

## CONTRACT INFORMATION

1. TITLE OF PROPOSED PROCUREMENT:

MEASUREMENTS OF PENETRATION OR RETENTION OF LIQUID COMPOUNDS BY HUMAN SKIN

2. TOTAL ESTIMATED COST:

3. CONTRACT REQUEST NO.:

4. PROJECT NUMBER: TITLE: COST BY PROJECT: TYPE OF FUNDS:

5. CONTRACT PROJECT OFFICER: NAME: DIVISION: PHONE NO.:

Millard M. Mersten

Tox

24257

ALTERNATE CONTR. PROJ. OFFICER: NAME: DIVISION: PHONE NO.:

Milton H. Joffe

Ch. of Asst. Dir. / MR

5150

6. SCOPE: A. 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 vivo and in vitro.
- (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:
- alteration of surface counts of radiolabel in skin.
  - migration of radiolabel, as determined by differences in skin surface count with time before and after scotch tape stripping.
  - detection of radiolabel in body fluids or biopsy specimens.
  - accumulation of penetrant in human epidermal cell space in amounts detectable by chemical or physical means at given intervals after application.
  - measurable alterations in normal structure, chemical composition, or enzymatic activity in the epidermal cell space or less superficial skin layer.
  - vesicator effects as indicated by local color or temperature changes.
  - 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 status. 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.
- (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:

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16. Scope (continued)

(4.) (cont)

- 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.

(6.) The Contractor shall be free to devote up to 50% of contract effort to aspects of microanatomy or physiology which become of interest during the studies detailed in items 2, 3 and 4, above, but which are peripheral to such studies.

6 B DRAWINGS AND SPECIFICATIONS INCLOSED

none

6 C MATERIALS TO BE FURNISHED

not applicable

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## 6D REPORTS BY CONTRACTOR

1. The contractor shall prepare and submit the following technical reports, which shall be prepared in accordance with Edgewood Arsenal format (CRDL 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, 15 March, 15 June, and 15 September, unless a

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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 addresses directly by the Contractor in the number of copies stipulated below:

a) Quarterly Letter Reports

(1) Three (3) copies of each of the required Quarterly Reports shall be furnished to  
Commanding Officer  
U.S. Army Chemical Research and Development Laboratories  
ATTN: Contract Project Officer (by name)  
Edgewood Arsenal, Maryland.

(2) One (1) copy to:  
Contracting Officer  
U.S. Army  
ATTN: Contract Negotiator and Administrator (by name)  
Edgewood Arsenal, Maryland. Procurement Agency

b) Semi-Annual Progress Report

- (1) Thirteen (13) copies and the reproducible masters to:
- (2) One (1) copy to:
- (3) Ten (10) copies to:

c) Final Comprehensive Summary Report

- (1)
- (2)
- (3)

3. The Contractor shall submit two (2) copies of a Monthly Status and Fiscal Report, SCAC 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:

Contracting Officer

U.S. Army

Procurement Agency

ATTN: Contract Negotiator and Administrator (by name)

Edgewood Arsenal, Maryland.

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3. GOVERNMENT ESTIMATE OF COSTS:

A. Materials . . . . . \$ 1800.00

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 \*

1	Pos. <u>2000</u>	hrs. at <u>2.40</u>	per hr. . . . \$ <u>4800.00</u>
1	Pos. <u>1000</u>	hrs. at <u>2.40</u>	per hr. . . . \$ <u>2400.00</u>
1	Pos. <u>500</u>	hrs. at <u>2.40</u>	per hr. . . . \$ <u>1200.00</u>
Fringe Benefits 7.5%			<u>630.00</u>

Total . . . . . \$ 9030.00

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. . . . . \$ 3,566.85~~  
~~75% of Item B. 3. . . . . \$~~

Total . . . . . \$ 3,566.85

D. Other direct costs

1. Special equipment and/or special facilities (Specify) . . . . .	***	\$ _____
2. Travel . . . . .		\$ <u>600.00</u>
3. Communication . . . . .		\$ <u>- 0 -</u>
4. Other <u>Honorariums for human volunteers</u> . . . . .		\$ <u>2,000.00</u>
Total . . . . .		\$ <u>2,600.00</u>

E. Consultation costs \_\_\_\_\_ days  
 At \$50 to \$100 per day . . . . . \$ - 0 -

F. GENERAL & ADMINISTRATIVE EXPENSE (N/A to Univ. & Res. Inst.)  
 10% of Items A thru E inclusive . . . . . \$ - 0 -

G. Total A thru F . . . . . \$ 16,996.85

H. FEE (8% of Item G) (N/A to Universities, etc.) . . . . . \$ - 0 -

I. Contingency (includes additional materials possibly needed) . . . . . \$ 1,003.15

J. Estimate for Fiscal Purposes . . . . . \$ 18,000.00

\* No charge for principal investigator or colleagues  
 \*\* Equipment cited in item 7 will be available without additional cost at Western Reserve Univ - will require outlay for transportation and installation elsewhere.

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## 7. GOVERNMENT FURNISHED PROPERTY:

ITEM	ESTIMATED COST	LOCATION
one (1) Temperature and Humidity Control Chamber, Model FR-2510, PO # 43320	cost \$1 4,398.00 Oct 1962	Lakeside Hospital Western Reserve Univ.
one (1) Pulsating Homogenizer Capacity 20-100 ml Voucher # D 215-2	cost \$30.00 May 1960	as above
two (2) Penetration Chambers # B 17913	cost \$75.00 ea. Feb 1960	as above
one (1) Power Supply Unit for Hydrogen Lamp B 2965 Order # USA 06-02	cost \$263.00 Jan. 1959	as above
one (1) Bookplate assembly for hydrogen lamp B 3240 Order # USA 06-02	cost \$86.00 Jan. 1959	as above

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 work 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 the contractor's volunteers — or ours. We 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.

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