

Dr. M. Herson, F1d Tox Branch
D/Med Res, Bldg. 3220 (355)

DMCR-4

Request for Negotiation of a Contract for Measurements of Penetration or Retention of Liquid Compounds by Human Skin, CRDL Request No. 2-57-4

Director, Procurement
ATTN: Ch, R&D Proc Div
101 Edgewood Arsenal, Md.

Deck Director
CRDL

21 SEP 1964
15-1000/2057/10

1. It is requested that a research and development contract be negotiated for measurements of penetration or retention of liquid compounds by human skin, for a period of one (1) year. The FY'64 funds, \$15,000.00, are chargeable to Project No. 15-1000-2-1 (Biological approach to New agents - U.S. 577, A.S. 5-374-01, ARPA appropriation. The remaining \$15,000.00 and \$5,000.00 will be funded in FY'65 and FY'66, respectively, as funds become available.

2. The proposed contractor shall undertake research as described in the attached inclosures.

FOR THE DIRECTOR

4 Inclos

- 1. ACRIC Form 5-44
- 2. Patent Rights Checklist
- 3. SF for Limitation
- 4. Res Request Checklist

S. D. J...
Director

Handwritten notes:
15-1000-2-1
2057/10

Distribution:

- 0 & 3 - Dir/Proc
- 1 - Med Mail & File
- 1 - Med Res Reading File
- 1 - CRDL Reading File
- 1 - Med Res Contract Off
- 1 - Contract Proj Off
- 1 - Ch, Toxicol Div
- 1 - PCO, CEB, CRDL

Handwritten signature:
J...
8/8 Oct 63

CONTRACT INFORMATION

DATE: 13 September 1963

1. TITLE OF PROPOSED PROCUREMENT: Measurements of Penetration or Retention of Liquid Compounds by Human Skin			
2. TOTAL ESTIMATED COST: 139,000.00		3. CONTRACT REQUEST NO.: 32-MT-4	
4. PROJECT NUMBER: 1352230LA079-31	TITLE: Biological Approach to New Agents (U)	COST BY PROJECT: \$15,000 FY64 \$18,000 FY65 \$5,000 FY66	TYPE OF FUNDS: RDT&I appropriation A.O. 5-374-20, C.C. 557 FY64 funds
5. CONTRACT PROJECT OFFICER: NAME: Dr. Millard W. Marshon		DIVISION: Toxicology	PHONE NO.: 24257
ALTERNATE CONTR. PROJ. OFFICER: NAME: Dr. Milton E. Joffe		DIVISION: Off of Asst/Dir	PHONE NO.: 5150

6. SCOPE:
1. Services to be performed:

(1) The contractor shall furnish the necessary facilities, personnel, equipment, materials and supplies to investigate microanatomy and physiology of human skin penetration by various substances applied in vitro and in vivo.

(2) The investigation shall include development of techniques for determining penetration rates of various liquid compounds applied on skin of human volunteers. Preferred techniques will measure penetration of compounds which do not produce overt physiological effects, but safe use with volunteers is the prime consideration. Changes to be measured may include, but are not limited to, the following:

- (a) Alteration of surface counts of radiolabel in skin.
- (b) Migration of radiolabel, as determined by differences in skin surface count with time, before and after scotch tape stripping.
- (c) Detection of radiolabel in body fluids or biopsy specimens.
- (d) Accumulation of penetrant in human epidermal cell space in amounts detectable by chemical or physical means at given intervals after application.
- (e) Measurable alterations in normal structure, chemical composition, or enzymatic activity in the epidermal cell space or less superficial skin layer.
- (f) Vasomotor effects as indicated by local color or temperature changes.
- (g) Alteration of skin function as by inhibition of sweating or sebaceous secretion, pilomotor activity, psychogalvanic skin response, etc.

(3) Applications on volunteers shall be preceded by studies to establish in vitro rates of penetration through freshly excised human skin. Such studies shall be conducted under conditions of controlled temperature and humidity approximating in vivo states. These studies shall be used to eliminate compounds which fail to penetrate skin at rates consistent with in vivo detection by radiotracer and/or other measuring techniques.

6. SCOPE (Continued)

(4) Studies shall be designed to characterize binding properties of keratinous layers in human skin. These studies may involve, but are not limited to, the following:

(a) Effects of humidity, temperature, sweating, or other environmental influences on "reservoir" functions of skin.

(b) Differences in reservoir effect with various compounds.

(c) Influences on penetration and/or reservoir effect resulting from keratin modification by hydration, surfactants, silicones, keratolytics, etc.

(5) Policies for selection of liquid test penetrants shall be established by agreement between the contractor and the Technical Representative of the Contracting Officer.

B. Drawings and Specifications: N/A

C. Materials to be Furnished by Contractor: N/A

D. Reports by Contractor:

(1) The contractor shall prepare and submit the following technical reports, which shall be prepared in accordance with Army format (CMDL Memo 335-1), to be supplied to the contractor by the Technical Representative of the Contracting Officer.

(a) Twenty-four (24) copies and a reproducible master copy (duplimate or ozalid) of a Semi-Annual Progress Report shall be submitted seven (7) months after initiation of work under this contract.

(b) Twenty-four (24) copies and a reproducible master copy (duplimate or ozalid) of a Final Comprehensive Summary Report, summarizing performance for the entire year, and including conclusions and recommendations, shall be submitted thirteen (13) months after initiation of work under this contract.

(c) Four (4) copies of an Informal Quarterly Letter Report shall be submitted on or before 15 December 1963, 15 March 1964, 15 June 1964 and 15 September 1964, unless a Semi-Annual or Final Comprehensive Report has been submitted within thirty (30) days of such date. These letters shall cover nature of work in progress, significant achievements since the previous report, difficulties being encountered, and plans for the following period.

(2) Distribution shall be made to the following addressees directly by the contractor in the number of copies stipulated below:

(a) Quarterly Letter Reports: Three (3) copies of each of the required Quarterly Reports shall be furnished to :

Commanding Officer
U. S. Army Chemical Research and Development Laboratories
AFTR: Contract Project Officer (by name)
Edgewood Arsenal, Maryland

5. SCOPE (Continued)

One copy of Quarterly Report shall be furnished to:

Director, Procurement

ATTN: Contract Negotiator and Administrator (by name)

U. S. Army Edgewood Arsenal, Maryland

(b) Semi-Annual Progress Reports

-1- Thirteen (13) copies of the report, plus a reproducible master copy, shall be forwarded to the Commanding Officer, U. S. Army Chemical Research and Development Laboratories, Edgewood Arsenal, Md., ATTN: Contract Project Officer (by name).

-2- One (1) copy of this report will be forwarded to the Director, Procurement, U. S. Army Edgewood Arsenal, Maryland, ATTN: Contract Negotiator and Administrator (by name).

-3- Ten (10) copies of this report shall be addressed to the Commander, Armed Services Technical Information Agency, ATTN: TIPCR, Arlington Hall Station, Arlington 12, Virginia.

(c) Final Comprehensive Summary Report

-1- Thirteen (13) copies of the report, plus a reproducible master copy shall be addressed as shown in paragraph D(2)(b)-1- above.

-2- One (1) copy of this report will be addressed as shown in paragraph D(2)(b)-2- above.

-3- Ten (10) copies of this report will be addressed as shown in paragraph D(2)(b)-3- above.

(3) The contractor shall submit two (2) copies of a Monthly Status and Fiscal Report, ACalC Form 3-9, showing the status of the work being accomplished, amount of contract funds expended during the report period, and estimated expenditures for the next period, to the Director, Procurement addressed as shown in paragraph D(2)(b)-2- above.

(4) The contractor shall furnish copies of material intended for publication or published, if such material has been supported in any degree by Department of Defense funds.

(5) Distribution shall be made to the following addressees directly by the contractor in the number of copies stipulated below:

(a) One (1) copy of any supported manuscript shall be submitted to the Commanding Officer, U. S. Army Chemical Research and Development Laboratories, Edgewood Arsenal, Md., ATTN: Contract Project Officer (by name), one (1) week or more, prior to release for publication.

6. SCOPE (Continued)

(b) Six (6) reprints of any supported publication shall be furnished, when available, to the Contract Project Officer, addressed as in paragraph D(5)(a) above.

(c) One (1) reprint of any supported publication shall be furnished, when available, to the Director, Procurement, U. S. Army Edgewood Arsenal, Maryland, ATTN: Contract Negotiator and Administrator (by name).

3. Phase Schedule and Completion Date:

This contract will be for a period of two (2) years, commencing on 1 December 1963 and ending on 30 November 1965.

7. GOVERNMENT FURNISHED PROPERTY:

<u>ITEM</u>	<u>ESTIMATED COST</u>	<u>LOCATION</u>
One (1) Temperature & Humidity Control Chamber, Model #FR-2510, PO#43320	Cost \$4,398; October 1962	Western Reserve Univ, Lakeside Hospital
One (1) Pulsating Homogenizer, Capacity 20-100 ml, Voucher #D 215-2	Cost \$50; May 1960	
Two (2) Penetration Chambers #B 17913	Cost \$75 each; February 1960	
One (1) Power Supply Unit for Hydrogen Lamp B2965, Order #USA 06-02	Cost \$263; January 1959	
One (1) Backplate Assembly Hydrogen Lamp B3240, Order #USA 06-02	Cost \$86; January 1959	
Labeled and Unlabeled chemicals not readily available to contractor	Unknown	USA CRDL, Edgewood Arsenal, Maryland

8. JUSTIFICATION:

Development of percutaneously effective agents is now directly related to penetration of human skin by liquid compounds. Unfortunately, little is known of penetration rates for liquids applied on man. The foregoing scope is intended to incorporate all essential steps for acquisition of a list of penetrants effective in vivo. These Laboratories urgently need such data for selection of vehicles and analysis of chemical or physical properties appropriate for design of new agents.

Scarcity of quantitative data on penetration of liquids, or solids, through intact human skin relates to inadequacy of methods for making such measurements. Therefore, development and utilization of a variety of techniques may be necessary to provide data on penetration rate for various non-drugs. Such techniques must be sensitive. They must also prove safe for human volunteers. We now must apply compounds and doses which produce measurable systemic effects, but measurement of local effects of small doses would be decidedly preferable.

Other benefits will accrue during development of measuring techniques. Knowledge of tissue binding of both water and applied compound will be gained during efforts to eliminate variables. Any information gained in these areas may contribute to our utilization of the "reservoir effect" for prophylaxis or military applications. Also, elucidation of barrier properties may aid in selection of decontaminants and additives to facilitate agent penetration.

9. GOVERNMENT ESTIMATE OF COSTS: FY1964 (1 Dec 63 - 31 July 64, eight months)

A. Materials \$ 1,200.00

B. Labor

1. Manufacturing or shop labor

_____ Pos. _____ hrs. at _____ per hr. . . \$ _____
 _____ Pos. _____ hrs. at _____ per hr. . . \$ _____
 _____ Pos. _____ hrs. at _____ per hr. . . \$ _____

2. Engineering labor

_____ Pos. _____ hrs. at _____ per hr. . . \$ _____
 _____ Pos. _____ hrs. at _____ per hr. . . \$ _____
 _____ Pos. _____ hrs. at _____ per hr. . . \$ _____

3. Research labor

Prin Investigator	Pos. <u>444</u>	hrs. at \$ <u>-0-</u>	per hr. . . \$ <u>-0-</u>
Med Lab Technician	Pos. <u>1333</u>	hrs. at \$ <u>2.40</u>	per hr. . . \$ <u>3,199.00</u>
Med Lab Technician	Pos. <u>667</u>	hrs. at \$ <u>2.40</u>	per hr. . . \$ <u>1,601.00</u>
Post Doc. Assistant(M.D.)	<u>333</u>	<u>2.40</u>	<u>799.00</u>
Total			\$ <u>5,599.00</u>

C. OVERHEAD (When actual rates are known, use such rates. Univ. and Res. Inst. usually apply one rate to all classes of labor)

150% of Item B. 1. \$ _____
 90% of Item B. 2. \$ _____
 50% ~~75%~~ of Item B. 3. \$ 2,800.00

Total \$ 2,800.00

D. Other direct costs

1. Special equipment and/or special facilities
 (Specify) . . . *See below \$ 3,000.00
 2. Travel \$ 400.00
 3. Communication \$ 50.00
 4. Other (Honoraria to Human Volunteers) \$ 1,400.00
 Total \$ 4,850.00

E. Consultation costs _____ days
 At \$50 to \$100 per day \$ _____

F. GENERAL & ADMINISTRATIVE EXPENSE (N/A to Univ. & Res. Inst.)
 10% of Items A thru E inclusive \$ _____

G. Total A thru F \$ 14,449.00

H. FEE (8% of Item G) (N/A to Universities, etc.) \$ _____

I. Contingency \$ 551.00

J. Estimate for Fiscal Purposes \$ 15,000.00

*Equipment: **Infra-red and radioactive detecting equipment.**

9. GOVERNMENT ESTIMATE OF COSTS: (FY1965) (1 August 1964 - 31 July 1965, twelve months)

A. Materials \$ 1,800.00

B. Labor

1. Manufacturing or shop labor

_____ Pos. _____ hrs. at _____ per hr. . . \$ _____
 _____ Pos. _____ hrs. at _____ per hr. . . \$ _____
 _____ Pos. _____ hrs. at _____ per hr. . . \$ _____

2. Engineering labor

_____ Pos. _____ hrs. at _____ per hr. . . \$ _____
 _____ Pos. _____ hrs. at _____ per hr. . . \$ _____
 _____ Pos. _____ hrs. at _____ per hr. . . \$ _____

3. Research labor

Prin Investigator	Pos. <u>637</u>	hrs. at <u>-0-</u>	per hr. . . \$	<u>-0-</u>
Med Lab Technician	Pos. <u>2000</u>	hrs. at <u>\$2.40</u>	per hr. . . \$	<u>4,800.00</u>
Med Lab Technician	Pos. <u>1000</u>	hrs. at <u>\$2.40</u>	per hr. . . \$	<u>2,400.00</u>
Post Doctoral Asst (M.D.)	<u>500</u>	<u>\$2.40</u>		<u>1,200.00</u>
Total				\$ <u>8,400.00</u>

C. OVERHEAD (When actual rates are known, use such rates. Univ. and Res. Inst. usually apply one rate to all classes of labor)

150% of Item B. 1. \$ _____
 90% of Item B. 2. \$ _____
~~50%~~ ~~100%~~ 50% of Item B. 3. \$ 4,200.00

Total \$ 4,200.00

D. Other direct costs

1. Special equipment and/or special facilities
 (Specify) \$ _____
 2. Travel \$ 600.00
 3. Communication \$ 75.00
 4. Other (**Honoraria for Human Volunteers**) . . . \$ 2,000.00

Total \$ 2,675.00

E. Consultation costs _____ days
 At \$50 to \$100 per day \$ _____

F. GENERAL & ADMINISTRATIVE EXPENSE (N/A to Univ. & Res. Inst.)
 10% of Items A thru E inclusive \$ _____

G. Total A thru F \$ 17,075.00

H. FEE (8% of Item G) (N/A to Universities, etc.) \$ _____

I. Contingency \$ 925.00

J. Estimate for Fiscal Purposes \$ 13,000.00

9. GOVERNMENT ESTIMATE OF COSTS: FY1966 (1 Aug 65 - 30 Nov 65, four months)

A. Materials						\$	<u>600.00</u>
B. Labor							
1. Manufacturing or shop labor							
_____ Pos. _____ hrs. at _____ per hr. . . .						\$	_____
_____ Pos. _____ hrs. at _____ per hr. . . .						\$	_____
_____ Pos. _____ hrs. at _____ per hr. . . .						\$	_____
2. Engineering labor							
_____ Pos. _____ hrs. at _____ per hr. . . .						\$	_____
_____ Pos. _____ hrs. at _____ per hr. . . .						\$	_____
_____ Pos. _____ hrs. at _____ per hr. . . .						\$	_____
3. Research labor							
<u>Prin Investigator</u> Pos. <u>222</u> hrs. at <u>-)-</u> per hr. . . .						\$	<u>-)-</u>
<u>Med Lab Technician</u> Pos. <u>567</u> hrs. at <u>\$2.40</u> per hr. . . .						\$	<u>1,301.00</u>
<u>Med Lab Technician</u> Pos. <u>333</u> hrs. at <u>\$2.40</u> per hr. . . .						\$	<u>799.00</u>
<u>Post Doctorate Asst (M.D.)</u> <u>167</u> hrs. at <u>\$2.40</u> per hr. . . .						\$	<u>401.00</u>
Total						\$	<u>2,801.00</u>
C. OVERHEAD (When actual rates are known, use such rates. Univ. and Res. Inst. usually apply one rate to all classes of labor)							
150% of Item B. 1.						\$	_____
90% of Item B. 2.						\$	_____
50% of 50% of Item B. 3.						\$	<u>1,401.00</u>
Total						\$	<u>1,401.00</u>
D. Other direct costs							
1. Special equipment and/or special facilities (Specify)						\$	_____
2. Travel						\$	<u>200.00</u>
3. Communication						\$	<u>25.00</u>
4. Other (Honoraria for human Volunteers)						\$	<u>600.00</u>
Total						\$	<u>825.00</u>
E. Consultation costs _____ days At \$50 to \$100 per day						\$	_____
F. GENERAL & ADMINISTRATIVE EXPENSE (N/A to Univ. & Res. Inst.) 10% of Items A thru E inclusive						\$	_____
G. Total A thru F						\$	<u>5,627.00</u>
H. FEE (8% of Item G) (N/A to Universities, etc.)						\$	_____
I. Contingency						\$	<u>373.00</u>
J. Estimate for Fiscal Purposes						\$	<u>6,000.00</u>

10. SECURITY & RECOMMENDED SOURCES

- a. Security Requirements Check List (DD 254) is attached
- b. Recommended Sources

POTENTIAL CONTRACTOR (Complete address and name of Principal Investigator, if known)	FACILITY CLEARED	CLEARANCE REQUESTED	EMPLOYEE CLEARANCE	
			Number Cleared	Requested (Date)
Lakeside Hospital Western Reserve University Cleveland 5, Ohio Dr. Richard B. Stoughton Chief, Section of Dermatology	Yes	---	1	1 Dec 63

11. CONTRACT DISTRIBUTION

Regular Distribution.

PROJECT OFFICERS PROCUREMENT CHECK LIST

1. Is the statement of the work (scope) to be performed complete?

Yes

2. Are needed drawings and specifications attached?

N/A

3. Has DD Form 254, Security Requirements Check List, been properly filled out and attached to the correspondence?

Yes

4. If competition should be limited, have the reasons been fully stated in the certificate which requests same? Is the Certificate Limiting Competition attached?

Yes

5. Have funds been allocated to the project?

Yes

6. Is a statement of the quantity, present availability, and value of Government property to be furnished to the Contractor included with the correspondence requesting the contract?

Yes

7. If the Contractor should supply written reports, have the number of copies of each report and the schedule of submission been indicated?

Yes

8. Has the completion date of the contract work been indicated?

Yes

9. If materials will be delivered by the Contractor, have the times and methods been stated?

N/A

10. Do recommended sources require additional facilities to perform the work? If so, have they been listed in detail?

Yes

11. Are the proper number of copies of each document included with the correspondence?

Yes

12. Has consideration been given to Small Business?

Yes

PATENT RIGHTS CHECKLIST

SUBJECT: Request for Negotiation of a Research and Development Contract for "Measurements of Penetration or Retention of Liquid Compounds by Human Skin."
CRDL Request No. 32-MT-4
DATE: 13 September 1963

	Yes	No
(a) Does the proposed contract or modification relate to a new technological field in which there is no significant nongovernmental experience? (Yes, No.) If so, is it probable that inventions which may be made under the proposed contract or modification will dominate the field or be of critical significance in it? (Yes, No.)		X
(b) Do the services of the contractor under the proposed contract or modification largely consist of coordinating and directing the work of others? (Yes, No.)		X
(c) Does the proposed contract or modification require work in a field directly relating to the health and safety of the public? (Yes, No.) If so, is it probable that the availability for public use of inventions arising out of such work will not depend on patent incentives? (Yes, No.)		X
(d) Does the proposed contract or modification involve circumstances similar to those of (a), (b), or (c) above? (Yes, No.)		X
(e) Does the proposed contract relate to atomic energy? (Yes, No.)		X
(f) Does the proposed contract cover work on behalf of the National Aeronautics and Space Administration? (Yes, No.)		X

MILLARD N. MERSHON

signed/Project Officer

WUCS-W

Request for Negotiation to be Limited to a Single Source, CHEL Request No. 32-WF-4

Director, Procurement
AFSA: Ch, R&D Proc Div
WPA Edgewood Arsenal, Md.

Tech Director
NSA CRODL

28 SEP 1968
Dr. Morrison/24257/D

1. Satisfactory performance of the subject requirements will entail physical features as follows:

- a. Dependable and frequent access to large areas of freshly excised human skin.
- b. Readily available sources of responsible human volunteers.
- c. Specialized equipment for determining surface counts of ^{32}P label on skin surfaces.
- d. Equipment for measuring penetration through excised human skin under conditions of controlled temperature and humidity.
- e. Facilities for tissue studies including both histology and histochemistry.

2. A satisfactory investigator must have qualifications including:

- a. The M.D. degree and license to practice at the facility.
- b. A dermatologist's knowledge of the structure, histochemistry, physiology, pathology and permeability of human skin in vivo and in vitro.
- c. Experience in measuring rates of skin penetration by various substances in vivo and in vitro.
- d. Willingness to undertake a contract for development of quantitative measurement of skin penetration rates for liquids lacking pharmacological effects.

3. The investigator and facility must be able to continue, develop and pursue special aspects of work currently in progress under Contract DA18-106-405-CNL-215.

4. It is requested that negotiation be limited to Western Reserve University, Cleveland, Ohio, for the following reasons:

- a. All of the above specifications are met by Dr. Richard B. Stoughton, designated principal investigator for the proposed contract and by the facilities at the Lakeside Hospital of Western Reserve University.

(See paragraph 6-104, Armed Forces Industrial Security Regulation)

DEPARTMENT OF DEFENSE
SECURITY REQUIREMENTS CHECK LIST
(CLASSIFICATION SPECIFICATIONS)
(FOR PRIME AND SUBCONTRACTS INVOLVING CLASSIFIED INFORMATION)

(See Section II, Industrial Security Manual for Safeguarding Classified Information)

1 THIS CHECK LIST IS FOR	2. CONTRACT NUMBER OR OTHER IDENTIFICATION NUMBER <i>(Prime contracts must be shown for all subcontracts)</i>	3. THIS CHECK LIST IS <i>(See note below)</i>	DATE	4. FACILITY SECURITY CLEARANCE REQUIRED FOR CONTRACT PERFORMANCE OR FOR ACCESS TO CLASSIFIED INFORMATION
<input checked="" type="checkbox"/> a PRIME CONTRACT	a PRIME	<input checked="" type="checkbox"/> ORIGINAL CHECK LIST	17 Sep 63	a TOP SECRET
<input type="checkbox"/> b SUBCONTRACT <i>(Use Item 15 to identify further subcontracting)</i>	b SUBCONTRACT	<input type="checkbox"/> b REVISED CHECK LIST <i>(Supersedes all previous lists)</i>		<input checked="" type="checkbox"/> b SECRET
<input checked="" type="checkbox"/> c INVITATION TO BID OR REQUEST FOR PROPOSAL	c INVITATION TO BID OR REQUEST FOR PROPOSAL Request No. 32-M-4	<input type="checkbox"/> c FINAL CHECK LIST FOR CONTRACT TERMINATION OR COMPLETION		c CONFIDENTIAL

5a NAME AND ADDRESS OF PRIME CONTRACTOR	b NAME AND ADDRESS OF COGNIZANT SECURITY OFFICE
6a NAME AND ADDRESS OF SUBCONTRACTOR <i>(If applicable)</i> <i>(Use Item 15 to identify further subcontracting)</i>	b NAME AND ADDRESS OF COGNIZANT SECURITY OFFICE

7 SECURITY REQUIREMENTS CHECK LIST FOR SUBCONTRACTING FROM THIS <input checked="" type="checkbox"/> PRIME CONTRACT <input type="checkbox"/> SUBCONTRACT WILL BE APPROVED BY	8. ARMED SERVICES TECHNICAL INFORMATION AGENCY (ASTIA) SERVICES		
a MILITARY ACTIVITY Director, Procurement	a REQUESTED	YES	NO
b. ADDRESS USA Edgewood Arsenal, Maryland	b APPROVED		<input checked="" type="checkbox"/>
	c. FIELD OF INTEREST REGISTER ISSUED		<input checked="" type="checkbox"/>

9. GENERAL IDENTIFICATION OF THE PROCUREMENT FOR WHICH THIS CHECK LIST APPLIES *(If classified, complete this item by separate correspondence)*

Title: Measurements of Penetration or Retention of Liquid Compounds by Human Skin.

10 PROPOSED PUBLICITY RELEASES SHALL BE SUBMITTED FOR APPROVAL PRIOR TO RELEASE DIRECT THROUGH *(Specify)*
Director, Procurement, ATTN: Ch, R&D Procurement Division, USA Edgewood Arsenal, Md.

TO THE OFFICE OF SECURITY REVIEW, OFFICE OF THE SECRETARY OF DEFENSE FOR REVIEW IN ACCORDANCE WITH THE INDUSTRIAL SECURITY MANUAL

11 RESTRICTED DATA IS NOT INVOLVED IN THIS CONTRACT *(If involved, check AEC/DOD Classification Guide)*

NOTE Original Check Lists (Item 3a) are authority for contractors to mark classified information. Revised and Final Check Lists (Items 3b and c) are authority for contractors to remark the regraded classified information. Such actions by contractors shall be taken in accordance with the provisions of paragraph 7 of the Industrial Security Manual

32-M-4

13	END ITEM PRODUCED UNDER CONTRACT	TOP SECRET	SECRET	CONFIDENTIAL	CONFIDENTIAL (Modified Handling Authorized)	UN-CLASSIFIED
a	CLASSIFICATION OF END ITEM					
b	EXTERNAL VIEW					
c	MILITARY APPLICATION					
d	NUMBERS CONTRACTED					
e	PRODUCTION AND PROGRAM SCHEDULES					
f	RATE OF DELIVERY					
g	NUMBERS DELIVERED					
h	DEGREE OF PROTECTION IN TRANSIT					
i	UNIT COST					
14.	ADDITIONAL (Attach additional sheets, if necessary)					
a	SCOPE					X
b	REPORTS					X
c						

15 REMARKS (Attach additional sheets if necessary and continue paragraph designation)

Items 12 and 13 are not applicable.

Although the contract is unclassified, a SECRET facility clearance has been in force, and is useful because the principal investigator utilizes background information up to and including SECRET. If classified information is anticipated in the future under contract, a revised DD 254 will be submitted.

REQUIRED DISTRIBUTION:

PRIME CONTRACTOR (Item 5a)

COGNIZANT SECURITY OFFICE (Item 5b)

DIRECTOR, FEDERAL BUREAU OF INVESTIGATION
WASHINGTON, D C (Only for Items 1a & 1b)
(2 copies)

SUBCONTRACTOR (Item 6a)

COGNIZANT SECURITY OFFICE (Item 6b)

ARMED SERVICES TECHNICAL INFORMATION AGENCY
ARLINGTON HALL, ARLINGTON, VIRGINIA
(Only when item 8b is marked "Yes")

ADDITIONAL DISTRIBUTION:

REFER ALL QUESTIONS PERTAINING TO THIS CHECK LIST TO THE APPROVING OFFICIAL BELOW

FOREGOING SECURITY REQUIREMENTS CHECK LIST APPROVED BY DEPARTMENT OF DEFENSE CONTRACTING OFFICER OR HIS REPRESENTATIVE

SIGNATURE

TYPED NAME AND TITLE OF APPROVING OFFICIAL
**MILLARD M. MERSHON, Contract Project Officer
Toxicology Division, USA CRDL**

CONTRACTING MILITARY ACTIVITY AND ADDRESS
**Director, Procurement
U.S. Army Edgewood Arsenal
Edgewood Arsenal, Maryland**

Information pertaining to classified contracts or projects, even though such information is unclassified, shall not be released for public dissemination except as provided by the Industrial Security Manual

ADCR-4

SUBJECT: Request for Negotiation to be limited to a single source, WDC Request No. 22-44

b. Past performance of this contractor has been exceptionally productive in terms of the mission of the Chemical Research and Development Laboratories.

c. The experience of Dr. Stoughton in this research field and in liaison with these laboratories gives him a unique advantage in understanding and coping with the problem for investigation.

d. No other potential contractor is known to have the combination of abilities and facilities needed to carry out the subject proposal. Acquisition of capability by other potential contractors is possible but is not feasible by reason of expense to such contractor.

e. A change of contractors would be of disadvantage to the Government for the reasons of unanticipated expense in advertising the new contractor, and in the transfer of nearly \$400,000 worth of Government furnished equipment. An unnecessary delay of 6 to 12 months before resumption of productive effort is anticipated in the event of such a change.

f. It is in the best interests of the Government to continue the services of Western Reserve University.

S. D. COLLIER, Ph. D.,
Director, Chemical Research and Development Laboratories

Bldg 355
Edgewood Arsenal, Maryland
21010
30 August 1963

Dear Dr. Stoughton:

I am enclosing a current draft of requirements which have been directed to our contract office. They are subject to revision at several points in the approximately 90 days course of procedure for issuance of requests for bids.

This draft is enclosed, for your comment, on an unofficial basis because procurement procedures are outside the scope of my duties. Accordingly, I can commit the Government in no way.

I am also enclosing a copy of a list of C14 labeled liquids which are listed as stock items by Nuclear-Chicago or Volk. Have you comments on use of these on volunteers?

Sincerely,

MILLARD M. MERSHON, VMD

* This letter was handwritten by Dr. Mershon while secretary was on leave.

C¹⁴ Labeled Liquids Readily Available

Solvents

Acetone
Acetonitrile
Ethyl acetate
Ethyl acetoacetate
~~Ethyl hexoacetate~~
n Hexadecane
n Octane
CCl₄

Alcohol

Methanol
Ethanol
Isopropanol
Glycerol

Other

Ethanolamine
Aniline

Aromatics

Benzene
Benzyl alcohol
Chlorobenzene
Toluene

Acids

Acetic
Butyric
Isobutyric
Oleic
Propionic

a. The contractor shall furnish the necessary facilities, personnel, equipment, materials, and supplies to investigate microanatomy and physiology of human skin penetration by various substances applied in vitro and in vivo.

b. The investigation shall include development of techniques for determining penetration rates of various liquid compounds applied on skin of human volunteers. Preferred techniques will measure penetration of compounds which do not produce overt physiological effects, but safe use with volunteers is the prime consideration. Changes to be measured may include, but are not limited to, the following:

- (1) Alteration of surface counts of radiolabel in skin.
- (2) Migration of radiolabel, as determined by differences in skin surface count with time, before and after scotch tape stripping.
- (3) Detection of radiolabel in body fluids or biopsy specimens.
- (4) Accumulation of penetrant in human epidermal cell space in amounts detectable by chemical or physical means at given intervals after application.
- (5) Measurable alterations in normal structure, chemical composition, or enzymatic activity in the epidermal cell space or less superficial skin layer.
- (6) Vasomotor effects as indicated by local color or temperature changes.
- (7) Alteration of skin function as by inhibition of sweating or sebaceous secretion, pilomotor activity, psychogalvanic skin response, etc.

c. Applications on volunteers shall be preceded by studies to establish in vitro rates of penetration through freshly excised human skin. Such studies shall be conducted under conditions of controlled temperature and humidity approximating in vivo states. These studies shall be used to eliminate compounds which fail to penetrate skin at rates consistent with in vivo detection by radiotracer and/or other measuring techniques.

-1-

d. Studies shall be designed to characterize binding properties of keratinous layers in human skin. These studies may involve, but are not limited to, the following:

- (1) Effects of humidity, temperature, sweating, or other environmental influences on "reservoir" functions of skin.
- (2) Differences in reservoir effect with various compounds.
- (3) Influences on penetration and/or reservoir effect resulting from keratin modification by hydration, surfactants, silicones, keratolytics, etc.

e. Policies for selection of liquid test penetrants shall be established by agreement between the contractor and the Technical Representative of the Contracting Officer.

SMUCR-M(T2)

Telephone Conversation of 22 August 1963 with
Dr. R. B. Stoughton, Western Reserve University

Actg Ch, Fld Tox Br
Ch, Tox Div

Fld Tox Br

3 September 1963
MMershon/bv/5217

1. Divergence between future plans of Dr. Stoughton (per his letter of 16 August) and needs of CRDL suggested the need for further clarification of our needs.

2. Dr. Stoughton was told that work with AHR-483 was of interest secondary to information on penetration of liquid compounds. He was also informed that renewal of his contract is not possible; that a new proposal must be subject to competitive bidding.

3. Dr. Stoughton was told to expect a request to bid from our procurement facility in the indefinite future.

Author:

MILLARD M. MERSHON, VMD
Contract Project Officer

Actg Ch, Fld Tox Br _____
HPAverill

Ch, Tox Div _____
BPMcNamara

Handwritten notes:
100-25-
100-100-11

Distribution:

- Orig & 1 cy: Fwd
- 1 cy: Fld Tox Br
- 1 cy: Tox Div
- 1 cy: Med Mail & File 0
- 1 cy: Cont 0

File Temp
MMershon/bv/5217
Proj. 4C08-02-024-07
Med Mail & File 0
3 Sep 63

Handwritten signature:
Jill
A. F. [unclear]

RICHARD B. STOUGHTON, M. D.
2048 ADELBERT ROAD
CLEVELAND 6, OHIO
RA 1-7060

aug 16th

Dear Dr. Mershan:

Enclosed is the proposal
for future work along with
a revised budget. We hope
there will be a possibility for
the Scintillation counter this
year.

I will be here Aug 20, 21 & 22
and away until Aug 28th.
If you have any questions, please
call me -
I enjoy seeing you this

wish an having a chance to talk
with you again —

Best regards,

Paul Stanton