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UNITED STATES
ATOMIC ENERGY COMMISSION

717190

LUMP SUM
RESEARCH CONTRACT

Contract No. AT-(40-1)-1081

THIS CONTRACT, entered into this 14th day of December, 1950, by the UNITED STATES OF AMERICA (hereinafter called the "Government"), acting through the UNITED STATES ATOMIC ENERGY COMMISSION (hereinafter called the "Commission") and Duke University, School of Medicine (hereinafter called the "Contractor"):

ARTICLE I - PURPOSE AND SCOPE

1. The Commission, in furtherance of its policy of assisting and fostering private research, desires to support the Contractor's fundamental research in the field of atomic energy.

2. The work shall consist of a study of the metabolism of the human bone marrow.

The plan of approach to the problem and the agreed upon program and budget for the project are described in Appendix "A", which is hereby made a part of this contract. The Contractor shall be guided by, but not bound to conform to the details of the budget described in Appendix "A".

3. The Contractor shall furnish all services, facilities, equipment, supplies and materials (except such services, equipment, supplies and materials as the Government has agreed to furnish herein) required for the performance of the research program described in Section 2 above.

4. The work will be carried out by the Contractor under the direction of L. M. Rundles as Project Leader

ARTICLE II - TERM OF CONTRACT

The initial period of performance for the research project covered by this contract will commence on January 1, 1951 and will end on December 31, 1951.
It is recognized that completion of the research work under this contract may involve a period of several years and that the term of this contract may be extended by mutual agreement.

ARTICLE III

1. Consideration. In consideration of the performance of the research activities described in Article I, the Government shall pay to the Contractor the sum of Twelve Thousand Forty-two Dollars ($ 12,042.00) for the initial period of performance.

2. Payment

a. On or before the date of commencement of work on the project described in Appendix "A", the Government shall pay to the Contractor, upon submission by the Contractor of a properly certified voucher, one-half the amount of the agreed consideration.

b. On or before the expiration of six months from the date of commencement of the project, the Government shall pay to the Contractor, upon submission by the Contractor of a properly certified voucher, the remaining one-half of the agreed consideration.

c. In the event that the term of the contract is extended, the Government shall pay to the Contractor, upon submission by the Contractor of properly certified vouchers, each six months in advance an amount equal to one-half the annual agreed consideration for the project as mutually agreed upon by the parties hereto.

3. Program and Budget for Subsequent Periods. At least three months before the end of the initial period of performance of the project, the Contractor will submit to the Commission a current statement of its expenditures for the project, an estimate of expenses to be incurred during the remainder of the period, and a proposed program and budget for the succeeding year, showing the proposed work to be financed by the Commission and the Contractor. The Contractor and the Commission shall then negotiate as to the amount to be paid by the Commission to the Contractor for the services to be performed during the ensuing period, taking into consideration any portion of payments theretofore made which will remain unexpended at the end of the initial period. The extended program, budget and the additional amount to be paid to the Contractor shall be incorporated into a formal modification to this contract.

ARTICLE IV - ADMINISTRATION OF CONTRACT BY COMMISSION

The Commission has assigned the responsibility for administering the technical and scientific aspects for the project to the Washington organizational unit set forth below, to be addressed as follows:

Medical Branch
Division of Biology and Medicine

U. S. Atomic Energy Commission
1901 Constitution Avenue, N. W.
Washington 25, D. C.

Responsibility for administering the business aspects of this contract, including contract negotiations, budget, payment, audit, etc., has been assigned by the Commission to:

Office of Research & Medicine
Oak Ridge Operations Office
U. S. Atomic Energy Commission
Post Office Box E
Oak Ridge, Tennessee

The Contractor may, as necessary, communicate directly with the appropriate office, as indicated above. The Contractor shall furnish information copies of communications, memoranda of telephone conversations, or other contacts to Oak Ridge Operations Office on all direct dealings with the Washington Office.

ARTICLE V - REPORTS, RECORDS AND INSPECTION

1. The Commission shall have the right to inspect in such manner and at such times as it deems appropriate all activities of the Contractor arising in the course of the work under this contract.

2. The Contractor shall make progress and other reports in such manner and at such times as specified in Appendix "C" which is attached hereto and hereby made a part of this contract. Progress reports shall include a list of personnel working on the project. Names appearing for the first time should be accompanied by a brief statement of the individual's background, training, and experience.

3. The Commission shall at all times be afforded access to the premises and to all technical records, correspondence, instructions, drawings, and memoranda of record value of the Contractor pertaining to said work.

ARTICLE VI - TITLE TO PROPERTY PURCHASED BY CONTRACTOR

In consideration of the Contractor's contribution to the research project described in Appendix "A" of this contract, title to all materials, tools, machinery, equipment and supplies, acquired from any source including the Government, or manufactured by the Contractor under this contract shall vest in the Contractor, except that title to items of property described in Section 2.c. of Appendix "A" shall vest in the Government.

ARTICLE VII - PURCHASE OF RADIOISOTOPES

The Contractor shall purchase, to the extent available in appropriate form, all radioisotopes, irradiation services and cyclotron time required in the performance of the work hereunder, through the Commission's Isotope Division, Post Office Box E, Oak Ridge, Tennessee.

ARTICLE VIII - GENERAL PROVISIONS

The provisions of Appendix "B", attached hereto, are hereby made a part of this contract.

ARTICLE IX - AUTHORIZATION

This contract is authorized by and has been executed under the Atomic Energy Act of 1946.

ARTICLE X - ALTERATIONS

The following alterations to this contract were made by mutual agreement of the parties prior to its execution:

Sentence 3 of Section 3 of Appendix "B" providing for the security clearance of the Project Leader is hereby deleted.

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

UNITED STATES OF AMERICA

BY: UNITED STATES ATOMIC ENERGY COMMISSION

BY: s/ C. Vanden Bulck
Contracting Officer

DUKE UNIVERSITY
(Contractor)

WITNESSES:

s/ A. S. Brower
Durham, N. C.
(Address)

BY: s/ A. Hollis Edens

TITLE: President

s/ June Johnson
Durham, N. C.
(Address)

ACCEPTANCE BY PROJECT LEADER

I have read the foregoing Contract and the Appendices attached hereto and made a part hereof, and I agree to be bound by the provisions of this document.

s/ R. N. Rundles, M. D.
Project Leader

APPENDIX "A"

Contract No. AT-(40-1)-1021

(Duke University, School of Medicine)

1. PROJECT

a. Scope and Present Status

The bone marrow differs from most organs and tissues in the body in that its main product is blood cells. Comparatively few studies have been made of its metabolism (Warren, J. Biol. Chem. 167:543, 1947; Guzman Barron, et al, J. Biol. Chem. 171:801, 1947, J. Exp. Med. 87:489 and 503, 1948, J. Gen. Physiol. 32:537 and 595, 1949, Bird and Evans, J. Biol. Chem. 178:289, 1949). Most investigators have used rabbit bone marrow. The findings in general indicate that oxygen utilization is 5 times less than that of highly respiring tissues. Glucose, pyruvate, acetate, and amino acids are utilized vigorously. Some evidence suggests that fatty substances may be especially important nutrients.

No attempts appear to have been made to study the metabolism of the human bone marrow. Since cellular morphology varies from species to species it is possible that metabolic activity does also.

The hemopoietic tissues furthermore are among the most vulnerable to the action of some destructive agents that may be employed in warfare and are frequently involved in clinical diseases. The latter include nutritional deficiencies (megaloblastic cell development), chemical or drug damage (aplastic anemia, agranulocytosis, some types of thrombocytopenic purpura and hemolytic anemia), radiation depression or damage, and malignant diseases (leukemia, sub-leukemia, multiple myeloma, etc.)

b. Outline of Work and Plan of Approach

Preliminary studies indicate that bone marrow cells can be aspirated from human subjects in sufficient quantity for in vitro studies using the Warburg apparatus. Adequate methods are available for separating the primitive blood cells from the erythrocytes, and for determining the rate of many metabolic processes/mg. of fat free tissue.

An attempt will be made to determine first the conditions for optimal survival of the marrow cells, or better growth and proliferation, if possible in a chemically defined medium. Then a study will be made of the rate of O_2 consumption, the utilization of glucose, pyruvate, acetate, and amino acids, essential and otherwise in normal and abnormal marrow as influenced by roentgen irradiation, the presence of P 32, urethane and other agents which have a well defined influence on marrow function.

Studies on amino acid uptake will require studies with synthetic radioactive amino acids, as well as amino acid analyses employing filter paper chromatography and microbiological assay.

The hematologic effects of urethane have been investigated in the Duke hematology laboratory for 3 years. The compound suppresses the growth of myeloid elements in myelogenous leukemia and plasma cells in multiple myeloma selectively and beneficially. An understanding of its metabolic effect in bone marrow is an important matter which may be studied advantageously in vitro and in vivo with the aid of the radioactive urethane.

c. Materials, Equipment and Facilities

The facilities of a small but well equipped hematology laboratory, organized and staffed as a consultation service for Duke Hospital patients, will be available for this investigation. An abundance of clinical material is available. An additional laboratory will be available in the Medical Research Building where electrophoretic and physico-chemical studies of proteins are being carried out. Expanded laboratory quarters in Duke Hospital will be available for use when current construction is completed.

Warburg equipment already purchased will be utilized on the project. Additional equipment and supplies as indicated in Section 2 of Appendix "A" purchased with Commission funds will be used in this investigation.

2. BUDGET

a. The Contractor will furnish the following:

(1) Salary of the Project Leader

(2) Laboratory Work Space

(3) Supplies normally provided for and salaries of personnel normally employed in the Hematology and other laboratories and research projects under the supervision and direction of the Project Leader.

(4) Salaries of R. W. Willett and Gordon R. McKinney from January 1, 1951 - June 30, 1951.

b. Cost to Commission

The sum of $12,042 to be paid by the Commission under this contract shall be used by the Contractor in accordance with Article I and the following schedule for the period January 1, 1951 - December 31, 1951:

(1)	Salaries and Wages	
	R. M. Willett (July 1, 1951 - December 31, 1951)	1,750.00
	G. R. McKinney (July 1, 1951 - December 31, 1951)	1,750.00
	1 Technician	2,400.00
(2)	Capital Equipment	
	Chromatography cabinets (3)	750.00
	Coleman Jr. Spectrophotometer	300.00
	Dubnoff Metabolic Shaking Incubator	300.00
	Warburg glassware	250.00
	Analytic balance	600.00
	Refrigerator-freezer	250.00
(3)	Expendable Equipment and Supplies, (Chemicals, reagents, glassware, experimental animals, etc.)	2,500.00
(4)	Communication and Travel	300.00
		$ 11,150.00
(5)	Institutional Overhead @ 8%	892.00
	TOTAL	$ 12,042.00

c. Items of property procured or manufactured by the Contractor under this contract, title to which will vest in the Government. See Article VI.

QUANTITY	DESCRIPTION
None	- -

APPENDIX "B"

GENERAL PROVISIONS

1. Patents

a. Whenever any patentable invention or discovery is made or conceived by the Contractor or its employees in the course of any of the work under this contract, the Contractor shall furnish the Commission with complete information thereon; and the Commission shall have the sole power to determine whether or not and where a patent application shall be filed, and to determine the disposition of the title to and rights under any application or patent that may result. The judgement of the Commission on these matters shall be accepted as final; and the Contractor, for itself and for its employees, agrees that the inventor or inventors will execute all documents and do all things necessary or proper to carry out the judgment of the Commission.

b. No claim for pecuniary award under the provisions of the Atomic Energy Act of 1946 shall be asserted by the Contractor or its employees with respect to any invention or discovery made or conceived in the course of any of the work under this contract.

c. Except as otherwise authorized in writing by the Commission, the Contractor will obtain patent agreements to effectuate the purposes of paragraphs a. and b. of this Article from all persons who perform any part of the work under this contract, except clerical and manual labor personnel who will not have access to technical data.

d. Except as otherwise authorized in writing by the Commission, the Contractor will insert in all subcontracts provisions making paragraphs a., b., and c. of this Article applicable to the subcontractor and its employees.

2. Publications. The Contractor shall have full freedom of publication of the results of the research under this contract and the Contractor is urged to disseminate the results of the work through customary scientific publication channels, except that "restricted data" as defined in the Atomic Energy Act of 1946 shall be governed by the provisions of Paragraph 3 of this Appendix "B". All publications shall include a reference that the results were developed under a Commission sponsored project.

3. Disclosure of Information.

a. It is understood that the work under this contract will not involve restricted data and the Contractor will perform such work as unclassified work. However, if in the course of such work any discoveries are made or any data used or developed that constitute restricted data, the Contractor shall promptly inform the Commission and shall classify and safeguard all discoveries and data in accordance with the requirements of the Commission. ~~It is understood that the person directing research work under this contract shall have been cleared by the Commission for access to restricted data.~~ The Contractor agrees that it will not permit any individual to have access to restricted data until the Federal Bureau of Investigation shall have made an investigation and report to the Commission of the character, associations and loyalty of such individual and the Commission shall have determined that permitting such person to have access to restricted data will not endanger the common defense or security. If doubt exists as to whether any discovery or data developed constitute restricted data, prior to the release of these data and before permitting any individual who has not received clearance from the Commission to have access to such data, the Contractor shall seek guidance from the Commission. Furthermore, the Commission reserves the right to require the classification of work whenever in its opinion restricted data are involved.

b. The continuation by the Contractor of work found to involve restricted data will be subject to mutual agreement of the Commission and the Contractor and shall be covered by a modification of this agreement. The phrase "restricted data" as defined in the Atomic Energy Act of 1946 and employed in this section shall mean "all data concerning the manufacture or utilization of atomic weapons, the production of fissionable material, or the use of fissionable material in the production of power; but shall not include any data which the Commission from time to time determines may be published without adversely affecting the common defense and security".

4. Disputes. Except as otherwise specifically provided in this contract, all disputes which may arise under this contract and which are not disposed of by mutual agreement shall be decided by a representative of the Commission duly authorized to supervise and administer performance under this contract, who shall reduce his decision to writing and cause a copy thereof to be mailed to the Contractor: said decision shall be final and conclusive, subject to the provisions of the sentence next following. Within thirty (30) days from the date of such mailing, the Contractor may appeal in writing to the Commission, whose written decision thereon, or that of its duly authorized representative, representatives, or board, not including the representative mentioned in the preceding sentence, shall be final and conclusive. Pending decision of a dispute hereunder, the Contractor shall proceed with the performance of its undertakings under this contract.

5. Safety and Accident Prevention - Inspections. The Contractor will comply with health and safety regulations of the Commission required for work of this nature, and permit the Commission and its designees to inspect the work conducted under this agreement.

6. Officials not to Benefit. No member of or Delegate to Congress, or Resident Commissioner shall be admitted to any share or part of this contract or to any benefit that may arise therefrom, but this provision shall not be construed to extend to this contract if made with a corporation for its general benefit.

7. Anti-Discrimination. The Contractor, in performing the work required by this contract, shall not discriminate against any employee or applicant for employment because of race, creed, color, or national origin.

8. Convict Labor. The Contractor shall not, in the performance of this contract, employ any person undergoing sentence or imprisonment at hard labor.

9. Termination.

a. The Commission may at any time upon 120 days written notice terminate this contract in whole or in part.

b. In the event of termination pursuant to subsection a., the Contractor will be reimbursed for the cost of the contract work already performed, together with reasonable costs of termination less the amount of all payments theretofore made. If the total payments theretofore made to the Contractor exceed the amount to which it is entitled hereunder, the Contractor shall promptly remit the amount of any such excess to the Government.

10. Eight-Hour Law. No laborer or mechanic doing any part of the work contemplated by this contract in the employ of the Contractor or any subcontractor contracting for any part of said work contemplated, shall be required or permitted to work more than eight (8) hours in any one calendar day upon such work at the site thereof, except upon the condition that compensation is paid to such laborer or mechanic in accordance with the provisions of this Article. The wages of every laborer and mechanic employed by the Contractor or any subcontractor engaged in the performance of this contract shall be computed on a basic day rate of eight (8) hours per day and work in excess of eight (8) hours per day is permitted only upon the condition that every such laborer and mechanic shall be compensated for

all hours worked in excess of eight (8) hours per day at not less than one and one-half (1½) times the basic rate of pay. For each violation of the requirements of this Article a penalty of Five Dollars ($5.00) shall be imposed upon the Contractor for each laborer or mechanic for every calendar day in which such employee is required or permitted to labor more than eight (8) hours upon said work without receiving compensation computed in accordance with this Article, and all penalties thus imposed shall be withheld for the use and benefit of the Government: provided, that this stipulation shall be subject in all respects to the exceptions and provisions of U. S. Code, Title 40, Sections 321, 324, 325, and 329, relating to hours of labor, as modified by the provisions of Section 303 of Public Act No. 781, 76th Congress, approved September 9, 1940, relating to compensation for overtime.

11. Definitions. As used in this contract the terms "United States Atomic Energy Commission", "Atomic Energy Commission" and "Commission" shall mean the United States Atomic Energy Commission or its duly authorized representative or representatives.

12. Fellowships. It is understood by the Contractor that none of the funds supplied by the Commission under this contract shall be used in any way to pay the stipend of any appointment for which commensurate services are not rendered under this contract; nor shall any of the funds be used to confer a fellowship, or to pay any part of the stipend of a fellowship, of any kind.

APPENDIX "C"

DISTRIBUTION AND SCHEDULING OF REPORTS FOR DIRECT AEC RESEARCH CONTRACTS

	Date	Copies and Distribution	Remarks
CONTRACTOR REPORTS			
1. Progress	On one of Following: March 15 June 15 Sept. 15 Dec. 15	(2) Appropriate Washington Division (See note) (2) Oak Ridge Operations Office (See note)	To be received on date listed which is nearest to end of nine month period from effective date of contract and annually thereafter on the same date
2. Summary 200 words on scope and purpose	1. On completion of contract negotiation 2. With progress reports	Prepared as a part of contract negotiations (2) Same as Progress Reports	1. Distribution by Oak Ridge Operations Office with Contract copies 2. Revised Summary to be included as part of Progress Report
3. Manuscripts	As available	(1) Patent Branch, Washington (1) Technical Library, Washington (1) Appropriate Washington Division (1) Oak Ridge Operations Office	
4. Reprints	As available	(2) Appropriate Washington Division (2) Technical Information Branch, Washington (1) Oak Ridge Operations Office	
5. Complete Scientific Report	On Contract Termination	(1) Same (1) as (1) for (1) manuscripts	Manuscripts prepared for publication may in some cases take the place of this report
6. Brief Reports	As desired by investigator	(1) Appropriate Washington Office (1) Oak Ridge Operations Office	Covering significant results or developments.

NOTE: Full Addresses as follows:

Washington Offices:	Oak Ridge Operations Office
Atomic Energy Commission (Add name of Division or Branch) 1901 Constitution Avenue, N. W. Washington, D. C.	Atomic Energy Commission Office of Research and Medicine Post Office Box E Oak Ridge, Tennessee

The appropriate Washington Divisions are:

Division of Biology and Medicine - for contracts in Biology and Medicine.

Division of Research - for contracts in physical research.

AEC, Oak Ridge, Tenn.-1-24-50—2000-A5369

Contract No. AT-(40-1)-1081
(Duke University, School of Medicine)
Modification No. 1

SUPPLEMENTAL AGREEMENT

THIS SUPPLEMENTAL AGREEMENT, entered into this 6th day of February, 1952, effective as of January 1, 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 DUKE UNIVERSITY, SCHOOL OF MEDICINE (hereinafter called the "Contractor");

WITNESSETH THAT:

WHEREAS, the Government and the Contractor entered into Contract No. AT-(40-1)-1081, dated December 14, 1950, for research by the Contractor into the metabolism of the human bone marrow; and

WHEREAS, the parties desire to extend the term of the Contract in order to continue the research project undertaken during the initial period, as described in TITLE II of Appendix "A"; and

WHEREAS, the 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)-1081 be modified in the following particulars, but in no others:

1. 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 second period of performance for the project covered by this Contract will commence on January 1, 1952, and will end on December 31, 1952."

2. Insert the subsection letter "a." between the words "Consideration" and "In" in Section 1 of ARTICLE III, and add the following new subsection b to Section 1 of ARTICLE III:

CERTIFIED A TRUE COPY
BY Jenks Nicholson

"b. In consideration of the performance of the work described in TITLE II of Appendix 'A', the Government will pay to the Contractor the sum of Eight Thousand Five Hundred Forty-Four Dollars ($8,544.00) for the second period of performance. It is expressly agreed and understood that the sum of One Thousand Five Hundred Dollars ($1,500.00) which has been previously paid to the Contractor by the Government but which remained unexpended at the end of the initial period of performance will be applied to the costs of the second period."

3. Insert the term "TITLE I" under the heading of Appendix "A" and add the following new TITLE II to Appendix "A":

"TITLE II

"January 1, 1952 - December 31, 1952

"1. PROGRAM

"A. PROJECT

"The general program will continue to be a study of the metabolism of the human bone marrow as described in TITLE 1. Methods for measuring lactic acid production, aerobic and anaerobic glucose utilization will be standardized. Filter paper chromatography methods for amino acid analysis will be set up.

"2. BUDGET - Second Period: January 1, 1952 - December 31, 1952

"A. The Contractor will furnish as its contribution to the project:

(1) Salaries of staff members, including the Project Leader, engaged in the work, except as provided in b (1) below.

(2) Use of laboratory work space and equipment and facilities on hand.

(3) Clerical and administrative expenses and other general and administrative type costs, including overhead, except as provided in b below.

"B. The Government will pay to the Contractor the sum of Eight Thousand Five Hundred Forty-Four Dollars ($8,544.00) which, together with the amount of One Thousand Five Hundred Dollars ($1,500.00) remaining unexpended from the Government's payments during the initial period of performance, will cover the Contractor's other expenses, estimated as follows, in the performance of the Contract during the second period:

(1)	Salaries	
	Dr. Roy Shipke, Professional Assistant	$ 5,600.00
	Technicians	4,000.00
(2)	Capital Equipment	
	Laboratory benches, cabinets, Warburg vessels and manometers, blood centrifuge equipment, etc.	500.00
(3)	Expendable Equipment and Supplies	
	Chemicals, reagents, glassware, etc.	1,000.00
(4)	Communication and Travel	200.00
		$ 9,300.00
(5)	Overhead @ 8%	744.00
		$10,044.00
	Less Unexpended Funds	1,500.00
	TOTAL	$ 8,544.00

"C. Items of property procured or manufactured by the Contractor under this Contract, 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 COMMIS

BY: s/ C. Vanden Bulck

TITLE: Assistant Manager, ORO

WITNESSES:

s/ L. W. Moore

Durham, N. C.
(Address)

DUKE UNIVERSITY, SCHOOL OF MEDICINE

BY: s/ A. Hollis Edens

TITLE: President

s/ A. S. Brower

Durham, N. C.
(Address)

ACCEPTANCE BY PROJECT LEADER:

I have read the foregoing Supplemental Agreement and I agree to be bound by the terms of this document.

s/ Wayne Rundles, M.D.
Project Leader

Contract No. AT-(40-1)-1081
Duke University, School of Medicine
Modification No. 2

SUPPLEMENTAL AGREEMENT

THIS SUPPLEMENTAL AGREEMENT, entered into this 31st day of January, 1953, effective as of January 1, 1953, by and between the UNITED STATES OF AMERICA (hereinafter referred to as the "Government"), represented herein by the UNITED STATES ATOMIC ENERGY COMMISSION (hereinafter referred to as the "Commission"), and DUKE UNIVERSITY, SCHOOL OF MEDICINE (hereinafter referred to as the "Contractor");

WITNESSETH THAT:

WHEREAS, the Government and the Contractor entered into Contract No. AT-(40-1)-1081, dated December 14, 1950, for a study by the Contractor of the metabolism of the human bone marrow, which contract was subsequently extended by Modification No. 1 thereto, dated February 6, 1952; and

WHEREAS, the parties desire to further extend the term of the contract in order to continue the research work; 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)-1081 is modified in the following respects, but in no others:

1. In ARTICLE II - TERM OF CONTRACT, add the following new section 3:

"3. The third period of performance for the project covered by this contract will commence on January 1, 1953, and will end on December 31, 1953."

2. In ARTICLE III, section 1, Consideration, add the following new subsection c:

"c: In consideration of the Contractor's performance of the research activities described in Table III to Appendix 'A', the Government shall pay to the Contractor the sum of Ten Thousand Dollars ($10,000.00) for the third period of performance."

3. In ARTICLE V - REPORTS, RECORDS AND INSPECTION, add the following new section 4:

"4. Examination of Records

"a. The Contractor agrees that the Comptroller General of the United States or any of his duly authorized representatives shall, until the expiration of three years after final payment under this contract, have access to and the right to examine any directly pertinent books, documents, papers and records of the Contractor involving transactions related to this contract.

"b. The Contractor further agrees to include in all his subcontracts hereunder a provision to the effect that the subcontractor agrees that the Comptroller General of the United States or any of his duly authorized representatives shall, until the expiration of three years after final payment under this contract with the Government, have access to and the right to examine any directly pertinent books, documents, papers, and records of such subcontractor involving transactions related to the subcontract. The term 'subcontract' as used herein does not include (i) purchase orders not exceeding $500, or (ii) contracts or purchase orders for public utility services at rates established for uniform applicability to the general public.

"c. Nothing in this contract shall be deemed to preclude an audit by the General Accounting Office of any transaction under this contract."

4. In Appendix "A", add the following Title III.

"Title III

"January 1, 1953 - December 31, 1953

"1. PROJECT

"a. Scope and Plan of Approach

During this period studies will be continued on the metabolism of mature and immature stages of human leukocytes obtained from normal and diseased patients. Aspects of the biochemistry

of the white blood corpuscles will be studied in relation to disease and the normal blood picture. Chemical substances which are used in clinical alleviation of abnormal bone marrow function will be studied with respect to their action upon leukocytes. Bone marrow tissue and isolated cells will be examined with respect to their metabolic picture. Studies will be continued on the metabolism of specific chemical compounds as energy sources.

"2. BUDGET - Third Period - January 1, 1953 - December 31, 1953

"a. The Contractor shall furnish as its contribution to the project:

(1) Salaries of staff members, including the Project Leader, and other personnel engaged in the work in excess of the Government's payments under b. (1) below.

(2) Use of laboratory work space, and equipment, materials and facilities needed for the project in excess of the Government's contribution under b. below.

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

"b. The Government's payment as provided in subsection 1 c. of ARTICLE III will cover the Contractor's other expenses, estimated as follows, in the performance of the contract during the third period:

(1) Salaries and Wages

Professional Assistant (Dr. T. Arends), January - March, 1953	$ 825.00
Technical Assistant (Mrs. E. Sullenberger), Full-time	3400.00
Technical Assistance, Part-time	2759.00

(2)	Expendable Equipment and Supplies	$2000.00
(3)	Communications and Travel	275.00
(4)	Overhead (8%)	741.00
	TOTAL	$10,000.00

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

5. In Appendix "B", GENERAL PROVISIONS, section 3, Disclosure of Information, subsection a, delete the third sentence thereof, and substitute therefor the following:

"Except as the Commission may authorize, in accordance with the Atomic Energy Act of 1946, as amended, the Contractor shall not permit any individual to have access to restricted data until the designated investigating agency shall have made an investigation and report to the Commission on the character, associations and loyalty of such individual and the Commission shall have determined that permitting such person to have access to restricted data will not endanger the common defense or security. As used in this paragraph the term 'designated investigating agency' means the United States Civil Service Commission or the Federal Bureau of Investigation or both, as determined pursuant to the provisions of the Atomic Energy Act of 1946, as amended by the Act of April 5, 1952, Public Law 298, 82nd Congress, 66 Stat. 43."

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

UNITED STATES OF AMERICA

BY: U. S. ATOMIC ENERGY COMMISSION

BY: [signature]
KENNETH [illegible]

TITLE: DIRECTOR OF RESEARCH AND MEDICINE

DUKE UNIVERSITY, SCHOOL OF MEDICINE

BY: [signature]
A. Hollis Edens

TITLE: President

WITNESSES:

[signature]
A. S. Brower
Durham, North Carolina
(Address)

[signature]
Patricia Silver
Durham, North Carolina
(Address)

Acceptance By Project Leader

I have read the foregoing Supplemental Agreement and agree to be bound by its provisions.

[signature], M.D.
Project Leader

L. D. MacKay, Director
Finance Division

November 22, 1954

Herman M. Roth, Director
Research and Medicine Division

CONTRACT NO. AT-(40-1)-1081 - DUKE UNIVERSITY SCHOOL OF MEDICINE

SYMBOL: OR:JER

This is to advise you that the work under Contract No. AT-(40-1)-1081 with the Duke University School of Medicine has been completed and the final report has been submitted.

The contract should therefore be closed out.

ORIGINAL SIGNED BY
HERMAN M. ROTH

Herman M. Roth

OK CC: J. R. Moore
F. E. McPherson

Roumsaville:lr

W-3498L

OFFICE ▶	OR	OR	OR	NOR	GKK
SURNAME ▶	Roumsaville	Carley	Haughton	KM	Calvert
DATE ▶	11-19-54	11/19/54	11/19	11/19	11-19-54

Form AEC-318 (Rev. 9-53) U.S. GOVERNMENT PRINTING OFFICE 16—62761-3

1110753

[illegible] January [illegible], 1954

[illegible] and Medicine Division, [illegible]

C. S. Shoup, Chief, Biology Branch, Research and Medicine Division, Oak Ridge

[illegible] CONTRACT W. AT-(40-1)-1081

[illegible]

We wrote Dr. Wayne Rundles on October 22, 1953, and again on January 7, 1954, regarding his submission of a final report on the subject contract.

We now have a letter from Dr. Rundles under date of January 21, 1954, stating that he will submit his final report in the form of reprints of publications resulting from work under the contract, transmitting the documents presently available in accordance with Appendix [illegible] of the contract, and mailing others to the same listing when the final papers are published and the reprints become available.

[illegible]:ef

TO-270

OFFICE ▶	ORB	ORB				
SURN ▶	CShoup	Smiley				
DATE ▶	1/26/54	1/27/54				

1110154

Duke University
DURHAM
NORTH CAROLINA

School of Medicine
Department of Medicine
Reply to Undersigned

January 21, 1954

Re: OR:JER

Dr. C. S. Shoup
Chief, Biology Branch
Research and Medicine Division
U.S. Atomic Energy Commission
Oak Ridge, Tennessee

Dear Dr. Shoup:

Thanks very much for your letter of January 7, 1954, regarding the final report on our Research Contract No. AT-(40-1)-1081. After your letter of October 22, 1953, had arrived, I had planned to make our final report in the form of reprints of publications as listed in our Progress Report dated October 1, 1953. We are just now receiving some of these reprints. One paper will appear in April, and one is still in the process of being written. I take it that you would like to have the report as final as possible and as soon as possible. We shall gather together all the reprints presently available and relay them to you within the next few days, and distribute others in accordance with Appendix C of our contract. When the last papers are published, we will then relay on reprints to complete the project report.

I hope this arrangement will be satisfactory with all concerned.

Very sincerely yours,

Wayne Rundles

Wayne Rundles, M. D.

WR:mc

cc: Chief, Medical Branch
Division of Biology and Medicine
U. S. Atomic Energy Commission
Washington, 25, D. C.

JAN 2 1954

D-41

1110755

In Reply
Refer To: [illegible]

Oak Ridge, Tennessee
January 7, 1954

Dr. R. W. Rundles
Duke University
School of Medicine
Durham, North Carolina

Subject: CONTRACT NO. AT-(40-1)-1081

Dear Dr. Rundles:

Reference is made to our letter of October 22, 1953, regarding the submission of the final report under the subject contract.

We would appreciate your advising us on the status of the report and the expected date of completion. The report should be distributed in accordance with Appendix C of the subject contract.

Your cooperation in this matter will be appreciated.

Very truly yours,

C. C. Shown
Chief, Biology Branch
Research and Medicine Division

Rounsaville:mah

W-43

CONTRACTS
Duke-1081

OFFICE	OR	OR	W43	OR		
SURNAME	Rounsaville	Corey	Cohoon	Shown		
DATE	1-5-54	1-6-54	1-6-54	1/7/54		

1110756

In Reply
Refer To: [illegible]

Oak Ridge, Tennessee
October 2[illegible], 1953

Dr. R. W. Rundles
Duke University
School of Medicine
Durham, North Carolina

Subject: CONTRACT NO. AT-(40-1)-1081.

Dear Dr. Rundles:

This will acknowledge the copy of your letter to Dr. J. F. Haggerty, in which you indicated that you do not anticipate continuing work on the contract subject.

We regret that you find it necessary to drop this interesting work. It is to be hoped that your group can continue it sometime in the future.

The final report prepared on your contract work may, if you so desire, be in the form of publications or manuscripts describing the results of your project. Directions for distribution will be found in Appendix C of your contract. We shall look forward to receiving these as they appear in print.

Very truly yours,

[illegible] Shoup
Chief, Biology Branch
Research and Medicine Division

Geckler:ec

X-3261

CONTRACTS — Number 1081

OFFICE ▶	ORA	OR	DOR			
SURNAME ▶	Shoup	Cooley	Roth			
DATE ▶	10/22/53	10/26/53	10/27/53			

Form AEC-318 U. S. GOVERNMENT PRINTING OFFICE 16—63761-2

1110757

October 1, 1953

Mr. James F. Haggerty
Medical Branch
Division of Biology and Medicine
U. S. Atomic Energy Commission
Washington, D. C.

Dear Dr. Haggerty:

Enclosed is a copy of our Progress Report on our research project "Metabolism of Human Bone Marrow," subsidized by the Atomic Energy Commission. We are enclosing, also, 6 reprints of publication #1.

This work has been extremely intriguing to us, and I am sure that many laboratories should continue work along these lines, in spite of any difficulties that have to be overcome. As far as I can see now, however, we shall have to suspend work in this field at the end of this year. Dr. Gordon R. McKinney, who has been a Fellow in our Department for the past 2½ years, has been appointed to a position in Pharmacology at the University of West Virginia, and will no longer be with us. He will probably continue with similar work there.

If an adequately trained individual would like to come here and continue the work, we should be most interested in encouraging him to do so.

Very sincerely yours,

Wayne Rundles

Wayne Rundles, M. D.

WR:ms

cc: Dr. C. S. Shoup

Enclosures

PROGRESS REPORT

on

Research Project Sponsored by the Atomic Energy Commission
"Metabolism of Human Bone Marrow"
R. W. Rundles, M. D., Duke University School of Medicine
Durham, N. C., October 1, 1953

During the past year the bulk of our work in which Dr. Gordon McKinney has been most active has concerned metabolic studies of mature, circulating leukocytes, and immature cells from patients with leukemia. The general methods have been outlined in previous Progress Reports and in a publication (1). The findings outlined have been extended to include immature cells obtained from the circulating blood of patients with leukemia. In contrast to most other normal tissues, normal human leukocytes possess a high rate of aerobic lactate production. Exposure of these cells to nitrogen does not appreciably increase this rate; i.e., normal leukocytes do not exhibit a Pasteur effect. The outstanding metabolic difference between mature and immature (leukemic) human granulocytes is the ability of the former to make lactic acid in the presence of oxygen. This metabolic difference may be a reflection of the aging process or it may provide a clue to the fundamental distinction between normal and leukemic leukocytes. Studies on the metabolic pathway of aerobic glycolysis have continued, in an attempt to account for the absence of the Pasteur effect in normal leukocytes and to compare these cells with those obtained from normal bone marrow and from patients with leukemia.

Aerobic Glycolysis of Normal Leukocytes:

Many of the experiments of the past year have attempted to provide an answer for the question--"does the lactic acid formed aerobically by normal human leukocytes arise by way of the Meyerhof-Embden scheme of glycolysis?" Certain data as outlined below provide evidence for an alternate pathway of lactate production.

(a) NaF, a specific inhibitor of enolase in the phosphorylating system of glycolysis, inhibited leukocytes glycolysis only in high concentrations (above final concentration of 0.01M). Low concentrations stimulated lactate formation.

(b) l-Glyceraldehyde normally condenses with dihydroxyacetone phosphate to form sorbose-1-phosphate which in turn inhibits hexokinase. dl-Glyceraldehyde did inhibit leukocyte glycolysis, but instead caused it to rise.

(c) Pyruvate, the immediate source of lactate in the Meyerhof-Embden scheme, only slightly elevated lactate production by broken cells. Whereas, in the same preparation, fructose-1,6-diphosphate gave rise to more lactate than did glucose.

(d) Oxamic acid, a specific inhibitor of lactic dehydrogenase, (Federation Proceedings 12:213, 1953) depressed lactate formation only slightly.

(e) Coenzyme I (diphosphopyridine nucleotide) incubated with leukocytes, markedly depressed their lactate production.

(f) While determining the effect of a nitrogen mustard on leukocyte respiration and glycolysis, it was noted that added glutathione not only protected against inhibition by methyl-bis-(beta-chloroethyl)-amine, but also increased oxygen utilization and decreased lactate appearance in control vessels.

On the basis of these observations a source of lactate outside the Meyerhof-Embden scheme was sought. Methyl glyoxal was considered as a possible precursor of the lactate produced by leukocytes, and subsequent experiments showed that human leukocytes contain a very active glyoxalase system. Cell per cell, leukocytes contain over 700 times more glyoxalase activity than erythrocytes (4). The enzyme activity did not increase when leukocytes were incubated, anaerobically. No final statement can be made at this time as to the significance of glyoxalase in leukocytes. If a significant amount of lactate is derived from it, it might explain the absence of the Pasteur reaction in mature leukocytes since glyoxalase activity was independent of oxygen tension. The lack of inhibition of glyoxalase activity by oxamic acid supports the possible importance of this enzyme in lactate production by white blood cells.

At this time no pathway is known for the synthesis of methyl glyoxal by any tissue. Manometric data have revealed that the total acid production (measured as carbon dioxide) of normal leukocytes from equimolar amounts of glucose and methyl glyoxal, present together, was essentially equal to the sum of either alone.

This observation indicates either that two independent pathways existed for the formation of lactate or that glucose is converted to methyl glyoxal. When glyoxalase activity was depressed by the addition of an excess of glutathione (coenzyme of glyoxalase) allowing methyl glyoxal to accumulate the results pointed to a net conversion of glucose to methyl glyoxal. In these experiments methyl glyoxal was measured colorimetrically, both by the reduction of arsenophosphotungstic acid by methyl glyoxal in the presence of KCN and $NaCO_3$ and by formation of the 2,4-dinitrophenylhydrazone. More definitive experiments are in progress to ascertain whether or not methyl glyoxal is on the direct pathway of carbohydrate breakdown to lactate in human leukocytes, and whether this system might account for the high rate of aerobic glycolysis and the absence of the Pasteur reaction in these cells.

Aerobic Glycolysis of Leukemia Leukocytes:

Of interest in reference to the presence of glyoxalase in leukocytes is the observation that a normal leukocyte contains approximately 3 times more glutathione than does an erythrocyte. Leukemic leukocytes contain an even greater amount with erythrocyte values remaining constant (8).

In contrast to normal leukocytes, leukemic cells are relatively unable to make lactate aerobically, but they do exhibit a Pasteur reaction. Additional studies have shown that these immature cells contain glyoxalase, since added methyl glyoxal

increased CO_2 production. Therefore, the lower capacity of leukemic leukocytes to make lactate may be due to some metabolic aberration where they cannot make the precursor, methyl glyoxal. Experiments are planned to study the capacity of leukemic cells to synthesize methyl glyoxal.

Effects of Glucose and Fructose on Aerobic Glycolysis of Normal Leukocytes:

Related studies on carbohydrate metabolism in normal leukocytes have indicated that they possess two mechanisms which provide for the entry of glucose and fructose into the cell, and that they appear to utilize glucose preferentially (2). However, leukocytes from patients with diabetes mellitus produced essentially equal amounts of lactate from either glucose or from fructose. The addition of insulin to the reaction mixture enabled diabetic leukocytes to make approximately a normal amount of lactate from glucose (5,6).

Human Bone Marrow Studies:

The interesting leads described above have directed the work away from bone marrow cells in recent months.

The use of high density media (e.g., plasma with increased protein and/or lactose concentration) for the separation of bone marrow leukocytes from accompanying erythrocytes has been explored. However, a high degree of morphologic damage has been constantly produced by these methods, and they have been abandoned. Control experiments have shown that exposure of mature leukocytes to

ethylenediamine tetraacetate (EDTA) in a concentration of 1-2 mg. per ml. did not alter their respiration or lactic acid production. Therefore, this agent can be used as an anticoagulant for metabolic studies. Preliminary experiments have shown that it is practical to suspend aspirated marrow particles in plasma containing EDTA and 5% dextran of intrinsic viscosity 0.46. Erythrocytes settle rapidly with gentle centrifugation and adequate concentrations of leukocytes suitable for study have been obtained. Preliminary observations have shown that their respiration is constant over a period of 4 hours.

SUMMARY: Normal human leukocytes have a uniquely high rate of aerobic glycolysis. Mature cells differ from immature leukemic leukocytes in that the former cells produce lactic acid in the presence of oxygen. A pathway of aerobic glycolysis outside the Meyerhof-Embden scheme has been sought, and evidence indicates that methyl glyoxal may be a precursor of lactate produced by leukocytes.

Leukocytes can utilize fructose but may preferentially consume glucose.

A method obtaining leukocytes from human bone marrow for metabolic studies has been developed.

Publications:

1. McKinney, G.R., Martin, S.P., Rundles, R.W., and Green, R.: Respiratory and glycolytic activities of human leukocytes *in vitro*. J. Applied Physiol. 8:335, 1953.

2. McKinney, G.R., Martin, S.P., and Green, R.: Effects of glucose and fructose on aerobic glycolysis of human leukocytes *in vitro*. Am. J. Med. 14:755, 1953. (Abstract)

3. Martin, S.P., Chaudhuri, S.N., Green, R., and McKinney, G.R.: Effect of bacterial products and hormones on human leukocytes. Clin. Res. Proc. 1:47, 1953. (Abstract)

4. McKinney, G.R.: Glyoxalase activity of human leukocytes. Arch. Biochem. In press.

5. Martin, S.P., McKinney, G.R., and Green, R.: Effect of glucose, fructose, and insulin on the leukocytes of diabetics. J. Clin. Invest. 32:586, 1953. (Abstract)

6. Martin, S.P., McKinney, G.R., Green, R., and Becker, C.: The influence of glucose, fructose, and insulin on the metabolism of leukocytes of healthy and diabetic subjects. J. Clin. Invest. In press. (Nov., 1953)

7. Martin, S.P., Chaudhuri, S.N., Green, R., and McKinney, G.R.: The effect of adrenal steroids on aerobic lactic acid formation in human leukocytes. J. Clin. Invest. In manuscript.

8. Green, R., Martin, S.P., and McKinney, G.R.: The glutathione content of human leukocytes in health and leukemia. In manuscript.

Personnel: Gordon R. McKinney, Ph.D., has worked full time on this project since July 1, 1951, under sponsorship of an American Cancer Society Fellowship. Dr. Julie Arends helped with blood processing and marrow studies until leaving to return to Caracas, Venzuela, on April 1, 1953. Dr. Robert Willett assisted part time on investigating marrow separation techniques January-May, 1953. He is supported by a Damon Runyon Fellowship.

Technical help in hematology was provided by Mrs. Elaine Sullenberger from January-July, 1963, and by Miss Lee Willard from June, 1963, to date. Miss Alicia Van Billiard has worked as a chemical technician, part time February-June, 1963, and full time since then. Catherine Carter has helped with unskilled work, cleaning glassware, etc., part time since June, 1963.

Expenditures: (January 1 - September 30, 1963)

Salaries:	Dr. Julio Arends	$ 825.00
	Mrs. Elaine Sullenberger (Jan.-June)	1,500.00
	Miss Lee Willard	615.00
	Miss Alicia Van Billiard	878.00
	Miss Catherine Carter	280.00
Social Security:		
Capitol Equipment		45.00
Expendable Supplies		817.81
Communications and Travel		103.23
University Overhead		405.12
		$5,469.16

We estimate that there will be a small balance remaining in this grant at the end of this year.

Plans for the Remainder of the Year: Some aspects of the work as outlined above can be carried through to completion and prepared for publication. Additional observations on the metabolism of aspirated marrow tissue will be made.

Wayne Rundles

Wayne Rundles, M. D.

WR:mc

1110766

SUBJECT: Final report on Contract AT(40-1)-1081

D-416

FILE DATE: 1/21/54

TO: Shoup

FROM: Rundles

SUMMARY:

BROUGHT FORWARD AND FILED WITH—

SUBJECT: Final report, Duke University Contract AT(40-1)-1081

W-270
Contracts
Duke 1081

FILE DATE: 1/26/54

TO: Faggerty

FROM: Shoup

U. S. ATOMIC ENERGY COMMISSION

CONTINUITY REFERENCE FORM

1110767

SUBJECT: Contract No. AT(40-1)-1081

N-43

FILE DATE: 1/7/54

TO: Rundles

FROM: Shoup

SUMMARY:

BROUGHT FORWARD AND FILED WITH—

SUBJECT: Final Report, Duke University Contract AT(40-1)-1081

W-270
Contracts
Duke 1081

FILE DATE: 1/26/54

TO: Haggerty

FROM: Shoup

U. S. ATOMIC ENERGY COMMISSION

CONTINUITY REFERENCE FORM

1110768

SUBJECT: Contract AT(40-1)-1081

A-3261

FILE DATE: 10/22/53

TO: Rundles

FROM: Shoup

SUMMARY:

BROUGHT FORWARD AND FILED WITH—

SUBJECT: Final Report, Duke University Contract AT(40-1)-1081

W-270
Contracts
Duke 1081

FILE DATE: 1/26/54

TO: Haggerty

FROM: Shoup

U. S. ATOMIC ENERGY COMMISSION

CONTINUITY REFERENCE FORM

1110769

DATE: 10-13-53

INDEX: Contr Duke 1061

TO: DRM

FROM: McCauley/Duke

SUMMARY: Voucher Submission C-5985

FILED: Contr Duke 289

INDEXER:

REMARKS:

U. S. ATOMIC ENERGY COMMISSION

CORRESPONDENCE REFERENCE FORM

1110770

John C. Bugher, Director, Division of Biology and Medicine, Washington

October 12, 1953

Kenneth Kasschau, Director, Research and Medicine Division

RENEWAL OF CONTRACTS

SYMBO: OR:JER

In reviewing our records we find that the following listed contract will expire during the month of October:

Contract Number	Institution	Project Leader	Expiration Date
1077	University of Arkansas	Dr. J. M. Siegal	10-31-53

We received the progress report and proposal for renewal on September 28.

The following listed contracts will expire during the month of December:

Contract Number	Institution	Project Leader	Expiration Date
1081	Duke University	Dr. R. W. Rundles	12-31-53
1345	Emory University	Dr. A. V. Beatty	12-31-53
1569	Emory University	Dr. H. D. Bruner	12-31-53
1542	University of South Carolina	Dr. M. H. Knisely	12-31-53
1335	Southern Research Institute	Dr. H. E. Skipper	12-31-53

We have received a letter from Dr. Rundles indicating that he will not request renewal of his contract. Letters of notification that the proposals are due were forwarded to the Project Leaders.

We would appreciate your advising us as soon as possible on the status of these contracts so that we may proceed with any contract action that may be required. We are particularly interested in receiving information on the contract due to expire during the month of October.

CONTRACTS Duke 108

Kenneth Kasschau

Rounsaville/mra

OK Y Emory - 1345
OK X " 1569
OK Y U of SC - 1542
OK X SR - 1335

X-3195

OFFICE ▶	OR	OR	ORB	OOR	OOR
SURNAME ▶	Rounsaville	Carley	CSShoup	Kelly	Kasschau
DATE ▶	10-12-53	10-12-53	10/14/53	10/14/53	10/15/53

Form AEC-318 U. S. GOVERNMENT PRINTING OFFICE 16—65701-2

1110771

OR FORM 368 (JULY 2, 1948)

SUBJECT: Contract No. AT-(40-1)-1081

C-5785 Contracts Duke 1081

FILE DATE: October 1, 1953

TO: Haggerty

FROM: Rundles

SUMMARY:

BROUGHT FORWARD AND FILED WITH—

SUBJECT: Contract Number AT-(40-1)-1081

Y-3261 Contracts Duke 1081

FILE DATE: October 22, 1953

TO: Rundles

FROM: Shoup

U. S. ATOMIC ENERGY COMMISSION

CONTINUITY REFERENCE FORM

1110772

DATE: Sept. 25, 1953

INDEX: Contracts Duke 1081 C-5724

TO: Office of Research and Medicine

FROM: McCauley, Duke Univ.

SUMMARY: Voucher Submission - Contract AT-(40-1)-1031, etc.

FILED: Contracts Duke 1031

INDEXER:

REMARKS:

U. S. ATOMIC ENERGY COMMISSION

CORRESPONDENCE REFERENCE FORM

1110773

J. W. Gald, Jr., Assistant General Counsel — January 5, 1953

R. G. Humphries, Assistant Director, Contract Division

REQUEST FOR PREPARATION OF RENEWAL CONTRACT FOR ONE YEAR WITH DUKE UNIVERSITY, SCHOOL OF MEDICINE, DURHAM, NORTH CAROLINA CONTRACT NO. AT-(40-1)-1081, DR. WAYNE RUNDLES, PROJECT LEADER

SYMBOL: AD:AMB

Forwarded is an approved proposal for renewal of subject contract for one year beginning January 1, 1953. The approval is covered by Procurement Directive No. PD-53-109, dated December 15, 1952, in the amount of $10,000.00.

It is requested that you prepare an appropriate modification to extend this contract for another year and provide for the payment of $10,000.00 in accordance with the enclosed revised budget.

Dr. C. S. Shoup will act as Technical Advisor on this contract.

R. G. Humphries

1. Memo fm Kaschau, 12/30/52.
2. Memo fm Washington, 12/15/52.
3. Ltr fm Dr. Rundles, 12/24/52.
4. Proposal.
5. Resume.

CC: C. S. Shoup
L. D. MacKay
Ed Ziegler
J. Nicholson

Brown:srb

CONTRACTS
AT-1081
C-71

1110774

Duke University
DURHAM
NORTH CAROLINA

School of Medicine
Department of Medicine
Reply to Undersigned

December 31, 1952

Dr. Sam Shoup
Atomic Energy Commission
Office of Research and Medicine
Post Office Box E
Oak Ridge, Tennessee

Dear Dr. Shoup:

It occurred to me after talking with you yesterday afternoon about our research budget (Contract No. AT - (40-1) - 1081) for the coming year that some phases of our work might be obscure to you. Almost every one of our Laboratory personnel contribute in one way or another toward this project, although only a few are supported by it.

As mentioned, Dr. Tulio Arends has been working as a professional assistant on this project, with his major assignment being the study of serum proteins. Media for our metabolic studies must contain protein, 2% or over, probably, and a high density medium must be developed for the differential separation of marrow elements. These protein solutions should be metabolically inert, with unstable proteins removed, and as well defined chemically as possible. We have used Conn's zinc-glycine method to make SPPS, which seems so far to be a suitable type of protein to use.

For these studies, Dr. Arends has become experienced in Tiselius electrophoretic methods, and has recently set up the more practical paper electrophoresis technique for our laboratory. To concentrate protein solutions, we have developed an ultra-filtration procedure by dialyzing in cellophane against buffered 20% PVP. All of these procedures are necessary for us to control the protein content and concentration in our metabolic medium.

We shall be sorry to lose Dr. Arends when he must return to Caracas this spring. We hope to carry on effectively, however, with the methods he has developed, with technical and other help.

On July 1, 1953, we shall have a new staff member working here, Dr. Wallace Jensen, now at Salt Lake City. Dr. Jensen has been using radio-active isotopes in his research work there. We hope that his talents and experience can be used to assist us in some aspects of the study as outlined.

The $2,000 allotted for expendable supplies this year is greater than for last year, when we found that we were about $700 short. We find that we paid out nearly $900 for blood from donors, 300 cc. for $15, each, to provide fresh white blood cells to study. A blood centrifuge may become available here soon which will enable

Duke University
DURHAM
NORTH CAROLINA

School of Medicine
Department of Medicine
Reply to Undersigned

us to obtain leukocytes from blood bank donors less expensively.

We are in the midst of remodeling our laboratory at this time, which poses another problem. The new quarters will be complete in about three months or so, we hope, and all of this work be carried out more effectively. Perhaps, it would be possible for you to visit us about this time and become acquainted with our activities at firsthand.

With many thanks for your interest, I am

Very sincerely yours,

Wayne Rundles

Wayne Rundles, M. D.

WR:mc

cc: Dr. James F. Haggerty
Medical Branch
Division of Biology and Medicine
U. S. Atomic Energy Commission
Washington 25, D. C.

John Moore, Director, Contract Division

December 30, 1952

Kenneth Kassehau, Director, Research and Medicine Division

REQUEST FOR PREPARATION OF A RENEWAL CONTRACT FOR ONE YEAR WITH DUKE UNIVERSITY, SCHOOL OF MEDICINE, DURHAM, N. C. CONTRACT NO. AT-(40-1)-1081, DR. WAYNE RUNDLES, PROJECT LEADER.

SYMBOL: ORB:CSS

We are in receipt of approval by the Division of Biology and Medicine for renewal for one year of the subject contract, and Procurement Directive No. RM-53-109 in the amount of $10,000. The budget submitted called for the sum of $12,420. On December 23, 1952, Dr. C. S. Shoup asked Dr. Rundles to submit a new revised budget in line with Washington recommendations.

The revised budget has now been received from Dr. Rundles under date of December 24, and is enclosed herewith. In the revised budget, Dr. T. Arends is to be on the project only until March, 1953, since soon after that time he will return to Venezuela. From March onward the main body of the technical work will be carried by additional personnel to be supplied who are trained in clinical biochemistry. It will be noted that the items under capital equipment in the original budget in the amount of $1000 are removed from the revised budget.

Dr. Rundles reports no remaining unobligated balance. We would appreciate the assistance of your office in preparation of this renewal contract in the amount of $10,000 including 8% overhead.

Dr. C. S. Shoup will serve as Technical Advisor for this Division. A summary of the research program is enclosed.

ORIGINAL SIGNED BY:
HERMAN M. ROTH

Kenneth Kassehau

5 Encls.:
1. Memo frm Nash.
2. Pro. Dir.
3. Ltr dtd 12/24/52 frm Dr. Rundles.
4. Proposal.
5. Resume.

K-18

CONTRACTS

Duke-1081

OFFICE ▶	ORB			
SURNAME ▶	Shoup:ss	Copley Roth for KR		
DATE ▶	12/30/52	12/31/52 12/31/52		

Form AEC-318

U. S. GOVERNMENT PRINTING OFFICE 16—62761-2

1110777

Duke University
DURHAM
NORTH CAROLINA

School of Medicine
Department of Medicine
Reply to Undersigned

December 24, 1952

Dr. Sam Shoup
U. S. Atomic Energy Commission
Office of Research and Medicine
Post Office Box E
Oak Ridge, Tennessee

Dear Dr. Shoup:

I appreciate very much your telephone call yesterday, regarding the budget for our AEC research project, "Study of the Metabolism of the Human Bone Marrow," for the calendar year, 1953. I have gone over our research program again in the light of the revisions suggested by your Committee. Some items of durable nature may be required during the course of the year, but we shall likely be able to obtain them from other sources. There will be some changes in our technical personnel during the course of the year.

The funds allotted for our work during the year, 1952, have been expended completely.

Enclosed is a revision of the budget for the coming year, which I believe will allow us to operate with close to maximum efficiency. We appreciate very much the support and interest of your Commission in our work here.

Very sincerely yours,

Wayne Rundles

Wayne Rundles, M. D.

WR:mc
cc: Dr. James F. Haggerty
Enclosure

U. S. Atomic Energy Commission

Research Contract No. AT - (40-1) - 1081

Budget, January 1, 1953 - December 30, 1953

Professional assistance (Dr. T. Arends, January-March, 1953)	$ 825.00
Technical assistance (Mrs. E. Sullenberger)	3400.00
Part-time technical assistance	2759.00
Expendable apparatus and supplies, chemicals, reagents, glassware, photographic material, electrodes, filters, blood from donors, blood packs, etc.	2000.00
Communications and travel	275.00
	$9259.00
Unexpended, 1952	0.00
	$9259.00
University Overhead, 8%	740.72
	$9999.72

Wayne Rundles

Wayne Rundles, M. D.

WR:mc

1110779

December 24, 1952

Dr. James F. Haggerty
Medical Branch
Division of Biology and Medicine
United States Atomic Energy Commission
Washington 25, D. C.

Dear Dr. Haggerty:

We were very pleased to receive your letter of December 18, informing us that your Commission will be able to continue the support of our research project, "Study of the Metabolism of the Human Bone Marrow," for another year. We anticipate that this year will be a most favorable one for productive research.

Dr. Sam Shoub called yesterday regarding the budget revision for next year. Enclosed is a copy of the budget, which we are forwarding to him today.

Very sincerely yours,

Wayne Rundles, M. D.

WR:mc
cc: Dr. Sam Shoub
Enclosure

UNITED STATES ATOMIC ENERGY COMMISSION
DIVISION OF BIOLOGY AND MEDICINE
WASHINGTON, D. C.

DATE: DEC 1

TO : Kenneth Kasschau, Director, Office of Research and Medicine
Oak Ridge Operations Office

FROM : James F. Haggerty, Medical Branch

SUBJECT: TRANSMITTAL OF RESEARCH PROPOSAL FOR CONTRACT NEGOTIATION

SYMBOL : [redacted]:JFH

This letter with enclosures, in triplicate, is sent in accordance with the procedure described in a letter from the General Manager to all Managers of Operations dated January 27, 1949.

1. Institution: Duke University - School of Medicine

2. Investigator (s): R. Wayne Rundles, M. D.

3. Title: "Study of the Metabolism of the Human Bone Marrow"

4. ( ) New Contract or (X) Renewal of Contract No. AT(40-1)1081

5. Duration - From: January 1, 1953 To: December 31, 1953

6. AEC Technical Supervision: Medical Branch

7. Recommended Support: $10,000.00, including overhead at 0%

Authorized by Procurement Directive No. [redacted]-109

Issued _____ $ 10,000.00

Activity No. 6300

8. Other Comments:

It is recommended that the budget be revised at a level of $10,000.00, with deletion of funds for purchase of manometers and analytical balance.

Since this constitutes the third year of support, there is no assurance of support beyond this contract year.

1110781

8. Comments (Continued)

9. Security Requirements:

In accordance with the provisions of GM-93 (Revised March, 1950), and the requirements of the Declassification Guide, the Division of Biology and Medicine has determined that the following security precautions should be taken in connection with the proposed research contract.

Since there is essentially zero chance that restricted data will be required or developed, no personnel security requirements should be imposed.

10. Reports: ( )X Reports are to be required as provided for by Memorandum Instruction of November 9, 1949, on subject "Direct Research Contract Reports".

( ) Special Reports Instructions are as follows:

Enclosures:
( )X "A" - Proposal, dated Undated
( ) "B" - Notification letter, dated _____
( ) "C" - Other correspondence, _____ letters
( )X "D" - Procurement Directive DMB-109

Distribution:

Addressee: Original (w encl.)
1st Copy (" ")
2nd Copy (" ")
Program Analysis Branch: White Copy (w/o encl.)

Division File: Yellow Copy (w encl.)
Pink Copy (w/o encl.)
Green Copy (" ")
Branch File: White Copy (w ")

1110782

[redacted]:JFH

DEC [illegible] 2

Dr. Wayne Rundles
Duke University
School of Medicine
Durham, North Carolina

Dear Doctor Rundles:

I am pleased to inform you that our Research Contracts Committee has approved continuation of support of your "Study of the Metabolism of the Human Bone Marrow" for an additional year. The contractual details will be handled in the usual manner by our Oak Ridge Operations Office, and you should hear from a representative of that office within a short time.

The Committee was pleased to note the progress made during the past year, and we trust that the ensuing year will be equally satisfactory.

Sincerely yours,

James F. Haggerty
Medical Branch
Division of Biology and Medicine

cc OROO - att: K. Kasschau

HAGGERTY:rmk

Medical

1110783

U. S. ATOMIC ENERGY COMMISSION

STATEMENT OF AUTHORITY

FORM OR 169 (May 9, 1947)

1. DELEGATED TO (Name, title, unit, location)	2. DELEGATED BY (Name, title, unit, location)
Chief, Biology Division Oak Ridge Operations Office	Director Office of Research and Medicine Oak Ridge Operations Office
3. NUMBER ASSIGNED TO THIS STATEMENT OF AUTHORITY: 1247	5. THIS STATEMENT OF AUTHORITY IS REDELEGATION NUMBER OF STATEMENT OF AUTHORITY NO.: 11 of 1173
4. EFFECTIVE DATE OF THIS STATEMENT OF AUTHORITY: March 15, 1952	

1. Pursuant to the authority vested in me you are hereby designated as a representative of the Commission and of the Contracting Officer, in connection with the performance of Contract No. AT-(40-1)-1081, Duke University, School of Medicine, with authority to take such action and make such decisions in connection therewith as are required of the Atomic Energy Commission with the exception that you are not authorized to (a) execute modifications of the contract, (b) make decisions relative to disputes, claims and appeals arising under the contract, or (c) approve any purchase or subcontract requiring Commission approval.

2. You shall establish such controls as may be necessary to maintain that portion of the program represented by the contract within budgetary limitations. You shall also develop and maintain liaison and coordination with others concerned to assure continuity of existing budgetary and administrative policies and agreement on new policies.

3. This Statement of Authority may not be redelegated to others; it will remain in effect until revoked.

Kenneth Kasschau, Director
Office of Research and Medicine

AEC, Oak Ridge, Tenn., 8-25-50—5,000-A27946

UNITED STATES ATOMIC ENERGY COMMISSION
DIVISION OF BIOLOGY AND MEDICINE
WASHINGTON, D. C.

DATE: NOV 2 6 1951

TO : Dr. Nathan Woodruff, Director, Office of Research and Medicine
Oak Ridge

FROM : L. W. Tuttle, Assistant Chief, Medical Branch

SUBJECT: TRANSMITTAL OF RESEARCH PROPOSAL FOR CONTRACT NEGOTIATION

SYMBOL : [redacted]:LWT

This letter with enclosures, in triplicate, is sent in accordance with the procedure described in a letter from the General Manager to all Managers of Operations dated January 27, 1949.

1. Institution: Duke University School of Medicine

2. Investigator (s): R. Wayne Rundles, M. D.

3. Title: "Metabolism of Human Bone Marrow"

4. ( ) New Contract or (X) Renewal of Contract No. AT(40-1)-1081

5. Duration - From: January 1, 1952 To: December 31, 1952

6. AEC Technical Supervision: Medical Branch

7. Recommended Support: $10,100.00, including overhead at 8%

Authorized by Procurement Directive No. BMB2-96

Issued [illegible] 1951 $ 10,100.00, including overhead at 8%

Activity No. 6300

8. Other Comments:
Due to limited funds available, it is suggested that the item for equipment be reduced to $500.00, and the item for Communications and Travel be reduced to $200.00.

Comments
Duke-1081

1110785

8. Comments (Continued)

9. Security Requirements:

In accordance with the provisions of GM-93 (Revised March, 1950), and the requirements of the Declassification Guide, the Division of Biology and Medicine has determined that the following security precautions should be taken in connection with the proposed research contract.

Since there is essentially zero chance that restricted data will be required or developed, no personnel security requirements should be imposed.

10. Reports: (X) Reports are to be required as provided for by Memorandum Instruction of November 9, 1949, on subject "Direct Research Contract Reports".

( ) Special Reports Instructions are as follows:

Enclosures:
(X) "A" - Proposal, dated October 1, 1951
( ) "B" - Notification letter, dated _____
( ) "C" - Other correspondence _____ letters
(X) "D" - Procurement Directive ~~DMSE-96~~

Distribution:

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	1st Copy (" ")		Pink Copy (w/o encl.)
	2nd Copy (" ")		Green Copy (" ")
Program Analysis Branch:	White Copy (w/o encl.)	Branch File:	White Copy (w ")

October 1, 1951

Proposal for Extension of Research Project Supported by the Atomic Energy Commission.

1. Title. Metabolism of Human Bone Marrow.
2. Institution. Duke University School of Medicine.
3. Investigators. R. Wayne Rundles, Ph.D., M.D., Gordon R. McKinney, Ph.D., and others.
4. Scope and Present Status. Summarized in Progress Report dated October 1, 1951.
5. Outline of work to be undertaken. As before.
6. Material, Equipment, and Facilities. As before.
7. Scientific Personnel. See Progress Report.
8. Budget, proposed for January 1-December 30, 1952, appended.
9. Other responsibilities of investigators, etc. (as previously given).

Proposed budget to be supplied by the Atomic Energy Commission, Jan. 1-Dec. 30, 1952.

Salaries:	Ray Shipke, M.D., professional assistant	3,600
	Technicians	4,000
Capital equipment:		
	Laboratory benches, Cabinets, Warburg vessels and manometers, blood centrifuge equipment, etc.	1,000
Expendable equipment and supplies:		
	Chemicals, reagents, glassware, etc.	1,000
Communication and travel:		400
		10,000
	Institutional Overhead	800
	Total	10,800

Principal Investigator

R. Wayne Rundles M.D.
Duke Hospital, Durham

Administrative Approval

Duke University

A. Brownell
Business Manager & Comptroller
Duke University

1110787

Progress Report,

Research Project Sponsored by the Atomic Energy Commission,

Metabolism of Human Bone Marrow, R. W. Rundles, M.D.,

Duke University School of Medicine, October 1, 1961.

The loss of professional assistants from our Laboratory early in 1951, occasioned by the needs of the Armed Forces, delayed the beginning of our study on the metabolism of the human bone marrow. Nevertheless, considerable progress has been made during the last few months in this intrinsically difficult investigation.

Nearly all past studies of tissue metabolism have utilized organs and tissues other than bone marrow. A standard of reference for the metabolic processes of bone marrow was considered necessary. It appeared that a satisfactory comparison could best be made with normal human leucocytes. The technical problem of obtaining adequate quantities of normal, living leucocytes has been overcome. From previous work it was apparent that contact with wettable surfaces, anticoagulants, strong centrifugal force, etc., would have to be avoided. All surfaces coming in contact with the cells should be coated with silicone, or be made of plastic. Coagulation should be prevented by ion exchange resin decalcification. A satisfactory blood donor kit incorporating these essentials has recently become available (Fenwal Laboratory) and has proved eminently suitable for our purposes. To separate red from white cells, the most satisfactory method has proved to be the addition of one part in twenty of 5% Swedish Dextran of specific viscosity 0.46, suspending the plastic container in a closed water filled vessel at 4°C, and allowing the erythrocytes to sediment. After the red cells have sedimented in a matter of 45-60 minutes the supernatent plasma, which contains a large percentage of

the leucocytes, can be forced into a collecting jar by increasing the water pressure surrounding the plastic bag. By centrifugation at 50-60 G., or less, one can obtain concentrated suspension of leucocytes, 20,000,000-30,000,000 per cc., relatively free of red blood cells. Experiments were performed regarding the effect on respiration of different media in which white cells were suspended. It was found that leucocytes were injured if they were suspended in protein-free electrolyte solutions, or in solutions containing only albumin. Most satisfactory rates of respiration were obtained with leucocytes suspended in plasma diluted with a balanced electrolyte solution. After respiratory measurements have been completed, the leucocyte protein content is determined by nitrogen analysis by the micro-Kjeldahl method. Satisfactory respiratory quotients have been obtained with leucocytes obtained and studied by these procedures.

The handling of bone marrow after aspiration was patterned on the above principles. Several methods for separating bone marrow particles from blood, utilizing differences in specific gravity, were explored with little success. Concentrated albumin solutions and gelatins were mechanically faulty, if not fatally injurious, to surviving cells. While a final method for separating marrow particles for metabolic studies has not been adopted, it appears at this time that placing the marrow in a plasma solution containing Dextran, followed by differential centrifugation will be satisfactory. The use of other red cell agglutinating agents, a phytohemagglutinin, a dextran with a molecular weight of about 440,000 and specific viscosity of 0.64, and a dextrin will be studied.

Warburg equipment has been assembled, calibrated and is in active use. A micro-Kjeldahl nitrogen analysis method is in

operation. Methods for measuring lactic acid production, aerobic and anaerobic glucose utilization are being standardized. Filter paper chromatography methods for amino acid analysis are being set up. Our hematology technicians have acquired skill in methods utilized in bone marrow examinations, cell counting, staining, etc. They have not had all of their time fully occupied on this project to date, but have helped maintain access to clinical material. The have, in addition, assisted with a research project begun earli the effects of Triethylene melamine in neoplastic disease. A publication dealing with our investigations in this field will b completed during the coming months, in which partial support by t Atomic Energy Commission will be acknowledged.

Personnel.

Gordon R. McKinney, Ph.D. Dr. McKinney finished his [redacted] He has worked full time on this project since July 1. He is supported this year by an American Cancer Society Fellowship.

George Chase, M.D. Dr. Chase finished [redacted] He was able to assist us with the early phases of this work from Jan.-June, 1951, before beginning his internship July 1, 1951.

Ray Shipke, M.D. Dr. Shipke finished his [redacted] Since July, 1951, he has assisted us in obtaining blood from donors, in preparing leucocyte suspensions, processing marrow specimens , and setting up chemical methods. He is now familiarizing himself with paper chromatographic methods which we

hope to be able to use for studying the utilization and incorporation into cellular protein of amino acids.

Mrs. Ella Hardy Shipke, a graduate medical technologist, has worked full time but is now working part time.

Miss Betty Simpson, a graduate medical technologist, was transferred to this project July 1, 1951, working full time.

Expenditures, (January 1, 1951 to September 15, 1951).

Capital equipment			$1,249.88
Salaries			
Dr. Gordon McKinney	$ 0.00	$ 0.00	
Dr. George Chase	200.00/mo.	1,080.00	
Dr. Ray Shipke	300.00/mo.	750.00	
Miss Betty Simpson	185.00/mo.	462.50	
Mrs. Ella H. Shipke	185.00/mo. 8 mos. 130/mo. currently	1,545.00	
		$3,837.50	$3,837.50
Expendable Supplies			462.09
Travel			155.98
			$5,705.45
	University Overhead		456.44
	Total Expenditure		$6,161.89

Salaries at the above rate will continue throughout this year. It is estimated that $800-$1,000 will remain unexpended at the end of the year.

Summary. Satisfactory progress has been made on this project so far and continued work should result in significant scientific advances.

Wayne Rundles, M.D.

J. Wallace Gald, Jr., Assistant General Counsel January 14, 1952

R. G. Humphries, Chief, Contract Coordination Branch

RENEWAL OF CONTRACT AT-(40-1)-1081 - DUKE UNIVERSITY SCHOOL OF MEDICINE

SYMBOL: RC:RGH

Forwarded is an approved proposal for extending research under Contract No. AT-(40-1)-1081 with Duke University with Dr. E. Wayne Rundles as Project Leader, as covered by Procurement Directive RB-52-96.

Washington has suggested and the Contractor has concurred in a reduction in the proposed capital equipment item to $500 and the communications and travel item to $200. With these adjustments the budget set forth in the Contractor's proposal is in the amount of $9300 before adding overhead at 8%, or $744, making a total of $10,044 for the second year. The Contractor's letter dated December 26, 1951, attached, reports there will be a balance at the end of the year of $1500. Deducting this balance from the approved budget leaves a net payment due for the second year in the amount of $8,544.

It is requested that you prepare an appropriate modification to extend the term of the contract to cover the research program and provide for a lump sum payment in the amount of $8,544.

Dr. C. S. Sheep will act as technical adviser on this contract action.

R. G. Humphries

Encls.:
Memo fm Knowlton 12-13-51 w/
Memo fm Tuttle 11-26-51
Contractor's proposal dtd. 10-1-51 & ltr 12-28-51

CC: ✓C. S. Sheep
L. B. Mosby
Ed. Ziegler
J. Nicholson

Humphries:lm

CONTRACTS
Duke-1081
B-295

1110792

John R. Moore, Chief, Contracts Division December 13, 1951

Kenneth Kasschau, Acting Director, Office of
Research and Medicine

RENEWAL OF CONTRACT NO. AT-(40-1)-1081 - DUKE UNIVERSITY
SCHOOL OF MEDICINE

SYMBOL: RM:AMC

We are enclosing a memorandum from the Division of Biology and Medicine, Washington, dated November 26, 1951, authorizing the renewal of the subject contract for a period of one year, beginning January 1, 1952.

Dr. C. S. Shoup will act as technical adviser for this office. We would appreciate your assistance in negotiating this contract.

Kenneth Kasschau

Enclosure
1. Procurement Directive dtd 11-26-51
2. Memo fm LWT to WHT dtd 11-26-51
3. Proposal
4. Ltr from Rundles to Shoup dtd 12-28-51
Carley:cc

CONTRACTS
Duke U. 1081

4-32

16—64000-1 GPO

OFFICE ▶	Reviewed	Reviewed	Rom	ORM		
SURNAME ▶	Carley	Shoup	RoMa	Kasschau		
DATE ▶	12-13-51	1-2-52	1-2-52	1/3/52		

1110793

UNITED STATES ATOMIC ENERGY COMMISSION
DIVISION OF BIOLOGY AND MEDICINE
WASHINGTON, D. C.

DATE: NOV 2 6 1951

TO : Dr. Nathan Woodruff, Director, Office of Research and Medicine
Oak Ridge

FROM : L. W. Tuttle, Assistant Chief, Medical Branch

SUBJECT: TRANSMITTAL OF RESEARCH PROPOSAL FOR CONTRACT NEGOTIATION

SYMBOL : BMM:LWT

This letter with enclosures, in triplicate, is sent in accordance with the procedure described in a letter from the General Manager to all Managers of Operations dated January 27, 1949.

1. Institution: Duke University School of Medicine

2. Investigator (s): R. Wayne Rundles, M. D.

3. Title: "Metabolism of Human Bone Marrow"

4. ( ) New Contract or (X) Renewal of Contract No. AT(40-1)-1081

5. Duration - From: January 1, 1952 To: December 31, 1952

6. AEC Technical Supervision: Medical Branch

7. Recommended Support: $10,100.00, including overhead at 8%

Authorized by Procurement Directive No. BM52-96

Issued NOV 2 6 1951 ; $ 10,100.00, including overhead at 8%

Activity No. 6300

8. Other Comments:
Due to limited funds available, it is suggested that the item for equipment be reduced to $500.00, and the item for Communications and Travel be reduced to $200.00.

1110794

In order to assist you in preparing an appropriate voucher there is enclosed an instruction sheet containing numbered instructions corresponding with numbers appearing on a specimen copy of the voucher form. Vouchers should be submitted to the Oak Ridge Operations office in one original (white) and four copies (yellow) addressed as shown in Article IV of the contract. It is assumed that you will give your business office the benefit of these instructions.

Your attention is called to the reporting requirements outlined in Appendix "C" to the contract, especially to Item No. 2 requiring the immediate submission of a 200 word summary statement describing the purpose and scope of your project.

For your information and guidance in purchasing isotopes through the Commission, in accordance with the provisions of Article VII, there is enclosed a copy of the latest radioisotope catalog, together with a set of application forms, which you will use in making purchases of isotopes.

Your particular attention is invited to Appendix "B", Section 12 - Fellowships.

It is believed that the remaining portions of the contract are self-explanatory, however, if you have any questions concerning the application or interpretation of any of the contract provisions I will be glad to furnish you with additional information pertaining thereto.

Very truly yours,

RBT

for C. Vanden Bulck
Assistant to the Manager
Oak Ridge Operations

Enclosures:
Contract (in trip.)
Vouchers & Instr. Sheets
Isotope Catalog & Applic. forms w/instr. sheet

Nicholson:jm

CC: Contracts ✓ C. Vanden Bulck A. M. Corley L. W. Tuttle (Washington)

1110795

Office Memorandum • UNITED STATES GOVERNMENT

TO : J. Wallace Ould, Jr., Assistant General Counsel DATE: November 13, 195

FROM : R. G. Humphries, Contract Coordinator

SUBJECT: REQUEST FOR PREPARATION OF LUMP SUM RESEARCH CONTRACT WITH DUKE UNIVERSITY

SYMBOL: CO:RGH

Forwarded is an approved research project in the amount of $12,642 with Duke University School of Medicine.

It is requested that you prepare an appropriate lump sum contract to cover this work. The portion of Section 3, Appendix "B" in the lump sum research contract form requiring clearance of the project leader should be deleted since the work is to be conducted on an unclassified basis.

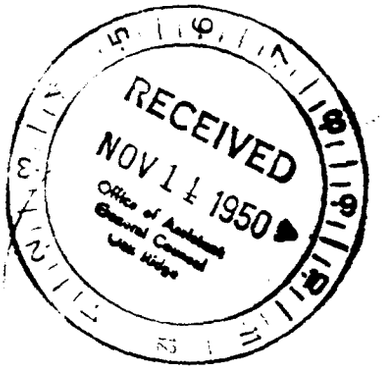
Dr. R. H. Rucker, Office of Research and Medicine, has been designated technical advisor on this contract. Please contact him on any technical questions.

R. G. Humphries

Enclosures:
Memo fm Roberson 11-3-50
Memo fm Tuttle 10-18-50 w/
Approved Project

CC: Dr. R. H. Rucker
Mr. S. Sobol
Mr. W. Stockburger (Finance)

Humphries:lm



1110796

Office Memorandum • UNITED STATES GOVERNMENT

TO H. G. Humphries, Contract Coordinator DATE: November 3, 1950

FROM John H. Roberson, Director of Research and Medicine

SUBJECT RESEARCH CONTRACT WITH DUKE UNIVERSITY, SCHOOL OF MEDICINE (R. W. RUNDLES)

SYMBOL: RM:AMC

We are enclosing a request for a research contract with Duke University, School of Medicine together with a memo from L. W. Tuttle to Dr. Roberson for the following project:

"Metabolism of Human Bone Marrow"

The technical Advisor for this contract is Dr. R. H. Rucker.

John H. Roberson

Enclosures:
1. Req. for Research Contract
2. Memo fm LWT to JHR 10-18-50

Corley:oc

Covered by Directive BM-51-44
Transmittal dated 10/20/50 — $12,042.00

1110797

UNITED STATES ATOMIC ENERGY COMMISSION
DIVISION OF BIOLOGY AND MEDICINE
WASHINGTON, D. C.

TO : Dr. John Roberson, Dir. Research and Medicine, Oak Ridge Operations Office
DATE: October 18, 1950

FROM : L. W. Tuttle, Asst. Chief, Medical Branch

SUBJECT: TRANSMITTAL OF RESEARCH PROPOSAL FOR CONTRACT NEGOTIATION

REFER TO SYMBOL: BMM:LWT

This letter with enclosures, in triplicate, is sent in accordance with the procedure described in a letter from the General Manager to all Managers of Operations dated January 27, 1949.

1. Institution: Duke University, School of Medicine, Durham, N.C.
2. Investigator(s): R. W. Rundles
3. Title: "Metabolism of Human Bone Marrow"
4. Duration - From: To: One year with provision for renewal
5. AEC Technical Supervision: Medical Branch
6. Recommended Support: ~~Including 8% overhead~~ $12,042.00 Procurement Directive BM-51-44
7. Other Comments:

The scope of the scientific work has been examined in the light of the requirements of the Declassification Guide and GM-93 (par. 4c Revised March 2, 1950). It is determined that the work falls in a category where there is essentially zero chance that restricted data will be required or developed during the investigations. It is recommended that the contract be set up on a completely unclassified basis.

Note
No clearance necessary.

AT-7307

1110798

8. Patents:

( ) In our opinion, patentable processes might be developed through the proposed work.
(x) In our opinion, there is no reason to expect patentable processes to be developed through the proposed work.

9. Restricted Data:

(x) Not likely to be required or developed.
( ) May be required or developed, and the following personnel should therefore be processed for security clearance:

10. Reports:

Three (3) copies of the following reports should be sent to the Washington Office directly, with additional copies as necessary to be sent to the Operations Office or others concerned.

( ) A scientifically accurate summary statement of approximately 200 words outlining the scope and purpose of the research: to be sent immediately after the completion of contract negotiations; a revised statement of the same sort due after nine months of activity on the project.
( ) A complete scientific report after one year of activity.
(x) Progress Reports to be received in Washington according to the following schedule:
March 15 ( ) September 15 (x)
June 15 ( ) December 15 ( )
( ) Brief reports to be submitted at any time Investigator wishes to call attention to significant results which have accrued.

11. Fund Allotments:

( ) The Budget Office has been requested to allot funds in the amount recommended for this contract.
( ) The Budget Office will be requested to allot funds as soon as you have advised us of the contract amount.
(X) Procurement Directive BM-51-44 in the amount of $12,042. has been issued to cover financing.

Enclosures:
( ) "A" - Proposal dtd August 16, 1950
( ) "B" - Notification ltr dtd _____
( ) "C" - Other correspondence (_____ ltrs)

Distribution:
To Addressee: Signed copy (with encl.)
Second copy (" ")
Third Copy (" ")
To Div. File: Yellow copy (with encl.)
Pink copy (without encl.)
Green copy (" ")
To Branch File: White copy (with encl.)
To Admin. Office: White copy (without encl.)

August 16, 1950

Proposal for the Support of Research Project by the Atomic Energy Commission

1. Title. Metabolism of Human Bone Marrow.

2. Institution. Duke University School of Medicine.

3. Investigators. R. Wayne Rundles, Ph.D., M.D.
Robert W. Willett, M.D.
Gordon R. McKinney, Ph.D. (July '51)

4. Scope and Present Status.

The bone marrow differs from most organs and tissues in the body in that its main product is blood cells. Comparatively few studies have been made of its metabolism (Warren, J. Biol. Chem. 167:543, 1947; Guzman Barron, et al, J. Biol. Chem. 171:801, 1947, J. Exp. Med. 87:489 and 503, 1948, J. Gen. Physiol. 32:537 and 595, 1949, Bird and Evans, J. Biol. Chem. 178:289, 1949). Most investigators have used rabbit bone marrow. The findings in general indicate that oxygen utilization is 5 times less than that of highly respiring tissues. Glucose, pyruvate, acetate, and amino acids are utilized vigorously. Some evidence suggests that fatty substances may be especially important nutrients.

No attempts appear to have been made to study the metabolism of the human bone marrow. Since cellular morphology varies from species to species it is possible that metabolic activity does also.

The hemopoietic tissues furthermore are among the most vulnerable to the action of some destructive agents that may be employed in warfare and are frequently involved in clinical diseases.

The latter include nutritional deficiencies (megaloblastic cell development), chemical or drug damage (aplastic anemia, agranulocytosi some types of thrombocytopenic purpura and hemolytic anemia), radiation depression or damage, and malignant diseases (leukemia, sub-leukemia, multiple myeloma, etc.)

5. Outline of work to be undertaken.

Preliminary studies indicate that bone marrow cells can be aspirated from human subjects in sufficient quantity for in vitro studies using the Warburg apparatus. Adequate methods are available for separating the primitive blood cells from the erythrocytes, and for determining the rate of many metabolic processes/mg. of fat free tissue.

We wish to determine first the conditions for optimal survival of the marrow cells, or better growth and proliferation, if possible in a chemically defined medium. ~~We can then~~ study the rate of O_2 consumption, the utilization of glucose, pyruvate, acetate, and amino acids, essential and otherwise in normal and abnormal marrow as influenced by roentgen irradiation, the presence of P 32, urethane and other agents which have a well defined influence on marrow function.

Studies on amino acid uptake will require studies with synthetic radioactive amino acids, as well as amino acid analyses employing filter paper chromatography and microbiological assay.

The hematologic effects of urethane have been investigated in ~~our~~ laboratory for 3 years. The compound suppresses the growth of myeloid elements in myelogenous leukemia and plasma cells in multiple myeloma selectively and beneficially. An

understanding of its metabolic effect in bone marrow is an important matter which may be studied advantageously in vitro and in vivo with the aid of the radioactive urethane.

6. Material, Equipment and Facilities.

The facilities of a small but well equipped Hematology Laboratory, organized and staffed as a consultation service for Duke Hospital patients, ~~is~~ (will be) available for this investigation. An abundance of clinical material is available. An additional laboratory ~~is~~ (will be) available in the Medical Research Building where electrophoretic and physico-chemical studies of proteins are being carried out. Expanded laboratory quarters in Duke Hospital ~~are planned~~ when construction ~~under~~ contract is completed.

Warburg equipment has been purchased from available funds. Additional equipment and supplies ~~requested~~ from the A.E.C. ~~to~~ be used in this investigation. ~~are itemized below.~~

7. Scientific Personnel.

R. W. Rundles, Assistant Professor of Medicine, Duke University. Outline of research experience and publications appended.

Robert W. Willett. Damon Runyon Clinical Research Fellow, 1950-51.

[redacted] Interne, Duke Hospital, April-June, 1948, Interne, Syracuse University Hospital, 1948-49; Assistant Resident in Medicine, Duke Hospital, 1949-50.

Publications:

Willett, R. W., and McPherson, H. T.: Some observations on intraocular ovarian transplants with special reference to the effects of progesterone. Thesis,

[redacted]

Gordon R. McKinney. U. S. Public Health Fellow, 1949-51, Department of Physiology and Pharmacology (Dr. Frederick Bernheim).

[redacted]

Publications:

McKinney, G. R.: A study of the action of a nitrogen mustard on cytochrome oxidase. Anat. Record, 101:34, 1948.

McKinney, G. R.: The effect of a nitrogen mustard on certa synthetic reactions in vitro. J. Pharmacol. and Exp. Therapy, 96:188, 1949.

McKinney, G. R.: The effect of colchicine on certain synthetic reactions in vitro. (Introduced by Frederick Bernheim) Fed. Proc., 9:301, 1950.

McKinney, G. R.: The effect of various drugs on certain phases of in vitro anabolism. J. Pharmacol. and Exp. Therapy. (in press)

McKinney, G. R.: The effect of certain compounds containing the aromatic ring on para-Aminohippurric acid synthesis in vitro. Arch. Biochem. (in press)

8. Budget. The salary of R. W. Rundles is supplied by Duke University and the Department of Medicine. Supplies for the routine services of the Hematology Laboratory are provided by Duke Hospital (about $4000 annually), as are salaries for 2 house officers and 1-2 student technicians rotating through the laboratory. The salary of one technician and a secretary is supplied by the

Department of Medicine. A research project, "Clinical, hematologic and chemical effects of urethane in multiple myeloma", under the direction of R. W. Rundles, is supported by the American Cancer Society ($9120 annually). It is anticipated that support from these sources will continue.

Additional supplies, salaries and equipment requested from the A.E.C. are itemized below.

The proposed study should extend over at least 2 years and will commence at least in part in October, 1950. Sponsorship by the Atomic Energy Commission is requested after January 1, 1951.

9. Other Responsibilities of Investigators.

R. W. Rundles. General medical rounds and teaching, 2-3 half days per week, care of private patients 2 half days per week. Balance of time spent in research in clinical hematology.

R. W. Willett. Medical Clinic 2-3 half days per week. Balance of time is spent in clinical hematology and research. Major research interest will be this project after October, 1950.

Gordon R. McKinney. Full time on this project, available after October, 1950.

Research funds of the Department of Medicine are fully utilized to provide salaries for the senior investigators and support research projects without outside subsidy.

Proposed Budget to be supplied by the Atomic Energy Commission, January 1, - December 30, 1951.

Salaries:

R. W. Willett (July 1, 1951-December 30, 1951	$1,750.00
Gordon R. McKinney (July 1, 1951 - December 30, 1951)	1,750.00
Technician ($200 monthly)	2,400.00

Capital Equipment:	
Chromatography cabinets (3)	750.00
Coleman Jr. Spectrophotometer	300.00
Dubnoff Metabolic Shaking Incubator	300.00
Warburg glassware	250.00
Analytic balance	600.00
Refrigerator-freezer	250.00
Expendable Equipment and Supplies, (Chemicals, reagents, glassware, experimental animals, etc.)	2,500.00
Communication and Travel	300.00
	$11,150.00
Institutional Overhead @ 8%	892.00
Total	$12,042.00

Principal Investigator — R. Wayne Rundles, M.D.

Approved by Executive Committee,
Duke University School of Medicine

Approved by Administration,
Duke University — A. A. Brower
Business Manager and Comptroller

Rundles, R. W.

[redacted] Assistant Instructor in Anatomy, Cornell University Medical College, 1933-37; Interne, Assistant Resident and Resident in Medicine, University of Michigan Hospital, 1940-43; Instructor in Internal Medicine, and Research Assistant, Simpson Memorial Institute, 1943-45; Duke University, 1945-49; Assistant Professor of Medicine, Duke University, 1949-

Partial Bibliography:

Rundles, R. Wayne: Fiber and cellular degeneration following tem lobectomy in the monkey, Cornell Thesis, 1937.

Rundles, R. W., and Papez, J. W.: Fiber and cellular degeneration following temporal lobectomy in the monkey. J. Comp. Neurol. 68:267, 1937.

Bethell, F. H., Sturgis, C. C., Mallery, O. T., and Rundles, R. W. Blood: A review of recent literature. Arch. Int. Med., 74: 36, 131, 197, 1944.

Rundles, R. W.: Diabetic neuropathy, general review with report of 125 cases. Med., 24:111, 1945.

Rundles, R. Wayne; Hemorrhagic telangiectasia with pulmonary artery aneurysm. Am. J. Med. Sci., 210:76, 1945.

Bethell, F. H., Sturgis, C. C., Rundles, R. W., and Meyers, M. C.: Blood: A review of the recent literature. Arch. Int. Med., 76:239, 358, 1945, and 77:89, 196, 1946.

Rundles, R. Wayne: Prognosis in the neurologic manifestations of pernicious anemia. Blood, 1:209, 1946.

Rundles, R. W., and Falls, Harold F.: Hereditary (sex-linked ?) anemia. Am. J. Med. Sci., 211:641, 1946.

Hodges, Fred J., Rundles, R.Wayne, and Hanelin, Joseph: Roentgenologic study of the small intestine. Radiology, 49:587 and 659, 1947.

Loge, J. P., and Rundles, R. W.: Urethane (ethyl carbamate) therapy in multiple myeloma. Blood, 4:201, 1949.

Schieve, James F., and Rundles, R. W.: Response of lingual manifestations of pernicious anemia to pteroylglutamic acid and vitamin B_{12}. J. Lab. & Clin. Med., 34:439, 1949.

McPherson, A. Z., Jonsson, U., and Rundles, R. W.: Vitamin B_{12} therapy in megaloblastic anemia of infancy. J. Ped., 34: 529, 1949.

Rundles, R. W., and Jonsson, U.: Metastases in bone marrow and myelophthisic anemia from carcinoma of the prostate. Am. J. Med. Sci., 218:241, 1949.

Rundles, R. Wayne, and Reeves, Robert J.: Multiple Myeloma. II. Variability of roentgen appearance and effect of urethane therapy on skeletal disease. Am. J. Roentgenol. (in press)

Rundles, R. Wayne, Dillon, M. L., and Dillon, Edith S.: Multiple Myeloma. III. Effect of urethane therapy on plasma cell growth, abnormal serum protein components and Bence Jones proteinuria. J. Clin. Invest. (in press)

Jonsson, Ulfar, Hansen-Pruss, O. C., and Rundles, R. W.: Hemolytic anemia in myelogenous leukemia with splenectomy. Blood (in press)

UNITED STATES ATOMIC ENERGY COMMISSION
DIVISION OF BIOLOGY AND MEDICINE
WASHINGTON, D. C.

TO : Dr. John Roberson, Dir. Research and Medicine, Oak Ridge Operations Office

DATE: October 18, 1950

FROM : L. W. Tuttle, Asst. Chief, Medical Branch

SUBJECT: TRANSMITTAL OF RESEARCH PROPOSAL FOR CONTRACT NEGOTIATION

REFER TO SYMBOL: RRM:LWT

This letter with enclosures, in triplicate, is sent in accordance with the procedure described in a letter from the General Manager to all Managers of Operations dated January 27, 1949.

1. Institution: Duke University, School of Medicine, Durham, N.C.

2. Investigator(s): R. W. Rundles

3. Title: "Metabolism of Human Bone Marrow"

4. Duration - From: To: One year with provision for renewal

5. AEC Technical Supervision: Medical Branch

6. Recommended Support: $12,042.00 Including 8% overhead Procurement Directive BM-51-44

7. Other Comments

The scope of the scientific work has been examined in the light of the requirements of the Declassification Guide and CM-93 (par. 4c Revised March 2, 1950). It is determined that the work falls in a category where there is essentially zero chance that restricted data will be required or developed during the investigations. It is recommended that the contract be set up on a completely unclassified basis.

8. Patents:

( ) In our opinion, patentable processes might be developed through the proposed work.
(X) In our opinion, there is no reason to expect patentable processes to be developed through the proposed work.

9. Restricted Data:

(X) Not likely to be required or developed.
( ) May be required or developed, and the following personnel should therefore be processed for security clearance:

10. Reports:

Three (3) copies of the following reports should be sent to the Washington Office directly, with additional copies as necessary to be sent to the Operations Office or others concerned.

( ) A scientifically accurate summary statement of approximately 200 words outlining the scope and purpose of the research: to be sent immediately after the completion of contract negotiations; a revised statement of the same sort due after nine months of activity on the project.
( ) A complete scientific report after one year of activity.
(X) Progress Reports to be received in Washington according to the following schedule:

March 15 ( )	September 15 (X)
June 15 ( )	December 15 ( )

( ) Brief reports to be submitted at any time Investigator wishes to call attention to significant results which have accrued.

11. Fund Allotments:

( ) The Budget Office has been requested to allot funds in the amount recommended for this contract.
( ) The Budget Office will be requested to allot funds as soon as you have advised us of the contract amount.
(X) Procurement Directive BM-51-44 in the amount of $12,042. has been issued to cover financing.

Enclosures:
( ) "A" - Proposal dtd August 16, 1950
( ) "B" - Notification ltr dtd _____
( ) "C" - Other correspondence (_____ ltrs)

Distribution:
To Addressee: Signed copy (with encl.)
Second copy (" ")
Third Copy (" ")
To Div. File: Yellow copy (with encl.)
Pink copy (without encl.)
Green copy (" ")
To Branch File: White copy (with encl.)
To Admin. Office: White copy (without encl.)

August 16, 1950

Proposal for the Support of Research Project by the Atomic Energy Commission

1. Title. Metabolism of Human Bone Marrow.

2. Institution. Duke University School of Medicine.

3. Investigators. R. Wayne Rundles, Ph.D., M.D.
Robert W. Willett, M.D.
Gordon R. McKinney, Ph.D. (July '51)

4. Scope and Present Status.

The bone marrow differs from most organs and tissues in the body in that its main product is blood cells. Comparatively few studies have been made of its metabolism (Warren, J. Biol. Chem. 167:543, 1947; Guzman Barron, et al, J. Biol. Chem. 171:801, 1947, J. Exp. Med. 87:489 and 503, 1948, J. Gen. Physiol. 32:537, and 595, 1949; Bird and Evans, J. Biol. Chem. 178:289, 1949). Most investigators have used rabbit bone marrow. The findings in general indicate that oxygen utilization is 5 times less than that of highly respiring tissues. Glucose, pyruvate, acetate, and amino acids are utilized vigorously. Some evidence suggests that fatty substances may be especially important nutrients.

No attempts appear to have been made to study the metabolism of the human bone marrow. Since cellular morphology varies from species to species it is possible that metabolic activity does also.

The hemopoietic tissues furthermore are among the most vulnerable to the action of some destructive agents that may be employed in warfare and are frequently involved in clinical diseases.

The latter include nutritional deficiencies (megaloblastic cell development), chemical or drug damage (aplastic anemia, agranulocytosis, some types of thrombocytopenic purpura and hemolytic anemia), radiation depression or damage, and malignant diseases (leukemia, sub-leukemia, multiple myeloma, etc.)

5. Outline of Work to be Undertaken.

Preliminary studies indicate that bone marrow cells can be aspirated from human subjects in sufficient quantity for in vitro studies using the Warburg apparatus. Adequate methods are available for separating the primitive blood cells from the erythrocytes, and for determining the rate of many metabolic processes/mg. of fat free tissue.

We wish to determine first the conditions for optimal survival of the marrow cells, or better growth and proliferation, if possible in a chemically defined medium. We can then study the rate of O_2 consumption, the utilization of glucose, pyruvate, acetate, and amino acids, essential and otherwise in normal and abnormal marrows as influenced by roentgen irradiation, the presence of P 32, urethane and other agents which have a well defined influence on marrow function.

Studies on amino acid uptake will require studies with synthetic radioactive amino acids, as well as amino acid analyses employing filter paper chromatography and microbiological assay.

The hematologic effects of urethane have been investigated in our laboratory for 3 years. The compound suppresses the growth of myeloid elements in myelogenous leukemia and plasma cells in multiple myeloma selectively and beneficially. An understanding

of its metabolic effect in bone marrow is an important matter which may be studied advantageously in vitro and in vivo with the aid of the radioactive urethane.

6. Material, Equipment and Facilities.

The facilities of a small but well equipped Hematology Laboratory, organized and staffed as a consultation service for Duke Hospital patients, is available for this investigation. An abundance of clinical material is available. An additional laboratory is available in the Medical Research Building where electrophoretic and physico-chemical studies of proteins are being carried out. Expanded laboratory quarters in Duke Hospital are planned when construction under contract is completed.

Warburg equipment has been purchased from available funds. Additional equipment and supplies requested from the A.E.C. to be used in this investigation are itemized below.

7. Scientific Personnel.

R. W. Rundles, Assistant Professor of Medicine, Duke University. Outline of research experience and publications appended.

Robert W. Willett. Damon Runyon Clinical Research Fellow, 1950-51.

[redacted] Interne, Duke Hospital, April-June, 1948, Interne, Syracuse University Hospital, 1948-49; Assistant Resident in Medicine, Duke Hospital, 1949-50.

Publications:

Willett, R. W., and McPherson, H. T.: Some observations on intraocular ovarian transplants with special reference to the effects of progesterone. Thesis, Duke University, 1948.

Gordon R. McKinney. U. S. Public Health Fellow, 1949-51, Department of Physiology and Pharmacology (Dr. Frederick Bernheim).

[redacted]

Publications:

McKinney, G. R.: A study of the action of a nitrogen mu on cytochrome oxidase. Anat. Record, 101:34, 1948.

McKinney, G. R.: The effect of a nitrogen mustard on se synthetic reactions in vitro. J. Pharmacol. and Exp. Therapy, 96:188, 1949.

McKinney, G. R.: The effect of colchicine on certain synthetic reactions in vitro. (Introduced by Frederick Bernheim) Fed. Proc., 9:301, 1950.

McKinney, G. R.: The effect of various drugs on certain phases of in vitro anabolism. J. Pharmacol. and Exp. Therapy. (in press)

McKinney, G. R.: The effect of certain compounds containing the aromatic ring on para-Aminohippurric acid synthesis in vitro. Arch. Biochem. (in press)

8. Budget. The salary of R. W. Rundles is supplied by Duke University and the Department of Medicine. Supplies for the routine services of the Hematology Laboratory are provided by Duke Hospital (about $4000 annually), as are salaries for 2 house officers and 1-2 student technicians rotating through the laboratory. The salary of one technician and a secretary is supplied by the Department of Medicine. A research project, "Clinical, hematologic and chemical

effects of urethane in multiple myeloma", under the direction of R. W. Rundles, is supported by the American Cancer Society ($9120 annually). It is anticipated that support from these sources will continue.

Additional supplies, salaries and equipment requested from the A.E.C. are itemized below.

The proposed study should extend over at least 2 years and will commence at least in part in October, 1950. Sponsorship by the Atomic Energy Commission is requested after January 1, 1951.

9. Other Responsibilities of Investigators.

R. W. Rundles. General medical rounds and teaching, 2-3 half days per week, care of private patients 2 half days per week. Balance of time spent in research in clinical hematology.

R. W. Willett. Medical Clinic 2-3 half days per week. Balance of time is spent in clinical hematology and research. Major research interest will be this project after October, 1950.

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January 1, - December 30, 1951.

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Total	$12,042.00

Principal Investigator — R. Wayne Rundles, M.D.

Approved by Executive Committee,
Duke University School of Medicine

Approved by Administration,
Duke University — A. S. Brawner, Business Manager and Comptroller

[redacted]

in Anatomy, Cornell University Medical College, 1933-37; Interne, Assistant Resident, and Resident in Medicine, University of Michiga Hospital, 1940-43; Instructor in Internal Medicine, and Research Assistant, Simpson Memorial Institute, 1943-45, Duke University, 1945-49, Assistant Professor of Medicine, 1949-

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McPherson, A. Z., Jonsson, U., and Rundles, R. W.: Vitamin B_{12} therapy in megaloblastic anemia of infancy. J. Ped., 34:589, 1949.

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