equipment</u>		
New scaling unit	800.00	
Other equipment	300.00	
	<hr/>	
Total Equipment		1,100.00
(3) <u>Isotopes</u> (C ¹⁴ -labeled compounds)		1,200.00
(4) <u>Animals</u>		200.00
(5) <u>Supplies</u>		
Glassware	500.00	
Chemicals	500.00	
	<hr/>	
Total Supplies		1,000.00
(6) <u>Travel</u>		300.00
(7) <u>Maintenance</u>		350.00
		<hr/>
		\$10,750.00
(8) <u>Overhead @ 8%</u>		860.00
		<hr/>
Subtotal		\$11,610.00
Less Unexpended Balance		3,797.35
		<hr/>
TOTAL		\$ 7,812.67

"c. Items of property procured or manufactured by the Contractor, title to which will vest in the Government (see Article VI): None.

"TITLE III

"1. PROJECT

"a. Scope and Plan of Approach

The program under this Title III continues to be research into the toxicity of P³² as related to the diet and to the chemical nature of the compound. The following outline shows the general nature of the work to be performed during this period:

(1) Protective Role of Vitamins

The Contractor will extend to other factors of the B, C, and E groups its systematic study on the protective role of vitamins against P³².

(2) Protective Role of Certain Hormones and Drugs

Experiments will be made with dihydrotestosterone (AT10). A study of the effects of cortical and other steroid hormones will be undertaken.

(3) Attempts to Increase the Mobilization of P³² from the Bones

The Contractor will explore the effects of the introduction of inactive pyrophosphate in this field.

(4) The Effects of Repeated Exposure to Internal Radiation

Mice will be given a sublethal dose of either P³² or of another bone seeking radioisotope. Then, after periods varying from two to six weeks, a larger dose of P³² in the middlelethal range will be injected. Controls run simultaneously will receive only the larger dose of P³².

"2. BUDGET - Fourth Period: July 1, 1952 - June 30, 1953

"a. The Contractor will furnish as its contribution to the Title III project:

- (1) Salaries of staff members, including the Project Leader, and other personnel engaged in the work in excess of the Government's payment under b.(1) below.
- (2) Use of laboratory work space; and materials, equipment and facilities required for the work in excess of the Government's contribution under b. below.
- (3) Clerical, administrative and overhead costs in excess of the Government's payment under b. below.

"b. Under this Title III the Government will pay to the Contractor the sum of Four Thousand Four Hundred Fifty-Nine Dollars and Ninety-Five Cents (\$4,459.95) which together with the sum of One Thousand Eight Hundred Four Dollars and Five Cents (\$1,804.05) (which amount the parties hereby agree shall be deemed to represent the amount by which the total of payments made by the Government under this Title III for the previous periods of performance exceeds total expenditures for the same periods) is to cover generally the following operating estimates:

(1) <u>Salaries</u>		
C. Downs (full-time) Technician	\$2,400.00	
Research Associate (part-time)	<u>1,600.00</u>	
Total Salaries		\$4,000.00
(2) <u>Permanent Equipment</u>		300.00
(3) <u>Isotopes</u>		600.00
(4) <u>Supplies</u>		500.00
(5) <u>Animals</u>		250.00
(6) <u>Travel</u>		250.00
		<u>\$5,800.00</u>
(7) <u>Overhead @ 8%</u>		464.00
		<u>\$6,264.00</u>
	Subtotal	\$6,264.00
	Balance from previous period	<u>1,804.05</u>
	TOTAL	\$4,459.95

"c. Items of property procured or manufactured by the Contractor during this period, title to which will vest in the Government (see Article VI): None."

IN WITNESS WHEREOF, the parties hereto have executed this Supplemental Agreement the day and year first above written.

UNITED STATES OF AMERICA

WITNESSES:

UNITED STATES ATOMIC ENERGY COMMISSION

Katherine Davis
Winston-Salem N.C.
(Address)

BY: John R. Moore
John R. Moore
TITLE: Director, Contract Division, ORO

Jane Linbeck
Winston-Salem, N.C.
(Address)

BOWMAN GRAY SCHOOL OF MEDICINE OF
PEAKE FOREST COLLEGE
BY: Harry O. Pinner
TITLE: Controller

ACCEPTANCE BY PROJECT LEADERS

I have read the foregoing Supplemental Agreement and agree to be bound by its provisions to the extent that they are applicable to the project for which I am responsible.

Roy T. Haull, Jr.
Project Leader, Title I

D. Camille Arton
Project Leader, Title II

Roy T. Haull, Jr. D. Camille Arton
Project Leader, Title III