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TYPED
PREPARED LLP
APPROVED

Contract No. AT-(40-1)-288
(The Bowman Gray School of Medicine of Wake Forest College)
Modification No. 2

RETURN TO CONTRACT SECTION

SUPPLEMENTAL AGREEMENT

THIS SUPPLEMENTAL AGREEMENT, entered into this 28th day of June, 1951, 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 (2) the toxicity of P^{32} as related to the diet and to the chemical nature of the compound; and

WHEREAS, the contract has been amended heretofore by Modification No. 1; and

WHEREAS, the Government desires to increase its payments under the second period of performance; and

WHEREAS, the parties desire to extend the term of the contract in order to continue and expand the research activities undertaken during the initial period, as described in Supplement No. 2 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. In order to increase by One Thousand Dollars ($1,000.00) the Government's payment to the Contractor for work under Title I to Appendix "A" during the second period, the following changes are made effective as of April 23, 1951:

a. In ARTICLE III, Section 1, line 3, delete "Fifty-Three Thousand Seven Hundred Forty-Eight Dollars ($53,748.00)"

and substitute therefor "Fifty-Four Thousand Seven Hundred Forty-Eight Dollars ($54,748.00)".

b. In ARTICLE III, Section 2b, add the following new sentence at the end of the section:

"On or after April 23, 1951, the Government will pay to the Contractor, upon submission by the Contractor of a properly certified voucher, the sum of One Thousand Dollars ($1,000.00)."

c. In Supplement No. 1 to Appendix "A", Title I, Section 2B (1) delete, in line 1, "$13,858.00" and substitute therefor "$14,858.00"; and in Section 2B (1) c, delete, in line 5, "$300.00" and substitute therefor "$1,300.00", and delete, in line 8, "$2,900.00" and substitute therefor "$3,900.00", and delete, in line 12, "$13,858.00" and substitute therefor "$14,858.00".

2. Insert the section number "1." before the first word of ARTICLE II - TERM OF CONTRACT, and add the following new Section 2 to ARTICLE II:

"2. The third period of performance for the project covered by this contract will commence on July 1, 1951, and will end on June 30, 1952."

3. Insert the sub-section letter "a." between the words "Consideration." and "In" in Section 1 of ARTICLE III - PROGRAM DEVELOPMENT AND FINANCING, and add the following new sub-section b to Section 1 of ARTICLE III:

"b. In consideration of the performance of the work under the three Titles described in Supplement No. 2 to Appendix 'A', the Government will pay to the Contractor the total sum of Thirty Thousand Seven Hundred Ninety-One and 96/100 Dollars ($30,791.96) for the third period of performance, the funds to be applied to the three Titles according to the budget provisions of Supplement No. 2 to Appendix 'A'. It is expressly agreed that the total sum of Two Thousand Five Hundred Thirty-six and 84/100 Dollars ($2,536.84) which had been previously paid to the Contractor by the Government (this sum includes the increase effected by change number 1 of Modification No. 2) but which will remain unexpended at the end of the second

period of performance will be applied to the costs of the third period of performance according to the amount remaining to each Title.

4. Add the following new Supplement No. 2 to Appendix "A":

"SUPPLEMENT NO. 2

"TITLE I

"1. PROJECT

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

"a. Standardization of methods

"Though much time and effort has gone into development of techniques in the past year and a half some of the techniques still must be standardized to be sure they are absolutely dependable. No data are available on normal values for some techniques and these must be established before definitive experiments can be attempted or the data on experiments in progress interpreted.

"The radiopotassium work in animals has just begun. The technique must be standardized and normal values established for K^{42} space or exchangeable K content in normal rabbits.

"Normal values must be established for the tissue content of total potassium and K^{42} in normal rabbits.

"Since potassium is found almost entirely intracellularly in association with tissue proteins, the interpretation of data in abnormal states becomes extremely difficult. In addition to the control values for normal animals not under stress, a second type of control experiment must be done. It has been

shown that simply putting normal persons to bed will increase the nitrogen excretion in the urine, presumably from destruction of tissue protein. It might be presumed that the potassium excretion would be increased under such circumstances and the total tissue potassium correspondingly reduced. The validity of this thesis must be established in experimental animals under some stress which is different from that to be induced later in definitive experiments. Therefore, a second group of animals will be starved to induce tissue breakdown under reasonably normal physiologic conditions and the above studies performed in order to determine the effect of this stress alone - without infection or immune reaction - on the total exchangeable potassium content or potassium space and the tissue content of potassium. This control should be valid since animals ill with an infection or serum disease are not likely to eat as much as would normal animals.

"In order to determine whether the correlation between radiopotassium content and urinary creatinine excretion reported in normal human males will hold in rabbits, urinary creatinine should be determined at the same time the potassium excretion is measured in both normal and starved animals.

"Normal values must be established for rabbits by the tagged serum protein technique utilizing I^{131} as a marker. The range of normal values in animals, utilizing not only rabbit albumin but rabbit globulin and perhaps even large protein molecules such as fibrinogen, must be done.

"Depending upon the relative alteration of Na^{24}, K^{42} and I^{131} values as determined in the above experiment, autoradiography of the organs should be attempted in order to locate the tissues into which ions and proteins leak in the course of infections and immune reactions. Though potassium and sodium are soluble, it is hoped that a technique utilising plastic fixation without dehydration will prove feasible so that the soluble ions will not be reached out. The problem should be less technically difficult with iodine tagged proteins which may be precipitated and left in situ.

"Preliminary experiments in human beings have given interesting and often unexpected results indicating a relationship between urinary creatinine and K^{42} excretion. These experiments should be considerably extended in a wide range of pathological conditions in order to serve as a control on the alterations in permeability in specific infectious diseases and in known demonstrable immune reactions. Experiments should be run particularly on disease processes which are known to affect the permeability of capillary or cellular membrances - such as acute rheumatic fever, glomerulonephritis and myxedema.

"Comparison of blood volumes, utilizing human albumin and human globulin tagged with I^{131} and the Evans blue techniques, should be done.

"b. Intracellular infections

"Since the experimental techniques to be utilized have not yet been completely standardized, it was not possible during the past year to evaluate experimental infections in animals. It will be necessary to standardise an infection in rabbits, preferably with an experimental Rocky Mountain spotted fever strain, which is at present established in guinea pigs. The guinea pig is not a suitable animal for the experiments contemplated and our techniques are all standardized for rabbits.

"As soon as a standardized dose is determined and a dependable reproducible infection induced, the techniques, utilizing Na^{24}, K^{42}, and I^{131} labeled rabbit serum fractions, developed will be applied. Serial studies at as close intervals as technical problems - such as rate of decay of isotopes - will permit will be done.

"If satisfactory autoradiographic techniques are developed, such studies will be done in fatal instances and representative animals sacrificed at appropriate intervals as a check on the physiologic method by an anatomic one.

"If time permits, an attempt will be made to tag the rickettsias with P^{32} by introduction of the isotope into the chick egg during growth of the rickettsias. The labeled organisms will then be injected into normal rabbits and rabbits previously immunized against the same strain of rickettsias, in order to study more accurately the localization of the parasite.

"In all of the experiments the physiologic measurements will be correlated with the immunologic responses and the data compared with the previous findings in clinical instances of Rocky Mountain spotted fever in human beings.

"c. Extracellular infections

"The experiments now in press on fluid changes in trichinosis - an extracellular infection - should be repeated with the application of the techniques now being standardized. Rabbits will be fed trichinous rat meat; the Na^{24}, K^{42} and I^{131} labeled protein fraction studies will be done at appropriate intervals. The physiologic data will be correlated with the immunologic response and the findings compared with the small amount of data available in clinical cases of trichinosis in human beings.

"The difficulty in reproducing standardized extracellular interstitial infections in rabbits with the pneumococcus, as compared with the difficulty in trichinella infections, is so much greater that it seems more profitable to return to the parasitic infestation and to abandon, at least temporarily, the bacterial infection.

"d. Immune reactions without infections

"Further attempts will be made to standardize a dependable passive transfer method for induction of serum sickness in rabbits.

"If these attempts are unsuccessful, the experiments completed and in press in which serum sickness was induced actively by injection of human albumin should be repeated and the techniques under standardization be applied. Sodium-24, potassium-42, and iodine-131 labeled protein fraction alterations should be determined in rabbits.

"e. Auto-antibody studies

"The limitations of time and available technical assistance have so far postponed the inauguration of autobody studies. If the above outlined studies with

experimentally induced intracellular and extracellular infections and immune reactions without infections can be completed, this year the following study should be started.

"An attempt will be made to produce auto-antibody to rabbit hear using as antigen a mixture of group A beta hemolytic Streptococcus somatic group specific fractions which have been combined with normal rabbit heart. If the attempt is successful, the immunologic and physiologic methods, utilizing Na^{24}, K^{42}, and I^{131} labeled rabbit serum fractions, will be applied to the animals. In an additional group of animals the antibody itself can be tagged with I^{131} for studies on the distribution of the antibody in normal and sensitized animals. The histologic lesions could be correlated with the physiologic changes by autoradiography.

"As a control, the effect of repeated sensitization of rabbits with the bacterial fractions alone would be studied, utilizing the same techniques, and the results compared with those obtained by the auto-antibody technique.

"f. Clinical studies

"The techniques developed and standardized in human beings are being applied to the study of infectious diseases in human patients. The development of more potent antibiotics, such as terramycin, continues to reduce the number of clinical instances of rickettsial spotted fever or other acute infectious diseases admitted to the hospital. Such cases as are appearing for study have almost invariably been treated with at least one antibiotic before admission so that the cases are hardly suitable for study. In such cases as are admitted before treatment, baseline studies can be obtained but the infection is usually arrested so quickly by therapy with antibiotics that the physiologic changes observed in prior years do not develop to the extent previously seen or do not develop at all. It is for this reason that emphasis is being shifted to the experimental animal. Clinical studies will still be conducted in human beings when at all feasible.

"In order to utilize personnel and facilities in the intervals between suitable cases of infection, the techniques developed and standardized will be applied to various pathologic states which are known to induce

alteration in permeability of membranes, as well as to some which at present are not thought to induce changes in permeability.

"Observations will continue to be made measuring the exchangeable potassium content in human beings. Up to the present only survey studies with single determinations have been possible. An attempt will be made to do serial studies during the acute phase of disease. Permission has been obtained from the Isotopes Division to repeat studies at relatively short intervals. The limiting factor in K^{42} experiments is the chemical toxicity of the potassium administered because of the relatively low specific activity, rather than the cummulative radiation dose.

"Studies on sodium-24 space, utilizing the technique already published, will be continued and expanded. The same types of disease processes will be studied as described in the preceeding paragraphs. The specific activity of Na^{24} is so high that no problem in chemical sodium intoxication has been encountered or is anticipated. Permission has been received from the Isotopes Division to enable repeating these studies serially at relatively short intervals in acute instances of disease. Heretofore, only single isolated observations have been done.

"Determination of blood volume and permeability of membranes to I^{131} labeled human serum fractions will be continued and expanded. The extravasation of protein fractions into serous cavities, cerebrospinal fluid space, or interstitial spaces, in instances where edema fluid collects, will be continued.

"The type of disease process so far studied by the above techniques includes myxedema, rheumatic fever, glomerulonephritis, exogenous obesity, hyperthyroidism, diabetes, syphilis, psychoneurosis, chronic ulcerative colitis, and others. Most of these have been chronic forms of the disease where the pathologic physiologic situation is reasonably stabilized. Attempts will be made to obtain more acute instances of disease for serial studies, for example, diabetic acidosis with coma and dehydration, acute congestive heart failure, and acute glomerulonephritis.

"2. BUDGET - Third Period: July 1, 1951 - June 30, 1952

"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.

PRIVACY ACT MATERIAL REMOVED

(2) Use of laboratory work space, and equipment, materials and facilities on hand as needed for the work.

(3) Clerical, administrative and overhead costs in excess of the Government's payment under b (7) below.

"b. The Government will pay to the Contractor the sum of Fifteen Thousand Nine Hundred Thirty and 59/100 Dollars ($15,930.59) which, together with the unexpended amount of Twenty-One and 1/100 Dollars ($21.01) remaining from the Government's payments under the second period of performance, will cover the Contractor's other expenses, estimated as follows, in the performance of the contract during the third period:

(1) Salaries

J. F. Aikawa	[redacted]
Technician, E. Rhoades	[redacted]
Technician, C. Taylor	[redacted]
House officer for clinical studies	400.00
Electronic engineer	300.00
(2) Permanent equipment	870.00
(3) Isotopes	2,750.00
(4) Animals	1,800.00
(5) Supplies	1,300.00
(6) Travel	300.00

(7)	Overhead at 8%	$1,181.60
	Total	$15,951.60

"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.

"TITLE II

"1. PROJECT

"In the preceding years, the formation of phospholipides has been studied on both intact animals and isolated tissues with the aid of P^{32}. The results have given indications on the synthesis of whole phospholipide molecule starting from the inorganic phosphate and on the dependence of this process upon the composition of the diets.

"All phospholipides contain phosphorus, but the various phospholipides differ in their nitrogenous constituents. The most important type of phospholipides, the lecithins, contains choline. This substance is also an essential dietary factor, the deficiency of which leads to serious disturbances (such as fatty infiltration of the liver). The Contractor has used a preparation of choline (labeled in the methyls with C^{14}) in order to study the synthesis of lecithins, as well as other metabolic pathways of choline in the liver. More specifically, during the past year, the investigations have progressed along the following lines: 1) lipide composition of liver mitochondria; 2) incorporation of inorganic P^{32} into the phospholipides of liver slices from rats on various diets; 3) incorporation of labeled choline into the lipides of isolated liver tissue; 4) metabolic pathways of choline in liver slices; 5) synthesis of C^{14}-methyl labeled dimethylethanolamine (a possible choline precursor); 6) disposal of formaldehyde in tissues. During this period the Contractor will continue and extend the above mentioned groups of investigations. The following seem the most promising and the Contractor will concentrate on them:

"a. Incorporation of the nitrogenous constituents into the phospholipides of the liver.

"The data obtained thus far indicate that the incorporation of choline into the phospholipides might proceed independently from the incorporation of the inorganic phosphate. It is therefore suggested that phosphatidic acids (= phospholipides less their nitrogenous moieties) may represent important intermediates in the synthesis of the complete phospholipide molecule as well as in the conversion of one kind of phospholipide into another. The results of experiments in which various substances were added to liver tissue in vitro seem to be in line with the interpretation that a competition occurs between choline and the other nitrogenous components of the phospholipides (or analogues of these components). Such type of experiments will be continued and extended further. It is also hoped to synthesize or obtain from other sources a preparation of C^{14}-labeled ethanolamine (the nitrogenous constituent of the cephalins). Thus the formation of the two main types of phospholipides, lecithins and cephalins could be followed together and with similar techniques, and perhaps it will be possible also to attack the problem of their biochemical relationships.

"b. Incorporation of labeled dimethylethanolamine into the phospholipides of the liver.

"On the basis of its chemical constitution, dimethylethanolamine is likely to represent the immediate precursor of choline. Methyl labeled dimethylethanolamine has been synthesized and added to surviving liver slices. Preliminary results indicate that the compound is incorporated into the phospholipides at approximately the same rate as lapeled choline. The future experiments should decide whether the compound is incorporated directly into the phospholipides or, if a preliminary methylation to choline must occur. The possibility of a methylation of the compound after its incorporation into the phospholipides can also be visualized. Methylation of dimethylethanolamine (either free or as a phospholipide moiety) would represent the final step in the synthesis of choline by the tissue, and should be investigated in detail from various points of view, such as oxygen requirement, nature of the methyl donors, characteristics of the enzymes involved, etc. The labeled

dimethylethanolamine will also be used in certain phases of the study of the metabolism of choline in tissues (see below).

"c. Metabolism of choline in isolated liver.

"In spite of its important roles, very little is known about the metabolic products and pathways of choline in the body. When choline is administered to animals or humans, only minimal amounts are excreted in the urine. In order to simplify the problem, the metabolism of methyl labeled choline has been studied with liver slices or homogenates. Preliminary experiments have suggested the following major pathways (in addition to the incorporation of the intact compound into the phospholipides): 1) oxidation of the methyl group presumably to formaldehyde, formic acid and CO_2; 2) formation of trimethylamine and trimethylamine oxide; 3) formation of compounds highly resistant to hydrolysis.

"The Contractor is of the opinion that the last mentioned compounds are organic esters of choline (such as choline phosphate ester) but it is planned to obtain a more convincing evidence of their identity. At the same time the Contractor will try to identify other likely products of choline metabolism such as betaine, betaine aldehyde and dimethylglycine. The separation of these products will not be easy because of the similarity in their chemical and physical properties. Consequently it is expected that much time and effort will be required for the elaboration of a satisfactory scheme of analysis. If attempts will be successful, a balance sheet of choline metabolism in the isolated liver could be prepared. A further step in the investigations will be the study of the changes in the relative importance of these various pathways under the influence of several physiological and pharmacological agents. Besides labeled choline and labeled dimethylethanolamine it is presumed that in these experiments, other methyl-labeled compounds, such as dimethylglycine, betaine, and methionine, could be used advantageously. If the compounds could not be obtained from other sources, the Contractor will attempt to prepare these materials with the proper labels

"d. Metabolism of formaldehyde.

"The importance of one carbon compounds as intermediates in a number of metabolic reactions, including methylations, is growing rapidly. In recent experiments it was discovered that the enzymatic disappearance of formaldehyde is greatly accelerated in the presence of pyruvic acid. Isotopic techniques confirm the hypothesis of the formation of a condensation product. It seems probable that the product, formed initially, is later changed to other compounds susceptible to oxidation by periodic acid. These investigations will be continued in an attempt to attain a definitive identification of the compound or compounds formed.

"2. BUDGET - Third Period: July 1, 1951 - June 30, 1952

"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 equipment, materials and facilities on hand as needed for the work.

(3) Clerical, administrative and overhead costs in excess of the Government's payment under b (9) below.

"b. The Government will pay to the Contractor the sum of Eight Thousand Nine Hundred Forty-Three and 34/100 Dollars ($8,943.34) which, together with the unexpended amount of Two Thousand One Hundred Sixty-Nine and 86/100 Dollars ($2,169.86) remaining from the Government's payments under the second period of performance, will cover the Contractor's other expenses, estimated as follows, in the performance of the contract during the third period:

PRIVACY ACT MATERIAL REMOVED

(1) Salaries

Technician, C. Terhune	[redacted]
Two part-time technicians	2,160.00
Investigator, M. Crowder	[redacted]
(2) Warburg apparatus and accessories	1,100.00
(3) Permanent equipment	360.00
(4) Isotopes	1,700.00
(5) Animals	200.00
(6) Supplies	1,000.00
(7) Travel	300.00
(8) Maintenance of radioactivity apparatus	350.00
(9) Overhead at 8%	831.20
Total	$11,113.20

"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.

"TITLE III

"1. PROJECT

"In the past two years a systematic study has been undertaken of the toxicity of radioactive phosphate in mice maintained on various diets. The acute toxicity (as measured by the LD_{50} at the 21st day) is lowest with diets low in fat and protein, and is not modified by fatty infiltration or toxic damage of the liver. A significant degree of protection was obtained by enriching the diets with inorganic phosphate. In experiments of longer duration the role of certain vitamins on the recovery of the damaged tissues has been studied. The importance of an adequate supply

of both vitamin B_{12} and folic acid could be demonstrated in animals receiving sulfasuxidine (in order to reduce the synthesis of the vitamins in the gastro intestinal tact).

The investigations will be continued essentially along the following main lines during this period:

"a. Effects of vitamins and hormones on the recovery from damage by P^{32}.

"In a continuation of the studies mentioned above, the influence of other vitamins will be studied. Since several of these vitamins are synthesized by the intestinal flora, an acute deficiency is not likely to occur in ordinary conditions. However, one may visualize the possibility that vitamin deficiencies develop as a result of the continued administration of antibiotics (such as it has been suggested precisely in the treatment of radiation injury). Moreover, a limited synthesis of at least certain vitamins occurs also in animal tissues; such a synthesis can probably be encountered by the administration of vitamin analogues. Accordingly, the Contractor will compare the toxicity of P^{32} in animals receiving either antibiotics, or vitamin analogues (e.g., desoxypyridoxin) with the toxicity of the isotope in animals generously supplied with the natural vitamins (e.g., pyridoxin).

"It is planned also to investigate if, and to what extent the administration of certain hormones (e.g., corticosterone or ACTH) might favor the recovery of the tissues from the damage induced by the radioactive isotope.

"b. Alkalosic and acidosic diets.

"Preliminary data indicate that acid-producing substances tend to decrease the survival of mice injected with P^{32}. In an extension of these experiments, the effects of the addition of alkaline salts to the diets are being studied. If significant differences will become apparent, an attempt will be made to correlate the data on the survival with the changes in pH and isotope content of the urine.

"c. Increased mobilization of P^{32} from the skeleton.

"Among the various experimental dispositions tested, only the enrichment of the diets with phosphate appeared clearly effective in this respect. To date, attempts to cause a simultaneous mobilization of calcium and phosphate from the skeleton by the admixture of citrate in the diet or by injection of parathyroid hormone were not successful. However, additional experiments are needed before definite statements on this point can be made.

"In addition, the Contractor will test the effects of the administration of other "chelating" agents (such as "versenes"), which are known to markedly reduce the concentration of calcium ions in blood. Polyphosphates which are also effective in this respect could possible be beneficial by another mechanism (hydrolysis by pyrophosphatase with increased concentration of non-isotopic phosphate on the surface of the bones). It seems likely that in experiments of this type larger animals should be used, in order to make possible the intravenous injection of large volumes of solutions and to determine calcium and phosphorus levels in blood.

"d. Distribution and toxicity of P^{32} injected as pyrophosphate.

"As a collateral investigation, it is planned to compare the distribution and the toxicity of radioactive pyrophosphate with those of the orthophosphate. Since pyrophosphate does not exchange directly with the inorganic phosphate, it seems likely that differences in the behavior of these two forms of P^{32} will chiefly depend upon the rate of hydrolysis of pyrophosphate to inorganic phosphate under the action of the pyrophosphatases in the various tissues. The results of such a study might even suggest some practical applications for the use of P^{32} in therapy.

"2. BUDGET- Third Period: July 1, 1951 - June 30, 1952

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

(1) Salaries of staff members, including the Project Leader, engaged in the work.

PRIVACY ACT MATERIAL REMOVED

(2) Use of laboratory work space, and equipment, materials and facilities on hand needed for the work.

(3) Clerical, administrative and overhead costs in excess of the Government's payment under b (7) below.

"b. The Government will pay to the Contractor the sum of Five Thousand Nine Hundred Eighteen and 3/100 Dollars ($5,918.03) which, together with the unexpended amount of Three Hundred Forty-Five and 97/100 Dollars ($345.97) remaining from the Government's payments under the second period of performance, will cover the Contractor's other expenses, estimated as follows, in the performance of the contract during the third period:

(1)	Salaries	
	Technician (½ time)	[redacted]
	Technicians (part-time)	[redacted]
(2)	Permanent equipment	700.00
(3)	Isotopes	500.00
(4)	Animals	500.00
(5)	Supplies	600.00
(6)	Travel	200.00
(7)	Overhead at 8%	464.00
	Total	$6,264.00

"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 on the day and year first above written.

UNITED STATES OF AMERICA

BY: UNITED STATES ATOMIC ENERGY COMMISSION

BY: C. Vanden Bulck

C. Vanden Bulck, Acting Manager, ORO

TITLE: Contracting Officer

WITNESSES:

Jane Linebeck

Bowman Gray School of Medicine
(Address)

Katherine Davis

Winston-Salem, NC
(Address)

BOWMAN GRAY SCHOOL OF MEDICINE
OF WAKE FOREST COLLEGE

BY: Harry O. Larson

TITLE: Controller

ACCEPTANCE BY PROJECT LEADERS:

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

Geo. T. Hamill
Project Leader, Title I

E. Camille Artom
Project Leader, Title II

E. Camille Artom
Project Leader, Title III