

TO : Addressees Listed Below

DATE: February 26, 1958

FROM : John R. Moore, Director, Contract Division

714694

SUBJECT: CONTRACTUAL DOCUMENTS FOR REVIEW, COMMENTS AND INITIALING

The document(s) listed below are forwarded for your review, comments and initials. Upon completion of your review, please attach your comments, if any, and forward to next in turn. Expeditious handling of this matter will be appreciated.

Modification 3 to Contract AT-(40-1)-2165 with the University of North Carolina

Addressees:	Division:	Init:	Date:	Remarks:
1. <del>R. G. Handley</del>	Contract	<del>RM</del>	<del>2/28/58</del>	
2. A. E. Miller	Budget	ARM	2/28/58	06-81-91(24) Fund
3. C. S. Shoup	Res. & Dev.	gik	3-3-58	
4. L. D. Mackay	Finance	<i>ML</i>	3-3-58	
5.				
6.				

*Jan 31  
to 3-6-58*

RETURN TO:

Alice Brown

Contract Division

Tel.: 4719

REPOSITORY Oak Ridge Operations  
 COLLECTION Records Holding area  
Documents 1944-94  
 BOX No. Contracts AT-(40-1)-2138-2172  
Loe 1 Bldg. 2714-H  
 FOLDER Backup Papers - Univ. of NC  
Contract No. AT-(40-1)-2165

*Office Memorandum* • UNITED STATES GOVERNMENT

TO : J. W. Guld, Jr., Assistant General Counsel

DATE: February 19, 1958

FROM : John R. Moore, Director, Contract Division

SUBJECT: REQUEST FOR MODIFICATION OF CONTRACT AT-(40-1)-2165 WITH  
UNIVERSITY OF NORTH CAROLINA, CHAPEL HILL, NORTH CAROLINA

SYMBOL: ACD:DS

Please prepare an appropriate modification to the subject contract to provide additional research, to be completed not later than June 30, 1958, with new funds in the amount of \$3,888. This contract action is covered by Contract Authorization No. BM-58-303.

Request for Contract Action from the Research and Development Division is enclosed for your use.

  
John R. Moore

## Enclosures:

1. Reqst for Cont. Action
2. Program Resume<sup>1</sup>
3. Budget breakdown
4. Memo in Wash. Div. of Biology & Med., dtd 2-3-58
5. Renewal proposal

CC: C. S. Shoup  
L. D. MacKay  
Alice Brown w/cy encls 1, 3 & 4

1. TO: J. R. Moore Chairman Contract Board. From: Res. & Dev. Div.

It is requested that the Contract Board take the necessary action to process the following described contract action in accordance with the provisions of Bulletin OR-O&M-19:

2. Nature of Action Requested

[ ] Selection of New Contractor and Negotiation of Contract.

[x] Modification of Contract No. AT-(40-1)-2165

Contractor: University of North Carolina Chapel Hill, North Carolina

[ ] Review and approval of Contract, Sub-contract or Purchase Order.

[ ] Other (Explain)

Number: Name:

3. Nature of Services to be Covered by Contract

Construction [ ] Architect-Engineer [ ] Other [x] (Explain) Research

4. Funding Amount to be Obligated by this Contract Action \$3,888.00

Source of Funds

Approved ORO Financial Plan, Quarter, Fiscal Year 19 Project No. or, Activity No. 6320 Funds to be Obligated: Allotment No. 06-87-91(200). 1958 Funds Procurement Directive No. 1077-58-303 Dated 2-3-58 Issuing Office Div. of Biology & Medicine

Concurrence in Funding Statement: (signed) R Miller Chief, Budget Branch

5. Project or Activity to be Covered by Contract Action:

Location of Work: Construction Directive No. Estimated Cost of Work to be Covered by this Contract Action \$ Schedule: Date Work to Start Estimated Completion Date Description of Project or Activity:

(If more space is required use separate sheets and attach hereto:)

<p>6. <u>Contract Board Docket</u> No. _____ (To be assigned by Board Secretary)</p>	<p>7. Request Submitted By: (signed) <u>G. C. Leonard</u> Date: <u>FEB 1 1958</u> Title: _____ C. S. SHOUP CHIEF, BIOLOGY BRANCH RESEARCH AND DEVELOPMENT DIVISION</p>
<p>8. <u>Complete Description of Services to be Furnished by Contractor:</u> Headquarters designated research contract TITLE: "A Study of Ion Transport Across Smooth Muscle Cell Membrane"  (If more space is required use separate sheets and attach hereto:)</p>	
<p>9. <u>Description of other changes to be covered by Modification:</u> Modify contract to provide additional research to be completed not later than June 30, 1958, with new funds in the amount of \$3,888.  (If more space is required use separate sheets and attach hereto:)</p>	
<p>10. <u>Negotiated Contracts.</u> (Show why it appears desirable to negotiate new contract or to negotiate modification to existing contract)  Memorandum from C. W. Shilling to S. R. Sapirie dated February 3, 1958.  (If more space is required use separate sheets and attach hereto:)</p>	
<p>11. <u>Contracts, Subcontracts, or Purchase Orders Submitted for Review and Approval:</u> (Furnish brief description of action in this space and attach pertinent documents)  None</p>	
<p>12. <u>Disputes:</u> Attach a statement summarizing the dispute together with pertinent documents and Background Material.  None</p>	

OK  
H  
2/19

1508

1097563

SUBMIT FOR CONFR-OPT NO. AT-(40-1)-2105  
1-1-58 - 3-31-58

<u>Salaries and Wages:</u>		\$3,425.00
Dr. B. G. Stall (1/3 of time)	\$1,225.00	
Technician, Diener, and Animal Care	2,100.00	
Secretary assistance	100.00	
<u>Supplies and Equipment:</u>		1,300.00
<u>Travel:</u>		200.00
<u>Overhead (29.2% of salaries and wages):</u>		1,002.84
	TOTAL	<u>\$5,927.84</u>

The AEC's contribution to the above budget will be \$3,888.

1097564

UNIVERSITY OF NORTH CAROLINA  
SCHOOL OF MEDICINE  
DEPARTMENT OF MEDICINE  
CHAPEL HILL, N. C.

CONTRACT NO. AT-(40-1)-2165

DR. BERNARD G. STALL, III.  
Assistant Professor of Medicine  
Project Leader.

A STUDY OF ION TRANSPORT ACROSS THE SMOOTH MUSCLE CELL MEMBRANE.

Resume'

The contractor will continue studies of factors regulating the flux and movement of ions across smooth muscle cell membranes and will relate these factors to variations in the contractile function of the muscle tissue. Free energy conditions, energy gradients, ion imbalance, bioelectric potentials, etc. will be investigated, and explorations will be made of the relationships between actual ion transport and carbohydrate metabolism.

J. S. Shoup

1097565

UNITED STATES ATOMIC ENERGY COMMISSION  
WASHINGTON, D. C.

Contract Authorization No. BM-58-303

FEB 6 1958

TO : S. R. Sapirie, Manager  
Oak Ridge Operations Office

FROM : C. W. Shilling, M. D., Deputy Director  
Division of Biology and Medicine, Washington

SUBJECT : FUND AUTHORIZATION AND TRANSMITTAL OF RESEARCH PROPOSAL FOR  
CONTRACT NEGOTIATION

REFERENCE : AEC 102/16 APPROVED OCTOBER 7, 1953, AS IMPLEMENTED BY MEMORANDUM  
TO MANAGERS, OPERATIONS OFFICES, DATED OCTOBER 23, 1953, JOINTLY  
SIGNED BY THE DIRECTORS OF THE DIVISIONS OF RESEARCH AND BIOLOGY  
AND MEDICINE.

SYMBOL : BMB:JRT

The research proposal described below has been approved by the Division of Biology and Medicine, funds are available, and you are authorized and requested to negotiate a contract in accordance with the following terms and conditions:

1. Institution: University of North Carolina
2. Investigator (s): Dr. Bernard G. Stall, III
3. Title: A Study of Ion Transport Across Smooth Muscle Cell Membrane.
4. ( ) New Contract, ( X ) Renewal of Contract No. AT(40-1)2165
5. Duration: January 1, 1958 thru June 30, 1958
6. AEC Technical Representative: Dr. John R. Totter *JRT*
7. Funds are authorized for the obligation of this contract as follows:

<u>Allotment No.</u>	<u>Budget Category</u>	<u>Previous</u>	<u>Amount This Action</u>	<u>Total</u>
<i>JRT</i> 06-81-91(62)	6320	-	\$3,936	\$3,936
_____	_____	_____	_____	_____
_____	_____	_____	_____	_____

FEB 6 1958

FEB 6 1958

1097566



Budget

GOBY

Proposed Contribution by:

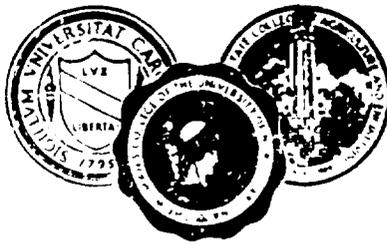
<u>Personnel, Scientific</u>	<u>AEC</u>	<u>UNC</u>
B. Stall (1/3 time)		\$1,225.00
<u>Other Personnel</u>		
Technician	\$1,900.00	
Diner and Animal Care	200.00	
Secretarial Assistance		100.00
<u>Permanent Equipment</u>		
	0	0
<u>Supplies and Expendable Equipment</u>		
Isotopes	600.00	
Animals	100.00	
Glassware, reagents, miscellaneous small items	500	
<u>Travel</u>		
	200.00	
<u>Overhead (8% AEC total)</u>		
	288.	
Administrative Overhead (29.28% of combined UNC and AEC Personnel)		714.84
less 8% AEC total	-	518.38
	3888.	
<u>Totals</u>	<u>\$4,536.00</u>	<u>\$2,843.38</u> 2039.84

(NOTE: By phone Dr. Stall indicates \$3,956 is correct figure - JRT - 1/21/58)  
3888.

SUMMARY

Proposed AEC Support	\$4,536.00	3888.
Proposed UNC Support	<u>2,843.38</u>	<u>2039.84</u>
Total Cost of Project	<u>\$6,379.38</u>	\$5927.84

Revised per telephone conversation between Dr. Sharp, Dr. Zetter,  
and Dr. Stall, 9 A. Branch, N.C. 2-10-54  
8075



THE UNIVERSITY OF NORTH CAROLINA *Co-located Office*  
University of North Carolina in CHAPEL HILL • North Carolina State College of Agriculture and Mechanical Arts in WELLSVILLE • College of Education in GREENSBORO

WILLIAM FRIDAY  
*President*

CHAPEL HILL

May 31, 1957

U. S. Atomic Energy Commission  
Research and Development Division  
Post Office Box E  
Oak Ridge, Tennessee

Gentlemen,

Enclosed, please find an application for the renewal of Contract No. AT-(40-1)-2165 in the amount of \$15,739.09 for research to be done by Dr. Bernard G. Stall, III, Assistant Professor of Medicine at the University of North Carolina.

We hope this application will merit your consideration.

Cordially,

  
William Friday

Enclosure

1097569

JUN 4 1957

1. Progress Report: Studies on ion flux across smooth muscle membrane were continued. The use of bovine arterial smooth muscle in these experiments has been satisfactory. This tissue is densely cellular and separated from intima and adventitia fairly easily.

In general the flux rates of potassium in this system have been quite rapid, so rapid that the inaccuracies in measurement have prevented valid comparisons among experimentally altered conditions. The use of Rubidium has been productive of somewhat slower fluxes.

Definition of optimal conditions for restitution of the initial potassium and sodium contents of tissue slices has been further pursued.

The basis of reference for K and Na content in the past has been non-collagenous protein. It is believed that tissue solids, after freeze drying, may be a consistent and valid reference to express these concentrations in the case of bovine arterial smooth muscle. Additional information regarding shifts in intracellular water would be thus obtained and considerable time would be saved should this reference prove satisfactory.

In general, the level of activity performed has followed that set forth in the contract fairly closely except for a lag period due to technical difficulties.

2. Reportable accidents and excessive radiation exposure: There have been none of these.
3. Renewal Proposal: There are no basic changes in the general objectives of this research which are to study the factors regulating ion flux across smooth muscle cell membrane and relating these to variations in contractile function of the tissue. However, the work has now reached a phase wherein it would be both helpful and interesting to determine the free energy involved in the reactions whereof the actively transported ions are moved against an energy gradient. It is proposed that an attempt be made to determine the free energy by placement of a microelectrode into the cells' interior. This type of measurement has been satisfactorily carried out for uterine muscle.

The relationship between the actual ion transport and the metabolism of carbohydrates is also to be explored.

1097570

G 4958  
JUN 4 1957

Scientific Personnel: No change

Other Personnel: No change

Other Financial Assistance: None

Materials, Equipment, and Facilities:

A. Available (or will be in near future): As of last May 1st, plus a radiation analyzer, gas flow counter, and Van Slyke gasometric machine.

B. Major Items to be procured:

- 1) Beckman Model D.U. spectrophotometer plus accessories
- 2) Analytical Balance

These items are needed to replace those currently in use and which will not be available hereafter.

Travel and Other Items: Funds are to be used for purposes of attending scientific meetings and programs germane to this project as well as other minor communication needs.

Budget

Proposed Contribution by:

AEC

UNC

Personnel, Scientific

1. Stall (1/3 time)

\$2,333.33

Other Personnel

Technician

\$3,600

Driver (and Animal care)

600

Secretarial Assistance

800

200

Permanent Equipment

1) Beckman Model DU

2) Spectrophotometer and accessories

1,850

3) Analytical Balance, Ainsworth

800

Supplies and Expendable Materials

Isotopes

1,500

Animals

200

Glassware, reagents, miscellaneous small items

1,200

200

Travel

250

Overhead (8% AEC total)

864

Administrative Overhead (29.28% combined UNC and AEC less 8% AEC total)

1,341.76

\$11,664.00

\$4,075.09

SUMMARY

Proposed AEC support

\$11,664.00

Proposed UNC support

4,075.09

Total Cost of Project

\$15,739.09

1097572

Statement of Current Expenditures

Contract No. AT-(4C-1)-2165, Second Period

	Expenditures 9/1/56 - 4/30/57		Estimated 5/1/57 - 8/31/57		TOTAL
	AEC	ERC	AEC	ERC	
<u>Salaries</u>					
Secretarial		100.00		100.00	200.00
Frances Morgan	2338.64		1169.32		3507.96
Bernard Stall		1555.52		777.76	2333.28
	2338.64	1655.52	1169.32	877.76	6041.24
<u>Equipment</u>	1067.85	—	797.15	—	1865.00
<u>Supplies and services</u>	1132.41	150.00	2259.45	50.00	3591.86
<u>Travel</u>	-0-	-0-	250.00	-0-	250.00
<u>Total direct costs</u>	<u>4538.90</u>	<u>1805.52</u>	<u>4475.92</u>	<u>927.76</u>	<u>11748.10</u>
<u>Overhead</u>					
@ 29.28%		1179.32		589.56	1768.88
@ 8.00%	363.11		358.07		721.18
	363.11	1179.32	358.07	589.56	2490.06
<u>Total Costs</u>	<u>4902.01</u>	<u>2984.84</u>	<u>4833.99</u>	<u>1517.32</u>	<u>14238.16</u>

TO : Addressees Listed Below

DATE: November 27, 1957

FROM : John R. Moore, Director, Contract Division

SUBJECT: CONTRACTUAL DOCUMENTS FOR REVIEW, COMMENTS AND INITIALING

The document(s) listed below are forwarded for your review, comments and initials. Upon completion of your review, please attach your comments, if any, and forward to next in turn. Expeditious handling of this matter will be appreciated.

Modification 2 to Contract AT-(40-1)-2165 with the University of North Carolina

<u>Addressees:</u>	<u>Division:</u>	<u>Initi</u>	<u>Date:</u>	<u>Remarks:</u>
1. <del>R. C. Humes</del>	<del>Contract</del>	<del>RM</del>	11/25/57	
2. <del>E. E. Miller</del>	Budget	RM	11/26/57	no additional funding
3. C. S. Shoup	Res. & Dev.	CS	11-27-57	
4. I. D. MacKay	Finance	IM	11-29-57	
5.				
6.				

RETURN TO:

Alice Brown

Contract Division

Tel.: 4719

1097574

# Office Memorandum • UNITED STATES GOVERNMENT

TO : J. W. Reid, Jr., Assistant General Counsel

DATE: November 15, 1957

FROM : John R. Moore, Director, Contract Division

SUBJECT: REQUEST FOR MODIFICATION OF CONTRACT AT-(40-1)-2165 WITH  
UNIVERSITY OF NORTH CAROLINA, CHAPEL HILL, NORTH CAROLINA

SYMBOL: ACD:DS

Please prepare an appropriate modification to the subject contract to provide for additional research, completion of which will be not later than December 31, 1957, without additional funds. There will be no significant change in the scope of the work.

Request for Contract Action from the Research and Development Division is enclosed for your use.

  
John R. Moore

Enclosures:

1. Reqst for Cont. Action
2. Memo fm Wash. Div. of Biology & Medicine dtd 10/29/57  
w/cy of ltr fm Dr. Stall fm Univ. of N. C.

CC: C. S. Shoup  
Alice Brown, w/cy encl 1

1097575

1469

1. TO: J. A. Moore Chairman Contract Board. From: Research & Development Div.

It is requested that the Contract Board take the necessary action to process the following described contract action in accordance with the provisions of Bulletin OR-O&M-19:

2. Nature of Action Requested

[ ] Selection of New Contractor and Negotiation of Contract.

[X] Modification of Contract No. AT-(110-1)-2165 Contractor: University of North Carolina Chapel Hill, North Carolina

[ ] Review and approval of Contract, Sub-contract or Purchase Order. Number: Name:

[ ] Other (Explain)

3. Nature of Services to be Covered by Contract

Construction [ ] Architect-Engineer [ ] Other [X] (Explain) Research

4. Funding Amount to be Obligated by this Contract Action \$ None

Source of Funds

Approved ORO Financial Plan, Quarter, Fiscal Year 19 Project No. or, Activity No. Funds to be Obligated: Allotment No. (F.Y. 19 Funds) Procurement Directive No. Dated Issuing Office

Concurrence in Funding Statement: (signed) Chief, Budget Branch

5. Project or Activity to be Covered by Contract Action:

Location of Work: Construction Directive No. Estimated Cost of Work to be Covered by this Contract Action \$ Schedule: Date Work to Start Estimated Completion Date Description of Project or Activity:

(If more space is required use separate sheets and attach hereto:)

6. **Contract Board Docket**  
No. \_\_\_\_\_  
(To be assigned by  
Board Secretary)

7. **Request Submitted By: (signed)**  
Date: NOV 1 1957 Title: A. Scherer, acting  
C. S. SHOUP  
CHIEF, BIOLOGY BRANCH  
RESEARCH AND DEVELOPMENT DIVISION

8. **Complete Description of Services to be Furnished by Contractor:**

Headquarters designated research contract.

Title: "A Study of Ion Transport across the Smooth Muscle Cell Membrane."

(If more space is required use separate sheets and attach hereto:)

9. **Description of other changes to be covered by Modification:**

Modify contract to provide for additional research completion of which will be not later than December 31, 1957, without additional funds.

There will be no significant change in the scope of the work.

(If more space is required use separate sheets and attach hereto:)

10. **Negotiated Contracts.** (Show why it appears desirable to negotiate new contract or to negotiate modification to existing contract)

Memorandum from C. D. Van Cleave to Harman M. Roth dated October 29, 1957.

(If more space is required use separate sheets and attach hereto:)

11. **Contracts, Subcontracts, or Purchase Orders Submitted for Review and Approval:** (Furnish brief description of action in this space and attach pertinent documents)

None

12. **Disputes:**

Attach a statement summarizing the dispute together with pertinent documents and Background Material.

None

1075

1097577

OK RE 11/13/57

*Office Memorandum* • UNITED STATES GOVERNMENT

TO : Herman M. Roth, Director, Research and Development Division, Oak Ridge Operations Office      DATE: October 29, 1957

FROM : C. D. Van Cleave, Medical Branch  
Division of Biology and Medicine, Washington

SUBJECT: CONTRACT NO. AT(40-1)-2165 - UNIVERSITY OF NORTH CAROLINA

SYMBOL: HMM:CDVC

The Medical Branch approves extension without additional funds of the subject contract for the period September 1, 1957 through December 31, 1957. Attached is copy of letter from Dr. Stall requesting this extension.

*OK. MMR*

NOV 1 1957

1097578

*Office Memorandum* • UNITED STATES GOVERNMENT

TO : Herman M. Roth, Director, Research and Development Division, Oak Ridge Operations Office      DATE: October 29, 1957

FROM : C. D. Van Cleave, Medical Branch  
Division of Biology and Medicine, Washington

SUBJECT: CONTRACT NO. AT(40-1)-2165 - UNIVERSITY OF NORTH CAROLINA

SYMBOL: EMM:CDVC

The Medical Branch approves extension without additional funds of the subject contract for the period September 1, 1957 through December 31, 1957. Attached is copy of letter from Dr. Stall requesting this extension.

*OK. MMR*

NOV 1 1957

1097579

THE UNIVERSITY OF NORTH CAROLINA

Chapel Hill

The School of Medicine  
Department of Medicine

October 22, 1957

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

Dear Sir:

It is requested that the research contract # AT-(40-1)-2165, modification #1 be extended without additional funds. There are approximately \$2,000 of uncommitted funds remaining in this account. This will allow the project to continue until a contract renewal or other financial support can be obtained.

A detailed progress report of the progress to date will be prepared in the near future and submitted for your consideration.

Thanking you for any consideration you may be able to give this request, I remain,

Yours very truly,

Bernard G. Stall, III, M. D.  
Assistant Professor of Medicine

BOS:hh

COPY

NOV 1 1957

1097580

THE UNIVERSITY OF NORTH CAROLINA  
CHAPEL HILL

THE SCHOOL OF MEDICINE  
DEPARTMENT OF MEDICINE

12 September 1956

Mr. John R. Moore, Director  
Contract Division  
Oak Ridge Operations  
U. S. Atomic Energy Commission  
Oak Ridge, Tennessee

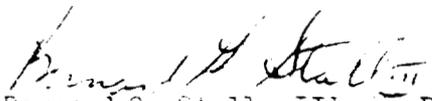
Re: ACC:ARB

Dear Mr. Moore:

Transmitted herewith are two properly signed copies of the modification No. 1 of Contract No. AT-(40-1)-2165.

Thank you very much for the expeditious manner in which this negotiation has thus far been handled.

Yours very truly,

  
Bernard G. Stall, III, M. D.

bgs;a  
Encs. *ok*

1097581

# Office Memorandum • UNITED STATES GOVERNMENT

TO : J. W. Ould, Jr., Assistant General Counsel      DATE: August 22, 1956

FROM : John R. Moore, Director, Contract Division

SUBJECT: REQUEST FOR MODIFICATION OF CONTRACT NO. AT-(40-1)-2165 -  
UNIVERSITY OF NORTH CAROLINA

SYMBOL: ACD:RGH

Please extend the period of the subject contract to August 31, 1957, with necessary funds in the amount of \$9,736. Also, please include provisions for compliance with AEC Manual Chapter 7510.

There is attached for your use a request for contract action from the Research and Development Division.

  
John R. Moore

Attachment:  
As Stated Above

CC: L. D. MacKay  
H. M. Roth  
J. Nicholson, w/encls.

225

1097582

225

1. Chairman  
TO: **J. R. Moore** Contract Board. From: **Res. & Dev. Div.**

It is requested that the Contract Board take the necessary action to process the following described contract action in accordance with the provisions of Bulletin OR-O&M-19:

2. Nature of Action Requested

- Selection of New Contractor and Negotiation of Contract.
- Modification of Contract  
No. **AT-(40-1)-2165**  
Contractor: **University of North Carolina  
Chapel Hill, North Carolina**
- Review and approval of Contract, Sub-contract or Purchase Order.  
Number: \_\_\_\_\_  
Name: \_\_\_\_\_
- Other (Explain) \_\_\_\_\_

3. Nature of Services to be Covered by Contract

Construction  Architect-Engineer  Other  (Explain) **Research**

4. Funding Amount to be Obligated by this Contract Action \$ **9,736.00**

Source of Funds

Approved ORO Financial Plan, \_\_\_\_\_ Quarter, Fiscal Year 19\_\_\_\_  
Project No. \_\_\_\_\_ or, Activity No. **6370**  
Funds to be Obligated: Allotment No. **06-71-91(2)** F.Y. 19**57** Funds)  
Procurement Directive No. **BH-57-40** Dated **8-3-56**  
Issuing Office **Div. of Biology & Medicine**

Concurrence in Funding Statement: (signed) \_\_\_\_\_

*Joseph J. Patten*  
Act. Chief, Budget Branch 8/10/56

5. Project or Activity to be Covered by Contract Action:

Location of Work: \_\_\_\_\_ Construction Directive No. \_\_\_\_\_  
Estimated Cost of Work to be Covered by this Contract Action \$ \_\_\_\_\_  
Schedule: Date Work to Start \_\_\_\_\_ Estimated Completion Date \_\_\_\_\_  
Description of Project or Activity: \_\_\_\_\_

(If more space is required use separate sheets and attach hereto:)

6. Contract Board Docket No. _____ (To be assigned by Board Secretary)	7. Request Submitted By: (signed) <u>C. S. Shoup</u> Date <u>AUG 17 1956</u> Title: _____ <small>C. S. SHOUP PLS. FILE</small>
---	--

8. Complete Description of Services to be Furnished by Contractor:

**Washington designated research contract.**

**Title: "A Study of Ion Transport Across Smooth Muscle Cell Membrane".**

(If more space is required use separate sheets and attach hereto:)

9. Description of other changes to be covered by Modification:

**Extend period of contract to August 31, 1957, with new funds in the amount of \$9,736. Include provisions for compliance with AEC Manual Chapter 7510.**

(If more space is required use separate sheets and attach hereto:)

10. Negotiated Contracts. (Show why it appears desirable to negotiate new contract or to negotiate modification to existing contract)

**Memorandum from C. W. Shilling to S. R. Sapirie, dated August 3, 1956.**

(If more space is required use separate sheets and attach hereto:)

11. Contracts, Subcontracts, or Purchase Orders Submitted for Review and Approval: (Furnish brief description of action in this space and attach pertinent documents)

**None**

12. Disputes:

Attach a statement summarizing the dispute together with pertinent documents and Background Material.

**None**

BUDGET FOR CONTRACT NO. AT-(40-1)-2165  
FOR PERIOD 9-1-56 - 8-31-57

(1) <u>Salaries and Wages:</u>		\$ 6,533.33
Dr. B. G. Stall, III (1/3 of time)	\$2,333.33	
Technician and Diener	4,000.00	
Secretarial Assistance	200.00	
(2) <u>Equipment:</u>		1,865.00
(3) <u>Supplies and Materials:</u>		3,100.00
<u>Travel:</u>		250.00
(4) <u>Overhead (30.32% of Salaries and Wages):</u>		1,980.91
	TOTAL:	<u>\$13,729.24</u>

The Commission's contribution to the above budget will be \$9,736.

1097585

UNIVERSITY OF NORTH CAROLINA  
SCHOOL OF MEDICINE  
CHAPEL HILL, NORTH CAROLINA.

CONTRACT NO. AT.\*40-1)-2165

Bernard G. Stall, M.D.  
Assistant Professor of Medicine,  
Project Leader.

A STUDY OF ION TRANSPORT ACROSS SMOOTH MUSCLE  
CELL MEMBRANE.

Resume'

Utilizing radioactive potassium and sodium, the contractor will continue studies of ion transport mechanisms into and out of smooth muscle cells and will direct the study to include the role of intermediate carbohydrate metabolism and the reactions and transformations that are of influence. The studies will include the definition of normal and altered cation and possibly anion fluxes across cell membranes, subjected to analysis in terms of CHO metabolism. The action of enzyme inhibitors will be studied with respect to energy utilization for maintaining K and Na ion balances and regulation of said balances in the cell. Related phenomena will be studied, and efforts will be made to experimentally determine by appropriate methods the factors involved in maintenance of differential ionic concentrations between the cell interior and the surrounding media.

U. S. Shoup

1097586

UNITED STATES ATOMIC ENERGY COMMISSION  
WASHINGTON, D. C.

Contract Authorization No. EM-57-40

AUG 9 1956

TO : S. R. Sapirie, Manager  
Oak Ridge Operations Office

FROM : Charles W. Shilling, M. D., Deputy Director  
Division of Biology and Medicine, Washington, D. C.

SUBJECT : FUND AUTHORIZATION AND TRANSMITTAL OF RESEARCH PROPOSAL FOR  
CONTRACT NEGOTIATION

REFERENCE : AEC 102/16 APPROVED OCTOBER 7, 1953, AS IMPLEMENTED BY MEMORANDUM  
TO MANAGERS, OPERATIONS OFFICES, DATED OCTOBER 23, 1953, JOINTLY  
SIGNED BY THE DIRECTORS OF THE DIVISIONS OF RESEARCH AND BIOLOGY  
AND MEDICINE.

SYMBOL : **EM:CVH**

The research proposal described below has been approved by the  
Division of Biology and Medicine, funds are available, and you  
are authorized and requested to negotiate a contract in  
accordance with the following terms and conditions:

1. Institution: **University of North Carolina**
2. Investigator (s): **Bernard G. Stall, III, M. D.**
3. Title: **"A Study of Ion Transport Across Smooth Muscle Cell  
Membrane"**
4. ( ) New Contract, (  ) Renewal of Contract No. AT(40-1)2165
5. Duration: **9/1/56 through 8/31/57**
6. AEC Technical Representative: **Clifford V. Harding** *CVH*
7. Funds are authorized for the obligation of this contract  
as follows:

<u>Allotment No.</u>	<u>Budget Category</u>	<u>Previous</u>	<u>Amount This Action</u>	<u>Total</u>
<u>06-71-91 (24)</u>	<u>6320</u>	<u>          </u>	<u>\$ 9,736</u>	<u>\$ 9,736</u>
<u>          </u>	<u>          </u>	<u>          </u>	<u>          </u>	<u>          </u>
<u>          </u>	<u>          </u>	<u>          </u>	<u>          </u>	<u>          </u>

1097587

7-6777  
AUG 7 1956

8. It is suggested that in the best interests of the government the following type contract be negotiated: **Lump-sum**
9. It is requested that the title to any capital equipment procured under this contract shall be vested with:
- the contractor;      (   ) the government.
10. If radioisotopes are to be used in this research, it is requested that the savings available to the contractor under the Radioisotope Research Support Program (Ref. AEC Manual Chapter 7510) be considered in the negotiation of the amount to be funded under this contract.
11. Other comments:

12. Security Requirements:

In accordance with the provisions of Chapter 3403 of the AEC Manual and the requirements of the Declassification Guide, it has been determined that the following security precautions should be taken in connection with the proposed research contract:

**Since there is essentially no chance for the development of restricted data, this project has been placed in Category I as defined in Chapter 3403 of the AEC Manual.**

13. Reports:  Reports are to be required as provided for by "Revised Guide for the Submission of Research Proposals" dated February 8, 1954.

(   ) Special reports instructions are as follows:

Enclosures:       "A" - Proposal, dated June 1, 1956  
                   "B" - Notification letter, dated AUG 3 1956  
                  (   ) "C" - Other correspondence, none letters

Distribution:

Addressee: Original (w encl.)	Division File: Yellow copy (w encl.)
1st copy (w encl.)	Pink copy (w/o encl.)
2nd copy (w encl.)	
	Branch File: White copy (w encl.)

Program Analysis Branch:  
                  White copy (w/o encl.)

3. Renewal Proposal: The ultimate objections of this project have been severely altered in the direction of being expanded. It seems very likely that not one, but many factors are involved in the maintenance of the differential cation concentrations between the cell interior and its surrounding water. For smooth muscle cells there are evidences from preliminary studies which suggest that many of the reactions and transformations of intermediate carbohydrate metabolism may bear directly or indirectly on the production and maintenance of this state. It is likewise probable that this process is likewise intimately associated with the various energy transformations involved in the behavior of myosin and actin during contraction and relaxation. Carrying this subject through to its ultimate conclusion would likely entail solution of most of the problems of cellular chemistry and physics. It is proposed, after accurate definition of normal resting cation and possibly anion fluxes across the membranes, to subject the system to analysis in terms of carbohydrate metabolism. Earlier work has shown that inhibition of high energy phosphorylation by any of several enzyme inhibitors effectively prevents the utilization of energy for maintaining high intracellular  $K^+$  and low  $Na^+$  suspended in an antithetically ionically constituted medium. Several other points of close association between these two broad phenomena have been demonstrated by numerous workers in the field in the case of other tissues. Relative importances and basic significance are unelucidated experimentally.

Scientific

Personnel: Unchanged since initial proposal.

Other Personnel: No change.

Other Financial Assistance: None.

Materials, Equipment, and Facilities:

- A. Available (or will be in near future): Adequate laboratory space, furnishings, and utilities, scintillation counter and scaler, flame photometer, Koller Smith Balance, analytical balance, pH meter, Kjeldahl digestion and distillation apparatus, transformers, Warburg apparatus, survey meter, personnel monitoring dosimeters, reagents, isotope handling and storage facilities.
- B. Major Items to be procured:
  - 1) Radiation Analyzer. The recent commercial availability of this apparatus for pulse height selection would allow several ions to be traced simultaneously in the same tissue slices. In addition to increasing the validity of such data over the case where separate ions were traced in different experiments using different tissue, there is the additional advantage of securing data from one experiment that otherwise would require several.
  - 2) Van Slyke Manometric Apparatus and Flow Counter. This is needed for counting of  $C^{14}$  in tracing metabolic fates of carbohydrate intermediates.

Travel and Other Items: Funds are to be used for purposes of attending scientific meetings and programs germane to this project as well as for other minor communication needs.

Budget

	Proposed Contribution by:	
	<u>AEC</u>	<u>UNC</u>
<u>Personnel, Scientific</u>		
B. Stall (1/3 time)		\$2,333.33
<u>Other Personnel</u>		
Technician	\$3,600	
Diemer (and animal care)	400	
Secretarial Assistance		200
<u>Permanent Equipment</u>		
1) Radiation analyser (plus alterations in present scaler to adopt it for this use)	1,000	
2) Van Slyke Manometric Apparatus	385	
3) Windowless Flow Counter	480	
<u>Supplies and Expendable Materials</u>		
Glassware, reagents, miscellaneous small items	1,200	200
Isotopes	1,500	
Animals	200	
<u>Travel</u>	250	
<u>Overhead (8% AEC total)</u>	721.20	
Administrative Overhead (30.32% combined personnel costs to UNC and AEC less 8% AEC total)		1,259.71
	<hr/>	<hr/>
	\$9,736.20	\$3,993.04

S U M M A R Y

Proposed AEC support	\$9,736.20
Proposed UNC support	<u>3,993.04</u>
Total Cost of Project	\$13,729.24

Statement of Current Expenditures

Contract No. AT-(40-1)-2165, First Period

	Expenditures 9/1/55 - 4/30/56		Estimated 5/1/56 - 8/31/56		TOTAL
	AFC	UNC	AFC	UNC	
Salaries and wages	\$2,266.64	\$2,133.28	\$1,433.32	\$1,066.72	\$ 6,899.96
Equipment	2,706.40	- 0 -	2,167.41	- 0 -	4,873.81
Supplies and services	1,244.47	145.00	1,550.84	55.00	2,995.31
Travel	- 0 -	- 0 -	- 0 -	- 0 -	- 0 -
Communication and publication	4.25	- 0 -	10.00	- 0 -	14.25
<b>Total direct costs</b>	<b>\$6,221.76</b>	<b>\$2,278.28</b>	<b>\$5,161.57</b>	<b>\$1,121.72</b>	<b>\$14,783.33</b>
Indirect cost*(30.32%)		\$1,334.06		\$ 758.01	\$ 2,092.07
" " (8.00%)	497.74	- 497.74	412.93	- 412.93	
	\$ 497.74	\$ 836.32	412.93	\$ 345.08	\$ 2,092.07
<b>Total costs</b>	<b>\$6,719.50</b>	<b>\$3,114.60</b>	<b>\$ 5,574.50</b>	<b>\$1,466.80</b>	<b>\$16,875.40</b>

\*Overhead rate 30.32% of direct salaries and wages determined by Army Audit Agency, based on our accounts for the fiscal year ended June 30, 1955.

## Office Memorandum • UNITED STATES GOVERNMENT

TO : J. W. Ould, Jr., Assistant General Counsel      DATE: October 5, 1955

FROM : John R. Moore, Director, Contract Division

SUBJECT: REQUEST FOR PREPARATION OF RESEARCH CONTRACT WITH UNIVERSITY OF  
NORTH CAROLINA, DR. B. G. STALL, PROJECT LEADER

SYMBOL: ADA:ARB

Enclosed is an approved proposal from the University of North Carolina for a research project entitled "A Study of Ion Transport Across Smooth Muscle Cell Membrane", with Dr. B. G. Stall as Project Leader. This action is covered by Contract Authorization No. EM-56-80, dated September 20, 1955, in the amount of \$12,794.

Please prepare an appropriate research contract to cover this program for a period of one year, beginning September 1, 1955, with Commission funds in the amount of \$12,294.00, in accordance with the attached budget.

John R. Moore 

## Enclosures:

1. Request for Contract Action
2. Budget for New Contract
3. Resume'
4. Contract Authorization EM-56-80
5. Proposal
6. Cy ltr fm Shoup to Stall, 9/28/55

CC: C. S. Shoup  
L. D. MacKay  
J. Nicholson, w/Encls. 1 and 2

1097592

1. Chairman  
 TO: J. R. Moore Contract Board. From: Research & Development Div.

It is requested that the Contract Board take the necessary action to process the following described contract action in accordance with the provisions of Bulletin OR-ORM-19:

2. Nature of Action Requested

- Selection of New Contractor and Negotiation of Contract.  
 University of North Carolina  
 Chapel Hill, North Carolina
- Modification of Contract  
 No. \_\_\_\_\_  
 Contractor: \_\_\_\_\_
- Review and approval of Contract, Sub-contract or Purchase Order.  
 Number: \_\_\_\_\_  
 Name: \_\_\_\_\_
- Other (Explain) \_\_\_\_\_

3. Nature of Services to be Covered by Contract

Construction  Architect-Engineer  Other  (Explain) Research

4. Funding Amount to be Obligated by this Contract Action \$ 12,294.00

Source of Funds

Approved ORO Financial Plan, \_\_\_\_\_ Quarter, Fiscal Year 19\_\_\_\_  
 Project No. \_\_\_\_\_ or, Activity No. 6320  
 Funds to be Obligated: Allotment No. 6-61-9A-4 (F.Y. 19\_\_\_\_ Funds)  
 Procurement Directive No. BM-56-80 Dated Sept. 20, 1955  
 Issuing Office Division of Biology & Medicine

Concurrence in Funding Statement: (signed) \_\_\_\_\_

*A. Miller*  
 Chief, Budget Branch

5. Project or Activity to be Covered by Contract Action:

Location of Work: \_\_\_\_\_ Construction Directive No. \_\_\_\_\_  
 Estimated Cost of Work to be Covered by this Contract Action \$ \_\_\_\_\_  
 Schedule: Date Work to Start \_\_\_\_\_ Estimated Completion Date \_\_\_\_\_  
 Description of Project or Activity:

(If more space is required use separate sheets and attach hereto:)

6. Contract Board Docket

No. \_\_\_\_\_  
(To be assigned by ,  
Board Secretary)

7. Request Submitted By: (signed) David F. Cope  
Date: 10-3-55 Title: \_\_\_\_\_

David F. Cope  
Acting Director  
~~Research & Development Div.~~

8. Complete Description of Services to be Furnished by Contractor:

washington designated research contract.  
Title: "A Study of Ion Transport Across Smooth Muscle Cell Membrane".

(If more space is required use separate sheets and attach hereto:)

9. Description of other changes to be covered by Modification:

New contract for the period of one year beginning September 1, 1955, with Commission funds in the amount of \$12,294.00.

(If more space is required use separate sheets and attach hereto:)

10. Negotiated Contracts. (Show why it appears desirable to negotiate new contract or to negotiate modification to existing contract)

Nemo to S. R. Sapirie from J. C. Bugher dated September 20, 1955.

(If more space is required use separate sheets and attach hereto:)

11. Contracts, Subcontracts, or Purchase Orders Submitted for Review and Approval: (Furnish brief description of action in this space and attach pertinent documents)

None

12. Disputes:

Attach a statement summarizing the dispute together with pertinent documents and Background Material.

None

1097594

Budget For New Contract - Dr. E. G. Stall

for Period 8/1/55 - 8/30/56

Salaries and wages:		\$ 7,200.00
<u>Dr. E. G. Stall</u> , (1/3 time)	\$3,000.00	
Research Assistants, Technicians, Etc.	4,000.00	
Secretarial Assistance	200.00	
1. <u>Equipment:</u>		4,571.00
2. <u>Supplies and Materials:</u>		2,725.00
3. <u>Travel:</u>		250.00
4. <u>Overhead</u> (36.11% of Salaries and Wages):		<u>2,599.92</u>
	Total	\$17,345.92

The Commission's contribution to the above budget will be \$12,294.00 and the Contractor's contribution will be \$5,051.92.

1097595

UNIVERSITY OF NORTH CAROLINA  
SCHOOL OF MEDICINE  
DEPARTMENT OF MEDICINE  
CHAPEL HILL, NORTH CAROLINA.

Bernard G. Stall, M.D.  
Assistant Professor of Medicine  
Project Leader.

A STUDY OF ION TRANSPORT ACROSS SMOOTH MUSCLE CELL MEMBRANE

Resume'  $Na^+$

The Contractor proposes to use radioactive potassium and sodium in the study of mechanisms transporting potassium and sodium ions into and out of smooth muscle cells, to relate variations in fluxes of  $Na^+$  and  $K^+$  in and out of the cells in various functional states on stimulation by various substances such as epinephrine, norepinephrine, acetylcholine, cholinesterase inhibitors, pitressin, sodium azide, etc. The effect, if any, of various biologically-active steroids on sodium and potassium movement will be studied in association with muscle function. It is hoped the variable and unpredictable reactivity of smooth muscle can be more correctly elucidated by the methods and experimentation proposed.

C. S. Shoup

1097596

In Reply  
Refer to: ONE:ER

Oak Ridge, Tennessee  
September 28, 1955

Dr. Bernard G. Stall  
Department of Medicine  
University of North Carolina  
Chapel Hill, North Carolina

Subject: RESEARCH CONTRACT

Dear Dr. Stall:

We have initiated action for the preparation of a research contract covering your work on "A Study of Ion Transport Across Smooth Muscle Cell Membranes". The contract will be for a period of one year beginning September 1, 1955, with the Commission contributing \$12,294 to the total cost of \$17,345.92. A copy of the budget to be included in the contract is enclosed for your information. The contract will be mailed to you for signature as soon as it is complete.

In accordance with your telephone conversation with J. E. Rounsaville, we deleted \$1,600 "Equipment" contribution by the University of North Carolina since the equipment is already on hand. We also reduced the amount allocated for "Isotopes" from \$1,500 to \$1,000 which was discussed with Mr. Rounsaville.

If you have any questions, or if we can be of assistance to you in any way, please do not hesitate to call upon us.

Very truly yours,

C. S. Sheep  
Chief, Biology Branch  
Research and Development Division

Enclosure:  
Budget

CC: C. E. Teague, North Carolina  
J. R. Moore ✓

Res. Serv. Br. Bio. Br.

Rounsaville:lr

9/

9/

1097597

UNITED STATES ATOMIC ENERGY COMMISSION  
WASHINGTON, D. C.

Contract Authorization No. EM-56-80

TO : S. R. Sapiro, Manager  
Oak Ridge Operations Office

SEP 20 1955

FROM : John C. Bugher, M. D., Director, Division  
of Biology and Medicine, Washington, D. C. *J. C. B.*

SUBJECT : FUND AUTHORIZATION AND TRANSMITTAL OF RESEARCH PROPOSAL FOR  
CONTRACT NEGOTIATION

REFERENCE : AEC 102/16 APPROVED OCTOBER 7, 1953, AS IMPLEMENTED BY MEMORANDUM  
TO MANAGERS, OPERATIONS OFFICES, DATED OCTOBER 23, 1953, JOINTLY  
SIGNED BY THE DIRECTORS OF THE DIVISIONS OF RESEARCH AND  
BIOLOGY AND MEDICINE.

SYMBOL : **EMM:PGL**

The research proposal described below has been approved by the  
Division of Biology and Medicine, funds are available, and you  
are authorized and requested to negotiate a contract in  
accordance with the following terms and conditions:

1. Institution: **University of North Carolina**
2. Investigator (s): **Bernard G. Stall, III, M. D.**
3. Title: **"A Study of Ion Transport Across Smooth Muscle  
Cell Membrane"**
4. (  ) New Contract, ( ) Renewal of Contract No. \_\_\_\_\_
5. Duration: **one year**
6. AEC Technical Representative: **Paul G. Lefevre**
7. Funds are authorized for the obligation of this contract  
as follows:

<u>Allotment No.</u>	<u>Budget Category</u>	<u>Previous</u>	<u>Amount This Action</u>	<u>Total</u>
<u>06-61-91 (24)</u>	<u>6320</u>	<u>          </u>	<u>\$12,794</u>	<u>\$12,794</u>
<u>          </u>	<u>          </u>	<u>          </u>	<u>          </u>	<u>          </u>
<u>          </u>	<u>          </u>	<u>          </u>	<u>          </u>	<u>          </u>

*E-6436*

1097598

8. It is suggested that in the best interests of the government the following type contract be negotiated: **Lump-sum**
9. It is requested that the title to any capital equipment procured under this contract shall be vested with:
- the contractor;      ( ) the government.

10. Other comments:

Please negotiate concerning the figure allotted for isotopes, in the light of the new pricing policy, and reduce accordingly the amount of the contract. (It is assumed that the reduction thus arrived at will be on the general order of \$1,000.)

The contract is to be negotiated with the starting date of September 1, 1955.

11. Security Requirements:

In accordance with the provisions of Chapter 3403 of the AEC Manual and the requirements of the Declassification Guide, it has been determined that the following security precautions should be taken in connection with the proposed research contract:

Since there is essentially no chance for the development of restricted data, this project has been placed in Category I as defined in Chapter 3403 of the AEC Manual.

12. Reports:     Reports are to be required as provided for by "Revised Guide for the Submission of Research Proposals" dated February 8, 1954.
- ( ) Special reports instructions are as follows:

Enclosures:     "A" - Proposal, dated \_\_\_\_\_  
                   "B" - Notification letter, dated SEP 20 1955  
                  ( ) "C" - Other correspondence, none letters

Distribution:

Addressee:    Original (w encl.)      Division File: Yellow copy (w encl.)  
                  1st copy (w encl.)      Pink copy (w/o encl.)  
                  2nd copy (w encl.)      Branch File:    White copy (w encl.)

Program Analysis Branch:  
                  White copy (w/o encl.)

## PROPOSAL

1. Title of Project: A Study of Ion Transport across Smooth Muscle Cell Membrane
2. Institution and Department in which work will be done: School of Medicine,  
University of North Carolina, Department of Medicine
3. Scientific Background of the Proposed Project:

Vertebrate smooth muscle cells in common with most animal and plant cells maintain a high concentration of potassium internally despite a relatively low concentration in the surrounding liquid phase. The other major cation of body fluid, sodium, is related reciprocally, being low in concentration intracellularly and high extracellularly. That this relation does not depend entirely upon unidirectional impermeability of the cellular membrane to these ions, but is due at least partly to an active transport of one or both ions thru the membrane, has now been established for a number of tissues both in vitro and in vivo with the use of radioactive tracers.

These include the red blood cell as demonstrated by Hahn, Hevesy, and Rebbe<sup>(1)</sup>, Cohn<sup>(2)</sup>, Dean, Noonan, Haege, and Fenn<sup>(3)</sup>, Raker, Taylor, Weller, and Hastings<sup>(4)</sup>, and others; in nerve axons by Hodgkin and Huxley<sup>(5)</sup>; in brain slices by Stern, Eggleston, Hems, and Krebs<sup>(6)</sup>; striated muscle by Fenn, Noonan, Haege and Mullins<sup>(7) (8)</sup>, Hevesy and Hahn<sup>(9)</sup>, Calkins, Taylor and Hastings<sup>(10)</sup>, and others; in rabbit cortex by Mudge<sup>(11)</sup>. So far as is known to the proposer no such studies have been reported in the case of smooth muscle.

The differential cation concentration between intra- and extracellular fluid has been shown to be associated with a difference in electrical potential across the membrane. In the case of nerve and muscle the chemical and electrical phenomena have been shown to be intimately related to the functional

response of these tissues to appropriate stimuli. The classical studies of Hodgekin and Huxley using the giant axon of squid have traced the sequential relationship of the chemical and electrical phenomena to impulse conduction along the nerve, refractoriness to further stimulation, and the eventual restriction of the resting, excitable state.

Studies done on a variety of types of smooth muscle by Bigg and Mannier have shown that stimulation via autonomic pathways or by autonomic agents resulted in a rapid influx of Na ions closely followed by a reversal of the membrane potential. Thus it seems possible that the sequence of events described in so detailed a fashion by Hodgekin and Huxley for squid axon may represent a phenomenon common to many or all excitable tissues.

Since the responsiveness of excitable tissue to an appropriate stimulus is ultimately dependent upon differential concentrations of K and Na inside and outside cells, information relative to the mechanisms by which these ions are transported and factors regulating these transport mechanisms seems eminently desirable.

The studies of Stern et al<sup>(6)</sup> on brain slices have shed light on the mechanism by which K<sup>+</sup> is transported into the cell. They showed that it was an enzymatic reaction dependent on the presence of oxygen, a "balanced" ionic constituency of the extracellular phase, and the presence of glucose and of glutamic or aspartic acid in the suspending medium. Studies with inhibitors suggested that the enzyme concerned might be carbonic anhydrase.

A relationship between acetylcholine, acetylcholinesterase, K<sup>+</sup>, and carbohydrate metabolism, and the function of nerve and muscle tissue has been suggested by numerous studies reviewed by Wilson and Nachmansohn<sup>(12)</sup>.

Interest in the project proposed here stems from participation in clinical studies on patients with essential hypertension in which an attempt was made by balance studies and isotope dilution techniques to find some difference in salt metabolism between hypertensive patients and normotensive controls in their responses to marked restriction of sodium intake with high, low, and average intakes of potassium. However, these studies failed to show any differences between hypertensives and normotensives or between the hypertensives who responded to sodium restriction with a decline in blood pressure and those who did not.

During the course of these studies it became evident that the methods available were too gross to detect a defect of salt metabolism in essential hypertensive patients. Likewise it became obvious that a rational approach to the study of hypertension in patients could not be made without more knowledge of the basic chemistry and physiology of the tissue responsible for the production of elevated blood pressure, i.e., arteriolar smooth muscle.

During the preceding 1-1/2 years studies on smooth muscle metabolism were carried out by the proposer at Brookhaven National Laboratory. Since arteriolar smooth muscle proved technically unsatisfactory, other sources of smooth muscle were tried and, of those available, the pigeon gizzard was found to be the most suitable. It proved to be densely cellular and homogenous and lent itself nicely to conventional tissue slicing techniques. Material could be obtained from a single animal for detailed experimental manipulation.

The project to date has centered around the tissue electrolyte response to the trauma associated with being sliced, definition of conditions necessary for restitution and maintenance of the electrolyte pattern of the basal,

resting state, and lately with measuring of  $\text{Na}^+$  and  $\text{K}^+$  in and out fluxes in the resting, steady state by means of isotopic tracers. This proposal is for continuation of this project which until recently was supported entirely by the A. E. C. thru Brookhaven National Laboratory.

#### Bibliography

- 1) Hahn, L. A., Hevesy, G. C., Rebbe, O. H. Biochemical J., 1939, 33, 1549.
- 2) Cohn, W. C., Am. J. Physiol., 1941, 133, 242.
- 3) Dean, R. B., Noonan, T. R., Haege, L., and Fenn, W. O. J. Gen. Physiol., 1941, 24, 353.
- 4) Raker, J. W., Taylor, I. M., Weller, J. M., and Hastings, A. E. Rate of Potassium Exchange of the Human Erythrocyte. J. Gen. Physiol., 1950, 33, 691.
- 5) Hodgkin, A. L., and Huxley, A. F. Currents Carried by Na and K Ions thru the Membrane of the Giant Axon of Loligo. J. of Physiol., 116:449 (1952a).
- 6) Stern, J. R., Eggleston, L. V., Hens, R. and Krebs, H. A. K Transport in Brain Slices. Biochem. J., 44:410 (1949).
- 7) Fenn, W. O., Noonan, T. R., Mullins, L. J., and Haege, L. Am. J. Physiol., 135:149 (1941/42).
- 8) Noonan, T. R., Fenn, W. O., and Haege, L. Am. J. Physiol., 132:474 and 614, (1941)
- 9) Hahn, L., and Hevesy, G. Effect of Exercise on  $\text{K}^{42}$  Interchange in the Gastrocnemius Muscle of the Rat. Acta Physiol. Scand., 2:51 (1941)
- 10) Calkins, E., Taylor, I. M., and Hastings, A. E. K Exchange in the Isolated Rat Diaphragm. Am. J. Physiol., 177:211 (1954).

- 11) Hodge, G. H. Electrolyte Metabolism of Rabbit Kidney Slices. Studies with Radioactive Potassium and Sodium. Am. J. Physiol., 173:511 (1953).  
12) \*

#### 4. Scientific Scope of the Proposed Research

The objectives of this research are: (1) To elucidate the mechanisms of  $K^+$  and  $Na^+$  transport into and out of smooth muscle cells, (2) To relate variations in the fluxes of  $Na^+$  and  $K^+$  into and out of smooth muscle cells with their functional state on stimulation by various substances to which they are known to be responsive, e.g., epinephrine, norepinephrine, acetylcholine, cholinesterase inhibitors, pitressin, Na azide, etc., (3) To ascertain the effect, if any, of various biologically active steroids on Na and K fluxes and in association therewith on muscle function.

It is hoped that the variable, unpredictable and apparently paradoxical reactivity of smooth muscle to various stimulating substances can be reduced to some common denominator, perhaps cation flux.

A plan of accomplishment for the first year's work is as follows:

- 1) Refinement of methods for measuring  $Na^+$  and  $K^+$  fluxes in smooth muscle tissue in the resting, steady state
- 2) A subsection of this system to various stimulating substances for observation of their effects on  $Na^+$  and  $K^+$  flux.
- 3) Test the effect of steroids on Na and K fluxes (A) by incubating tissue slices with the steroid, (B) pretreatment of the animals with steroids.

#### 5. Scientific Personnel

Senior Investigator: Bernard G. Stall

\* Wilson, I. B. and Nachmansohn, D. Generation of Bioelectric Potentials. Symposium on Ion Transport Across Membranes. Edited by Hans T. Clarke. Academic Press, Inc., New York, N. Y., 1954.

5. Scientific Personnel (continued)

Highest Academic Degree: M. D.

Position in Institution: Assistant Professor, Department of Medicine

Scientific Experience:

- 1) Rockefeller Institute for Medical Research - Assistant to Institute, Assistant Physician to its hospital - February 27, 1950 - February 19, 1951. Full time research in essential hypertension and electrolyte physiology of sweat.
- 2) Brookhaven National Laboratory - Associate Physician in Department of Medicine, Division of Physiology - January 11, 1953 - May 13, 1955. Full time research on essential hypertension and smooth muscle metabolism.

Publications:

- 1) Methods for Local Induction and Quantitative Analysis of Human Sweat. Bernard G. Stall, Vincent A. Dole, and Irving L. Schwartz. Proc. Soc. for Exper. Biol. & Med., 77:412, 1951.
- 2) Algunas Alteraciones Endocrinas en la Enfermedad de Graves. F. Malcefy y Bernard G. Stall. Archivos Medicos de Cuba No. 1, Vol. 5, Enero 1954.
- 3) Metabolic Effects of Marked Sodium Restriction in Hypertensive Patients: Changes in Total Exchangeable Sodium and Potassium. Lewis K. Dahl, Bernard G. Stall and George C. Cotzias. J. Clin. Invest., 33:1397, 1954.
- 4) Metabolic Effects of marked Sodium Restriction in Hypertensive Patients: Skin Electrolyte Losses. Lewis K. Dahl, Bernard G. Stall and George C. Cotzias. J. Clin. Invest., 34:462, 1955.
- 5) Metabolic Effects of Marked Sodium Restriction in Hypertensive Patients: III. Comparison of Normals vs. Hypertensives. (submitted for publication)

6. Other Personnel

Technician - 1; full-time

7. Other Financial Assistance: None

8. Materials, Equipment and Facilities Available:

Laboratory, instrument room and office space

Utilities (heat, water, gas, air and vacuum outlets)

Warburg apparatus

Major Items to be Procured:

- 1) Scintillation Counter, well type, with decade scaler, photomultiplier, crystal, and pig - installed. This is needed for radioactivity measurement in association with cation exchange studies using  $\text{Na}^{24}$  &  $\text{K}^{42}$  as tracers.
- 2) Flame Photometer - needed for Na and K analysis
- 3) Balance, Roller-Smith type - for weighing tissue slices
- 4) Balance, torsion - for weighing reagents used in preparation of media
- 5) pH Meter, for measuring pH of media before and after incubation of tissues; and for glucose determination by potentiometric titration with Ceric Sulfate.
- 6) Digestion Apparatus - for digesting tissue slices for K and Na analysis
- 7) Micro-Kjeldahl Distillation Apparatus (2) - for measuring tissue nitrogen
- 8) Variac Transformers (2) for operation of digestion & distillation apparatus.
- 9) Air Conditioner, 3/4 ton - needed to provide a suitable environment for proper functioning and maintenance of radioactive counting equipment in the room in which it is to be housed. The available room has a southwestern exposure and would not otherwise be suitable.

9. Travel

For purpose of attending scientific meetings germane to proposed research project.

10. Budget (see sheet attached)

*Bernard G. Stall*

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Bernard G. Stall, III, M. D.  
Responsible Investigator  
Department of Medicine

*H. D. Carmichael, Jr.*

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H. D. Carmichael, Jr.  
Vice-President and Controller  
University of North Carolina

10. Budget

	Proposed Contribution by:	
	<u>AEC</u>	<u>UNC</u>
<u>Personnel, Scientific</u>		
B. Stall (1/3 time)		\$ 3,000
<u>Other Personnel</u>		
Technician	\$ 3,600	
Secretarial Assistance		200
Diener (and animal care)	400	
<u>Permanent Equipment</u>		
1) Warburg Apparatus, complete		1,600
2) Scintillation Counter, well type, complete with decade scaler, mounted crystal in lead pig, and photo-multiplier, including installation	2,200	
3) Flame Photometer	650	
4) Balance, Koller-Smith, 0-500 mg.	201	
5) Balance, Torsion	175	
6) pH Meter, Beckman Model H-2	220	
7) Digestion Apparatus, micro	150	
8) Micro-Kjeldahl Distillation Apparatus (2)	150	
9) Variac Transformers (2)	100	
10) Air-Conditioning Unit (3/4 ton)	600	
11) Demineralizer (water) and cartridges	125	
<u>Supplies and Expendable Materials</u>		
Glassware, reagents, miscellaneous small items	1,400	200
Isotopes (including shipping charges from Oak Ridge)	1,500	
Animals	125	
<u>Travel</u>	250	
<u>Overhead (8% AEC total)</u>	947.68	
Administrative Overhead (36.11% UNC and AEC personnel contribution minus 8% AEC total)	\$12,793.68	1,652.24
		<u>\$6,652.24</u>

(See next page for "Summary")

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S U M M A R Y

Proposed AEC support	\$ 12,793.68
Proposed UNC support	6,652.24
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Total Cost of Project	\$ 19,445.92

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