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& draft letter
& Gordon
Schmid

October 4, 1973

John C. Cutler, M.D.
Director, Population Division
Graduate School of Public Health
University of Pittsburgh
Pittsburgh, Pennsylvania 15261

Dear Dr. Cutler:

Thank you for your letter dated July 6, 1973, and please accept my apology for this delayed response. It appears that the mail is very slow and then I was out of the office much of the last two months.

I think you are correct in noting a renewed interest here in prophylaxis as means of control of venereal disease. Thank you for the information you sent us. I also hope we can get together to discuss this important area. Individuals like yourself with a long interest and established expertise in venereal disease control may, at times, feel that "us youngins" have lost historical perspective relative to gonorrhea control particularly. I for one certainly hope this is not true of the research section in the Venereal Disease Branch. I know I personally could profit from discussion with you.

In keeping with our attempt to open rather than close avenues of communication, I'd like to mention a recent discussion I've had with Dr. Gordon of Julius Schmid, Inc. They have reported to us a clinical study claiming efficacy of dioctyl sodium sulfosuccinate in the treatment of gonococcal urethritis in men. I noted with interest, facts which you are probably aware. This compound is very commonly used now as a stool softener (Colace). But of more interest, it is one of the ingredients of Vaginex (a Julius Schmid product offered in vaginal suppository form for trichomoniasis). If I can use the word, cross-fertilization regarding this suppository as prophylaxis between yourself and Julius Schmid, Inc. might result in some useful application. I've suggested that they contact you. You may have spoken to them in the past, but a reexplanation of the subject might prove fruitful.

Again, thank you for your letter.

Sincerely yours,

Paul J. Wiesner, M.D.

in the History of Medicine Division, National Library of Medicine. NOTICE: THIS MATERIAL MAY BE PROTECTED BY COPYRIGHT LAW (TITLE 17

2001-011 JOHN CUTLER
From the
HSCOME

6/29
Dr. Fausto Moreira

RUA GIL VICENTE, 58-2.

TELEFONE 972488

AREOSA, 21st June 1982

4445 Ermesinde
PORTUGAL

Dear Doctor Cutler,

Many thanks for your kind letter of 23th May as well as for the reprints therewith enclosed.

I feel very happy to see that our views on VD prevention are quite coincident and I full agree with the reasons you point out for the slow awakening of Medical Authorities for prophylaxis against VD.

In this country in spite of want of uptodate official statistics the STD have been increasing notorially and I am wondering why besides efforts of clinical treatment and campaigns for sexual education developed by Health Authorities nobody seems aware of prevention systems and measures.

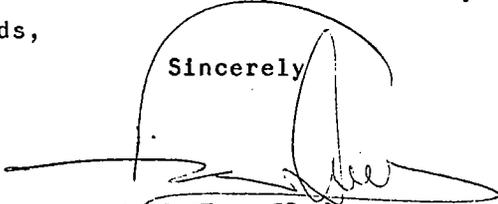
The old preventing agents are almost vanished from the market and completely out of current use and nothing has been made(at least in Portugal) for replacing them by others more modern and effective.

So, your clear-cut works with vaginal contraceptives in VD prevention appeal to me very much and I believe that they show the way for reaching the prophylaxis of future. Having this in mind I dare to ask you, Dear Dr.Cutler, to keep me informed on every progress you may take acquaintance with this field.

Please do accept once again my best thanks for your kind cooperation and do not hesitate to contact me everytime you need no matters what from me.

Looking forward to be of any service to you accept my kindest regards,

Sincerely



Dr. Fausto Moreira

6/29
Dr. Fausto Moreira

RUA GIL VICENTE, 58-2.

TELEFONE 972468

AREOSA, 21st June 1982

4445 Ermesinde
PORTUGAL

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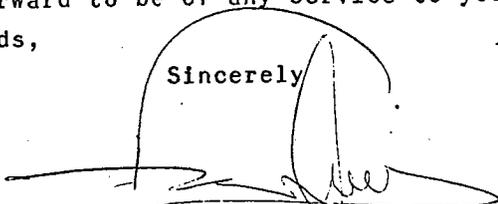
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Sincerely



Dr. Fausto Moreira

Discussed to

Griffin

Pand

Ho

March 31, 1970

all approved.

AID 1420-18 (1-69)

OFFEROR'S ANALYSIS OF COST PROPOSAL

BUDGET BURI
24-R006
APPROVAL E
December,

INSTRUCTIONS TO OFFERORS

1. The "Offeror's Analysis of Cost Proposal" form is a standardized document which an offeror must submit to the Agency for International Development (A.I.D.) in connection with all negotiated procurements. (See AIDPR 7-3.807.2(c).)

2. Use of this form is mandatory, unless the Contracting Officer waives this requirement in writing. Where a particular cost element is not appropriate for the procurement, indicate "Not Applicable" or "NA" on the form.

3. The offeror must also submit the supplementary data as detailed in the footnotes on the reverse side. If a Certificate of Current Cost or Pricing Data is required by FPR 1-3.807-3 and 1-3.807-4 for the procurement, it should also be appended to this form.

4. By submission of this proposal, the offeror grants to the Contracting Officer or his authorized representative, the right to examine, for the purpose of verifying the cost or pricing data submitted, those records, documents, and other supporting data which will permit a fair and equitable evaluation of such cost or pricing data, together with the computer projections used therein. This right may be exercised in connection with any negotiations prior to contract award.

5. The footnotes on the reverse side, in addition to detail required supplemental data, provide information which will be required in completing the "Cost Proposal" below.

I. Salaries 1/		MAN-MONTHS	ESTIMATED COST
A. U.S. Personnel			
Home Office Professional			\$ 51,300.00
Home Office Nonprofessional			\$ 82,800.00
Field Staff Professional			\$
Field Staff Nonprofessional			\$ 12,000.00
Total U.S. Salaries			\$ 146,100.00
B. Cooperating or Third Country Nationals			
Field Staff Professional			\$ 56,000.00
Field Staff Nonprofessional			\$ 64,400.00
If these salaries will be paid in U.S. dollars, enter the amount here:			\$ 120,400.00
If these salaries will be paid in local currency, enter the amount and currency below:			
7% INCREASE ON SALARIES FOR 2nd and 3rd YEAR			11,112.00
II. Consultants 2/			
Consultant Fees (Domestic)			\$ 18,900.00
Consultant Fees (Overseas)			\$
Total Consultant Fees			\$ 18,900.00
III. Fringe Benefits (Payroll Costs) 3/			
IV. Overhead 4/			
	BASE	RATE	
Home Office (On-campus)	\$152,548.00	% 48.8%	\$ 69,953.00
Field Staff (Off-campus)	\$115,346.00	% 29.5%	\$ 34,028.00
Total Overhead			\$ 103,981.00
V. Travel and Transportation 5/			
U.S. Travel (Personnel and Dependents)			\$ 16,350.00
International Travel (Personnel and Dependents)			\$ 5,220.00
Other Personnel Travel			\$
Transportation of Household Effects, Baggage & Vehicles			\$
Storage of Household Effects & Vehicles			\$
Other (Describe)			\$
Total Travel & Transportation			\$ 21,570.00
VI. Allowance 6/			
Category			
Post Differential			\$
Quarters			\$
Temporary Lodging			\$
Education			\$
Educational Travel			\$
Supplemental Post			\$
Separate Maintenance			\$
Per Diem			\$
Total Allowances			\$
VII. Other Direct Costs 7/ (Specify)			
Telephone & Postage			\$ 12,600.00
Publications			\$ 2,000.00
Services & Clinical Pathologist			\$ 15,000.00
Total Other Direct Costs			\$ 29,600.00
VIII. Equipment, Vehicles, Materials and Supplies 8/			
Equipment (Title in cooperating country)			\$ 46,560.00
Equipment (Title retained in A.I.D.)			\$
Material and Supplies			\$ 18,600.00
Vehicles			\$
Freight			\$
Total Equipment, Vehicles, Materials and Supplies			\$ 65,160.00
IX. Participant Training 9/			
Number of Participants:			
Training (Tuition, Fees, etc.)			\$
Travel and Subsistence			\$ 356.00
Total Participant Training			\$ 356.00
X. Subcontracts 10/ (Specify)			
			\$ 56,000.00
			\$
			\$
			\$

XI. General & Administrative Rate ^{11/}			ESTIMATED COST
Base:	Rate	%	\$ - 0 -
XII. Subtotal (Estimated Cost Exclusive of fixed Fee or Profit)(Items I - XI)			\$ 600,939.00
XIII. Fixed Fee or Profit ^{12/}			\$ - 0 -
Base:	Rate	%	
XIV. Grand Total (Items XII & XIII)			\$ 600,939.00

If more space is required and for items XV thru XX where additional information is necessary, please use separate sheet. Indicate item number to which answer applies and staple to form.

XV. Has any government agency performed an audit of your organization within the past 12 months?
 Yes No DCCA Pgh. Br. office thru 6/30/68
 (If yes, identify the contract, the agency, the date, and the number of the audit report.)

XVI. Will you require the use of any government property in performing this contract?
 Yes No (If yes, specify) as specified in budget

XVII. Will the source of all commodities procured under this contract be the United States? ^{13/}
 Yes No (If not, list the exceptions.)

XVIII. Have you performed any contracts for A.I.D. or other government agencies in the past ten years?
 Yes No (If yes, identify by Agency and contract number.) AID/IA362, AID/AFN 284, etc.

XIX. Will you require an advance payment or a Federal Reserve Letter of Credit (to be filled in by educational institutions and nonpro organizations only).
 Yes No (If yes, in what amount?) Federal Reserve Letter of Credit

XX. Is there any overtime included in this cost proposal?
 Yes No (If yes, explain the amount and what it will be used for.)

XXI. What is the average number of days per year used in the calculation of the above cost proposal for: (Standard Un. proceed
 Vacations _____ Holidays _____ Other (explain) _____ May have to be reflected as Professional
 Sick Leave ? Home Leave 0 _____ and non professional

and Field Testing of supplementary data, is submitted for use in connection with RFP _____ or the proposal titled 'Development of Combined Prophylactic-Contraceptive Preparation' and reflects our best estimates, as of this date, in accordance with the Instructions to Offerors and Footnotes.

TYPE NAME AND TITLE	SIGNATURE
Paul Solyan-Comptroller & Assistant Treasurer	
FIRM	DATE
University of Pittsburgh	

FOOTNOTES

In addition to the cost analysis on this form, the offeror is required, in good faith, to submit with this form the additional data, supporting schedules, and substantiation which are reasonably necessary for the conduct of an appropriate review and analysis in light of the facts of this particular procurement. In order to obtain a reasonable and equitable contract price, it is essential that there be a clear understanding of: (a) the existing, verifiable data; and (b) the judgmental factors applied in projecting from known data to the estimated price. In short, the offeror's estimating process should be clear to the negotiator.

The footnotes below include questions and explanations of the items of the Cost Analysis. The supplementary data should include all the following information, where applicable, as well as any other pertinent facts.

1. Salaries (U. S. Personnel and Cooperating or Third Country Nationals)

A. An individual is considered a professional if he is engaged in an occupation requiring advanced training in some liberal art or science, usually involving mental rather than manual work and who is qualified in his field by the standards of the profession. Examples are: professors, teachers, engineers, economists, scientists, and research associates.

The nonprofessional category includes those not considered professional such as graduate or undergraduate assistants, secretaries, clerks, technicians, administrative aides, research assistants, and trainees.

B. What are the position titles in each category? How many man-months are anticipated in each position? What is the anticipated salary of each position? Will each position involve work under this contract on a full-time basis? If not, what percentage of each position's time will be used for work under this contract?

2. Consultants — in what fields is the need for consultants anticipated? How many consultants are needed? How many man-days are anticipated for each consultant? What is the anticipated fee per man-day for each consultant?

3. Fringe Benefits — Which fringe benefits are included in this amount? What is the rate of each fringe benefit? Are fringe benefits included in your established personnel procedure? (Enclose a copy, if available, of your established personnel procedure concerning fringe benefits, allowances, leave, etc.)

4. Overhead — What costs are included in the overhead pool? Which direct costs are included in the overhead base? What were the rates established by the most recent government audit?

5. Travel and Transportation — Indicate how many round or one-way trips to where, an estimate of how many dependents will be traveling, and the anticipated weight of household effects which will be shipped and/or stored, etc.

6. Allowances — A.I.D. employs the "Standardized Government Travel Regulations" or "Standardized Regulations (Government Civilians Foreign Areas)" as applicable, in establishing the rates of, and criteria for, travel and overseas allowances. If the allowances used in the cost analysis exceed the rates permitted by these Regulations, explain. Indicate which allowances are applicable, and how much of each is anticipated, (i.e., educational travel for four dependents, 20 days per diem).

7. Other Direct Costs — Enumerate all other direct costs, such as medical examinations, communications, etc.

8. Equipment Vehicles, Materials, and Supplies — List the types of equipment, materials, and/or vehicles in each category which will be purchased for use under the contract, and the cost of each.

9. Participant Training — Where will participants be trained? In what fields will they be trained? What is the tuition per participant? What do the fees cover? How much travel is involved? Where? How much is allowed for subsistence?

10. Subcontracts — What type of work will be subcontracted? Approximately what percentage of the total scope of work is it? Will you subcontract with? What is the anticipated amount of subcontract?

11. General and Administrative Rate — Show, in detail, the price by which you arrived at the General and Administrative rate.

12. Fixed Fee or Profit — Show, in detail, the process by which arrived at the fixed fee or profit.

13. Source Certificate — The following conditions should apply to any commodity procurement financed under the proposed contract in U.S. dollars:

A. The source of the commodity shall be the United States, an area of Free World, or through manufacturing, processing, or assembly produced in the United States. The term "source" means the country from which a commodity is shipped to the cooperating country or the cooperating country if the commodity is located there at the time of purchase. If, however, a commodity is shipped from a free or bonded warehouse in the form in which it is received therein, "source" means the country from which the commodity was shipped to the port or bonded warehouse.

B. A produced commodity purchased in any transaction will contain any component from countries other than the United States, as defined in A.I.D. Geographic Code 899.

2. Contain components which were imported into the country of production from such Free World countries other than the United States; and

(i) such components were acquired by the producer in the form in which they were imported; and

(ii) the total cost of such components (delivered at the time of production) amounts to more than 10 per cent, or such percentage as A.I.D. may prescribe, of the lowest price (excluding the cost of ocean transportation and marine insurance) at which the supplier of the commodity available for export sale (whether or not financed by A.I.D.).

C. Exception for Printed or Audio-visual Teaching Materials — The geographic source of teaching materials (printed or audio-visual) procured with funds charged against A.I.D. appropriations, may, to the extent necessary, be progressively expanded to include the aid recipient country, Code 901 countries, and Code 899 countries, in addition to the United States when:

1. Effective use of the printed or audio-visual teaching materials depends on their being in the local language.

2. Such materials are intended for technical assistance projects or activities financed by A.I.D. in whole or in part.

3. Other funds, including U. S.-owned or -controlled currencies, are not readily available to finance the procurement of such materials.

Geographic Code 899 is defined as "any area or country of Free World, excluding the cooperating country itself, when such area or country is a possible source of A.I.D.-financed purchases. Geographic Code 901 is defined as "any area or country in the Free World, excluding the cooperating country itself and the following developed countries: Australia, Austria, Belgium, Canada, Denmark, France, Germany (Federal Republic), Italy, Japan, Luxembourg, Monaco, Netherlands, New Zealand, Norway, South Africa, Spain, Sweden, Switzerland, and the United Kingdom."

F.	PUBLICATIONS	\$ 2,000.00
G.	POSTAGE	3,600.00
	TELEPHONE	9,000.00
	CLINICAL PATHOLOGY-regional laboratories	5,000.00
	SERVICES - (payment for prostitutes for samples for laboratory testing) (100 prostitutes at \$5.00 per week for 2 yrs.)	10,000.00
	SUPPLIES -for the laboratories in Mexico and Jamaica	10,000.00
	typewriter, desk, file cabinet - one each for Mexico and Jamaica	1,440.00
H.	OVERHEAD (48.8% of salaries on campus)	69,953.00
	" (29.5% of salaries off campus)	34,028.00
I.	SUB-CONTRACTS	56,000.00

Arrangements will be made for sub-contracts
for services in prophylactic and contraceptive
testing.

TOTAL - - - - - \$ 600,939.00

E. TRAVEL EXPENSES

J.C. Cutler
H.M.D. Utidjian
B. Singh

each of the above will make 2 trips each year to Mexico and Jamaica
at 3 days each

Mexico plane + expenses -----	\$4,320.00
Jamaica plane + expenses -----	4,900.00

Project Director in Mexico and Jamaica

1 trip each year from Mexico and Jamaica to Pittsburgh
for 7 days each

Mexico plane +expenses-----	900.00
Jamaica plane +expenses-----	1,000.00

Consultant Travel

2 trips each year to Pittsburgh
5 consultants

plane and expenses-----	10,450.00
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B. Singh (to observe the VD service & research laboratories)

1 trip to Baltimore, Maryland to Johns Hopkins for 3 days

plane and expenses -----	102.00
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1 trip to Atlanta, Georgia to C.D.C. for 3 days

plane and expenses-----	156.00
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1 trip to Detroit, Michigan to Parke Davis

plane and expenses-----	98.00
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Total - - - - - \$ 21,926.00

C. Non-expendable - equipment

Conversion of a room (200 sq. ft.) and fixtures for VD Research laboratory	\$10,000.00
Metal cages for individual rabbits (100) and stainless steel unit-stands for cages	11,000.00
Darkfield microscope	1,500.00
Incubator--Co ₂ type	2,000.00
Refrigerator	250.00
Balance	300.00
Water bath	250.00
Anaerobic jar (5)	300.00
Maintenance of Equipment services @ \$600.00 per year (autoclave, centrifuge etc.)	1,800.00
Animal Operating table & lights	500.00
Calculator-Monroe 990 Electric	1,000.00
Typewriter, desk and file cabinet	720.00

D. Expendable equipment and supplies

Instruments (1st year \$700. next 2 years \$400. each)	1,500.00
Glassware (1st year \$2000. and next 2 years \$1000. each) (disposable & undisposable type)	4,000.00
Rabbits (male, treponema free)	10,000.00
Chemicals, media etc. (1st year \$1000 next 2 years \$300. each)	1,600.00
Other supplies \$1,000. per year	3,000.00
Feeding and bedding of animals	4,000.00

Total - - - - - \$ 53,720.00

PERSONNEL

	<u>% Participation</u>	<u>Annual Rate of Pay</u>	<u>Amount for Proposed Res.</u>
<u>I. A. In Pittsburgh</u>			
J.C. Cutler, M.D., Project Director	10%	3,100.00	9,300.00
H.M.D. Utidjian, M.D. " "	10%		
B. Singh, D.V.M., Ph.D. Microbiologist	100%	14,000.00	42,000.00
V. Ashmun, M.Sc., Research Assistant	100%	7,000.00	21,000.00
J. Gerende, M.Sc., Statistician	50%	4,920.00	14,760.00
Laboratory Technician	100%	6,000.00	18,000.00
Project-Secretary	100%	4,680.00	14,040.00
Animal Caretaker/attendant	100%	5,000.00	15,000.00
Health Educator (2 yrs. only)	100%	6,000.00	12,000.00
 <u>In Mexico</u>			
Physician-Project Director (1) 2yrs. only)	100%	14,000.00	28,000.00
Registered Nurse-Mexican (1) "	100%	3,000.00	6,000.00
Social Worker (1) "	100%	3,000.00	6,000.00
Laboratory Technician (1) "	100%	4,500.00	9,000.00
Records clerk/secretary "	100%	3,600.00	7,200.00
 <u>In Jamaica</u>			
Physician Project Director (1) 2yrs. only)	100%	14,000.00	28,000.00
Laboratory Technician (1) "	100%	4,500.00	9,000.00
Health Educator (1) "	100%	4,000.00	8,000.00
Social Workers (2) "	100%	6,000.00	12,000.00 (both)
Records clerk/secretary "	100%	3,600.00	7,200.00
		110,900.00	266,500.00
7% increase on salaries for 2nd and 3rd year			11,112.00
FRINGE BENEFITS (10% on salaries only)			27,760.00
this includes the 7% increase on the 2nd & 3rd years			
 <u>B. Consultants in Venereology</u>			
Dr. R.C. Arnold	14 days each	6,300.00	18,900.00 (all 3)
Dr. T.B. Turner	per each year		
Dr. Bruce Webster	@ \$150. per day		
Consultants from WHO/PAHO (2)	pro rata		<u>no salary</u>
		Total - - - - -	\$ 324,272.00

1 Informed Consent.

Consent to act as a subject in an experimental study: Vaginal Contraceptives as Prophylactic Agents Against Gonorrhea and C. Trichomatis Infection.

Dr. John C. Cutler

Source of Support: Grant NICHD

This study is designed to determine whether or not the use of a vaginal contraceptive as directed for contraceptive purposes may also provide some degree of protection against infection with gonorrhea or Clamidia trachomatis, the organism responsible for many cases of pelvic inflammatory disease.

If you enter the study you will be given for your use a contraceptive agent which is being tested or a placebo which looks exactly like the contraceptive agent. The reason for receiving either one or the other is, in order to carry out a study with certainty, it is necessary that we also know the risk of reinfection of the disease that initially brought you into the clinic if you are not protected by an agent placed in your vagina just like a contraceptive. You will be randomly chosen to receive one or the other preparation and will be expected to continue to follow the same pattern of sexual behavior as is your custom. However, it is necessary that you use the preparation as directed for each contact.

As has been discussed, since the placebo is not a contraceptive, and since the vaginal contraceptive does not provide absolute protection against pregnancy you may enter the study only if you are protected against unplanned pregnancy through the use of the IUD, an oral contraceptive or voluntary sterilization.

You will have been examined and given any necessary treatment before entering the study. In order to protect your health and to observe your protection from risk of infection, we at the clinic will arrange to have you pay one visit each month at a minimum. At the time of examination, cultures

will be taken to determine whether or not you are free from disease and you will be given a new supply of the preparation for your use. As discussed with you in the initial briefing, it will be necessary for you to keep a record of your sexual contacts and the use of the preparation given you. Should you have health problems requiring treatment, possibly acquiring another disease during the course of the study, this will be determined during your regular visits and you will be treated. Should you have any symptoms at any time, such as lower abdominal pain between visits, you should come to the clinic during clinic hours. If something serious occurs outside clinic hours, you should call the emergency number _____ and arrange to be seen.

At the end of 6 months you will receive the last of your monthly examinations and the study will have been completed as well as any needed treatment.

You will be expected to come to the clinic during the regular clinic hours unless in the case of an emergency you will be seen by a member of the Allegheny County Health Department VD staff which includes those involved in the study who will carry out the examinations, review your history and progress with you, and provide you with the necessary supplies.

In order to cover any costs you may incur, such as travel or care of member(s) of your family, etc., you will receive \$2.00 for transportation and \$5.00 for related costs for each visit. Should there be any needed treatment for disease or conditions related to the use of the preparation, this will be provided to you at no cost.

In view of the fact that the preparations being studied have been on the market for a number of years for contraceptive purposes, and in view of the fact that you are not at greater risk of infection, it is safe to say you are undergoing no additional risks by taking part in the study and you will benefit by the close observation at monthly intervals which will ensure your freedom of disease or treating you when disease is discovered. As a consequence of your participation in the study your health should be better.

As is the usual case in the Allegheny County Health Department VD Clinic, no member of your family or other person(s) will be informed of your treatment or participation in this study.

It should be understood that, if you have any concern about this study as time goes on, you are free to withdraw at any time. Should you so decide, you will not be contacted further and your responsibility will end. It should also be pointed out that in the event of physical injury or illness resulting from the research procedure, no monetary compensation will be made, but any immediate medical emergency treatment necessary will be made available without charge.

The only possible ill-effects that you or your partner may experience are occasional symptoms of irritation of the genitalia. If such should occur, you are to report to the clinic where appropriate treatment will be given.

I certify that I have read the preceeding and understand its contents. Any questions I have concerning this research have been or will be answered by Dr. _____. A copy of this consent form will be given to me. My signature below testifies that I freely agree to participate in this experimental study.

Date

Participant's Signature

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U.S. CODE
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2. Summary and Workscope

It is proposed to carry out a clinical study of the possible effects of a vaginal contraceptive approved by the F.D.A. and used as directed for contraceptive purposes in preventing infection of the female by N. gonorrhoea and/or C. trachomatis. This study will build upon the experience of the investigators in a previous study (Development and Field Testing of Combined Prophylactic Contraceptive Preparations, AID CSO 288) but will be modified and expanded to study C. trachomatis, to provide a placebo-using control group, and to "blind" both users and investigators.

The study will be carried out in cooperation with, and using the clinical and laboratory facilities of the Allegheny County Health Department, and with staff drawn from both the University of Pittsburgh and Allegheny County Health Department.

Laboratory studies using standardized techniques employed in the previous study will be carried in vitro to test all currently marketed vaginal contraceptives with respect to action on the two organisms. Similar studies will be carried out to select the appropriate placebo.

While these studies are being done the Allegheny County Health Department laboratory personnel and facilities will be prepared for routine testing of C. trachomatis; the clinical personnel will be trained in culture techniques, and the system for routine testing will be established and carried out in concert with gonorrhoea testing.

All female patients of the V.D. clinic will be screened routinely for CT as well as GC. Those 21 years of age or over, found positive for either, will be informed of the study and invited to take part. Only those using either the IUD, oral contraceptives or are sterilized, will be entered. There will be randomized selection with the investigators and patients "blinded" for use of agent or placebo. The patient will be entered into the study after treatment and proof of cure carried out in accord with the Allegheny County Health Department standards.

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The clinic (research) staff will fully manage the patient, secure informed consent, and will carry out follow-up at monthly intervals including review of patient contact history, preparation use, pattern of partners, etc., and will provide new supplies and any other relevant care or referral. Intensive care will be provided as needed by any patient problems. The pattern of repeat infections or freedom therefrom will indicate the response to the agent or placebo.

3. Research Proposal

a) Introduction

All vaginal contraceptive products currently approved by the F.D.A. will be subjected to laboratory evaluation to determine the in vitro effectiveness against *N. gonorrhoea* and *C. trachomatis*.

The procedure used for *N. gonorrhoea* will be that utilized in the previous study of vaginal contraceptives as prophylaxis against gonorrhoea. Similar procedures, based upon this experience, will be developed for testing their effectiveness on *C. trachomatis*.

All manufacturers will be requested to supply samples of the base without the spermicidal agent(s), and these will be subjected to the same testing procedures. Since, in the previous study, varying degrees and patterns of germicidal properties were found in all preparations tested, it is expected that similar findings will be observed in testing *C. trachomatis*. Thus, in order to select a placebo it will be necessary to identify those bases which are minimally lethal so that one can be selected which has the same physical characteristics and packaging potential as the preparation selected for study.

The manufacturer of the product selected will be asked to supply the placebo in appropriate packaging. The manufacturer will also be asked to supply the contraceptive selected for testing, without a label. In addition, the manufacturer will be asked to label the placebo and active preparation as "A" or "B"

and not to divulge the code to the investigator until completion of the study. The patients will be selected from the population attending the Allegheny County Health Department V.D. clinics. At present all females are cultured for gonorrhea by cervical culture. Routine testing of all females for C. trachtomotis will be instituted. All females, 21 years of age and over, found positive, will be treated using standard A.C.H.D. protocol, and checked for proof of cure. The usual procedures to provide therapy to their contacts will be followed.

Upon diagnosis of infection, in addition to the usual contact interview, the patient will be informed of the study and invited to participate. If she agrees, the usual informed consent will be secured, she will be randomly assigned to use either preparation "A" or "B", and will be fully instructed with respect to follow-up and the use of the preparation. If she is not contracepting with either the IUD, oral contraceptive(s) or tubal ligation or willing to contracept by one of these methods as part of the experiment, she will not be accepted.

The patient will be seen at monthly intervals; however, if there are any problems or symptoms she will be seen in usual clinic sessions unless an emergency problem develops. The patients will be given an emergency number(s) to call if needed and appropriate arrangements will be worked out.

At the routine visits, medical and sexual behavior history will be taken, physical examinations and cultures will be done, the contact log will be collected, new experimental supplies and contact logs will be given out, and a detailed interview will be carried out.

It is planned, in view of past experience, to pay each participant \$7.00 per visit; \$2.00 for transportation and \$5.00 for time spent or lost since many will have to take time off from work or pay baby sitters at home while away.

The patient will be seen in the A.C.H.D. VD Clinics, the laboratory work will be done by the A.C.H.D. laboratory, and the research staff will be A.C.H.D. staff whose time is purchased by the project, and additional staff employed through the project to supply the additional necessary resources to manage the patients and to carry out the laboratory tests.

As was done in the previous study on prophylaxis, the research team will function as a part of the Allegheny County Health Department Venereal Disease clinic staff. Once potential participants are identified in the clinic population, the research personnel will be alerted and the group consisting of nurse-educator, epidemiologists (contact tracer) and physicial will work with each patient to recruit and then to instruct as to product use, follow-up procedures, data collection, record keeping, etc. On the basis of past experience it is anticipated that the time spent on patient education and follow-up by phone, household visits, etc. will have to be sustained and intensive in order to assure monthly visits for clinical and laboratory examination, supply replacement, history review, etc.

The previous study was based on the comparison of the rates of reinfection in product users as compared to non-user controls. Because of the variations in numbers of sexual partners of the females and frequency of sexual contact, and because of the fact that most male partners were presumed not to be limited to a single partner--that is the female patient under study, a presumption frequently con firmed when the infected male was treated and interviewed in the VD clinic--there seems to be no feasible way to standardize the element of number of partners or contacts for the study. Thus, the volunteer will enter the study and the measure will be the difference in rate of reinfection in the two groups.

4. The period of performance is calculated to be as follows:

Phase 1: 6 months

- a) Laboratory tests carried out to select product for testing.
- b) A.C.H.D. staff trained in analytical testing.
- c) Clinic staff assembled and integrated with the A.C.H.D.;
procedures for patient management developed, tested and standardized.

Phase 2: 18 months

- a) Clinical trial initiated.
- b) Last patients entered at end of 12 months and followed through to 18 months.

Phase 3: 4 months

- a) Data Analysis
- b) Report preparation

E. Resource Information

Principal Investigators: Cutler, Singh, Dixon, Sarandrid, Balisky

Staff: Clinical physician - 2 (part-time)
Clinic nurse-educator - 2
VD epidemiologist - 1
Laboratory technician - 1-2
Project administrative Secretary - 1
Student Assistant - 1
Statistician - 1 (part-time)

Laboratory and clinical procedures - A.C.H.D. (as follows):

F. Qualifications

1) Experiences - The principal investigators, Cutler, Singh and Balisky were members of the team that carried out the study entitled Research Service Directed Toward the Development of a Combined Agent for Disease Prophylaxis and Contraception, AID/CSD 2822. The formal published reports on the project is as follows: Cutler, J.C., Singh, B., et al., "Vaginal Contraceptives as Prophylaxis Against Gonorrhea and Other Sexually Transmissible Diseases", Advances in Planned Parenthood, 12, No. 1, 45-56, 1977. The present AID member who could be contacted and who is familiar with the study is Dr. Joseph Spiedel, Acting Chief, Research Division, Office of Population, Bureau of Technical Assistance, Department of State, Agency for International Development, Washington, D.C. 20523. The director of the A.I.D. Population Program at that time, one whose concept was also reflected in it, is Dr. Reinert T. Ravenholt, presently Assistant Director of Epidemiology and Research, National Institute for Drug Abuse, Room 10-05, Parklawn Building, Rockville, Maryland 20857, phone (301) 443-6480.

Because of the interest of the World Health Organization, they have given the designation of WHO Collaborating Centre on Prophylactic Methods of Prevention of Sexually Transmitted Diseases to the program at the Graduate School of Public Health, University of Pittsburgh, headed by Drs. Cutler and Singh.

2) Personnel

The principal investigators will have shared, collaborative, and individual responsibilities as follows:

Cutler: Overall administrative control, coordinator of program and personnel at the Graduate School of Public Health, University of Pittsburgh, Allegheny County Health Department, School of Medicine, University of Pittsburgh, relationship with the contracting agency, suppliers of products tested, and used, reporting and cooperation in experimental design.

Singh: Establishment of laboratory program for C. trachamosis and N. gonorrhoea studies. Design, supervision of, and participation in laboratory testing to select preparations to be used. Developing laboratory protocols for patient follow-up and monitoring program. Monitoring of and participating in laboratory component of field trial; cooperation in experimental design.

Dixon: Planning for, supervision of, and assistance in provision of clinical services for management of study patients, both under preliminary examination, therapy, direct trial, etc.

Sarandrid: As Director of the A.C.H.D. diagnostic laboratory, will be responsible for performance of routine screening and follow-up testing for GC and CT as a part of the routine service (with CT studies added to present services) in support of the VD control administration of the Health Department.

Balisky: As administrator of the A.C.H.D. VD control program will have responsibility for establishing and maintaining the proposed research program as an integral component of the ACHD VD control activity. He will be responsible for assuring the full integration of reserach components into standard clinic operations and for the overall personnel management.

Other Key Personnel: Nurse-interviewer-educator (2 full-time). Responsible for public health nursing aspects of patient management and follow-up within clinic. Working with the physician and other team members will have primary responsibility for securing informed consent, for detailed patient instruction, follow-up interviews and other related activities.

Contact-tracer epidemiologist (1) Responsible, in accord with stated clinic procedure, to assist in interviews and follow-up of contacts and to assure reporting of contacts for work-up and treatment. Will also assume primary responsibility for follow-up of non-reporting study patients.

Secretary - one full time secretary will be required to serve both the clinic needs and administrative support needs.

Statistician - consultant service to assist in developing statistical element of research study design and in continuing review and analysis of data.

Laboratory Staff - Sarandrid and Singh.

G. Review of Work of Other Investigators

In the pre-chemotherapeutic and pre-antibiotic era, the importance of prophylaxis of STD's was recognized and played an important role in VD control programs as in the U.S. Military in World Wars I and II. This is summarized in the report of the Medical Department, U.S. Army, Preventive Medicine: World War II, Volume V, Communicable Diseases, USGPO, 1960. This combined prophylactic/contraceptive concept and its public health potential was recognized by the founders of Planned Parenthood at its inception but was not further investigated because of the public relations problem they saw if family planning was linked to VD control.

With the decline in interest in prophylaxis resulting from the perceived simplicity and economic advantage of treatment resulting from antibiotics discoveries, the U.S. Public Health Service discontinued prophylactic research (with which Dr. John C. Cutler was associated at the VDRL) in the early 1950's. At about the same time the Military discontinued prophylactic emphasis because of the simplicity of treatment.

However, the pro-con concept remained of interest to a few researchers. In 1965 Masters and Johnson reported on their pioneering laboratory studies with both standard vaginal contraceptives and a currently available prophylactic preparation, Progonosyl, and found strong laboratory evidence of potential prophylactic value. (Johnson, V.E. and Masters, W.H., "A Product of Dual Import: Intravaginal Infection Control and Conception Control", Pacific Medicine & Surgery, 73:267-271, 1965. No clinical trials were carried out, but on the basis of their work with human female subjects in simulated coitus,

they concluded "a product that simultaneously will provide conception control and protection against inter-current vaginal infection is indeed a valuable adjunct to the medical armamentarium."

With the rise in interest in population and family planning in the late 1960's , and the resultant increase in USAID funding in this field, came the concurrent recognition of the need to integrate family planning and health programs for both strategic political and health reasons. This was reflected in the award of U.S.A.I.D. contract Development and Field Testing of Combined Prophylactic Contraceptive Preparations, AID/CSD 2822 to the Graduate School of Public Health. The published report is: Cutler, J.C., Singh, B., et al., "Vaginal Contraceptives as Prophylaxis Against Gonorrhea and Other Sexually Transmissible Diseases", *Advances in Planned Parenthood*, 12, No. 1, 45-56, 1977.

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The product Conceptrol, with nonoxynal 9 as the active ingredient, was selected for field trial in cooperation with the Allegheny County Health Department VD program. The basis for selection was both the packaging - which was felt necessary for promotion of use by the group at risk - and the laboratory performance. A decision was made not to use a placebo because of the bactericidal properties of the emulsifier and other agents used in compounding of this vehicle for spermicides. Previous experiences of Cutler, et al., is research carried out abroad and in the U.S.A. with the USPHS-VDRL and demonstrated this relatively low risk of gonorrhoeal infections. Thus it was felt preferable not to use a placebo which would also lower the risk of infection.

Clinical findings showed a 90% reduction in the reinfection rate for the first six months of the trial. Following such protection from reinfection and the resultant loss of fear of the disease, there seemed to develop a sense of complacency and loss of fear of further risks so that the majority of patients then ceased follow-up visits in spite of follow-up efforts. They then had no further protection and no supplies were picked up. The next contact with the patient was usually when she returned to the clinic with symptoms of an infection acquired when not using any protective measures.

A similar study was carried out by Cole, Archer, et al., in the Tampa-Orlando, Florida Health Department VD Control Program. Because of the preference of a large part of their patient population for use of vaginal suppositories, and in view of the University of Pittsburgh's laboratory findings with respect to the bactericidal properties of the Lorophyn contraceptive suppository containing phenylmercuric acetate, they selected this preparation. Their study showed a significant reduction in the reinfection rate in the user population. Cole, C.H., Archer, T.A., et al, "Vaginal Chemoprophylaxis in the Reduction or Reinfection in Women with Gonorrhea - Clinical Evaluation of the Effectiveness of a Vaginal Contraceptive", Br. J. Ven. Dis., 56:314-318, 1980.

The studies by Rendon, A.L., Covarriubias, J., et al., reported in "A Controlled Comparative Study of Phenylmercuric Acetate, Vaginal and Placebo Vaginal Suppositories as Prophylactic Agents Against Gonorrhea", Curr. Ther. Res. 27:789-793, 1980, showed a similar risk reduction, approximately 70% in the users of the contraceptive suppository containing phenylmercuric acetate. The 40% reduction in users of the suppository containing nonoxyl 9 was not statistically significant in relation to the placebo group.

Criticism has been made of previous studies for various reasons, particularly with respect to experimental design. Furthermore, the mercury compounds are no longer approved by the F.D.A. Of particular concern in experimental design was

lack of use of a placebo and the lack of "blinding" of the investigators and subjects. In addition there was concern about the relatively small size of the various study groups and the problem of lack of compliance with respect to use of the preparation. The problem is perhaps best illustrated by the experience in a study carried out in Thailand by the IFRP (J.C. Cutler as consultant) working with a group of licensed prostitutes. The women, many of whom were married yet practicing prostitution to make a living for the family, refused to use the preparation when with their husbands. "It would be undignified". Thus the study was terminated.

The experience in studies on the population group at high risk of STD's highlights the relationship of social and behavioral habits and attitudes and the resultant problem in carrying out scientifically rigid studies in the group. However, the experiences of the past in the use of prophylaxis as an important element of VD control, as well as the indication of effectiveness of various preparations as shown by the studies of recent investigators using varying preparations and experimental design offer strong evidence of the importance of continuing this research approach with experimental designs which may recognize and overcome criticism of past studies yet deal realistically with the social and behavioral beliefs and patterns of behavior of the group.

H. Facilities and Equipment

The clinical and laboratory studies will be carried out in the facilities of the Allegheny County Health Department. The laboratory serves the needs of a population of _____ while the VD clinic serves primarily an area of approximately _____ population. The quality of service and experience of the official agency VD services may perhaps be summarized by the fact that the STD rates (specific) of Allegheny County rank _____ in the last of _____ SMSA's of more than 1 million population.

The case load of the clinic is as follows:

In order to provide chamydial testing services, the laboratory will require

The additional research operation of the VD clinic will require

The Graduate School of Public Health will use existing resources.

2. Summary and Workscope

It is proposed to carry out a clinical study of the possible effects of a vaginal contraceptive approved by the F.D.A. and used as directed for contraceptive purposes in preventing infection of the female by N. gonorrhoea and/or C. trachomatis. This study will build upon the experience of the investigators in a previous study (Development and Field Testing of Combined Prophylactic Contraceptive Preparations, AID CSO 288) but will be modified and expanded to study C. trachomatis to provide a placebo-using control group, and to "blind" both users and investigators.

The study will be carried out in cooperation with, and using the clinical and laboratory facilities of the Allegheny County Health Department, and with staff drawn from both the University of Pittsburgh and Allegheny County Health Department.

Laboratory studies using standardized techniques employed in the previous study will be carried in vitro to test all currently marketed vaginal contraceptives with respect to action on the two organisms. Similar studies will be carried out to select the appropriate placebo.

While these studies are being done the Allegheny County Health Department laboratory personnel and facilities will be prepared for routine testing of C. trachomatis; the clinical personnel will be trained in culture techniques, and the system for routine testing will be established and carried out in concert with gonorrhoea testing.

All female patients of the V.D. clinic will be screened routinely for CT as well as GC. Those 21 years of age or over, found positive for either, will be informed of the study and invited to take part. Only those using either the IUD, oral contraceptives or are sterilized, will be entered. There will be randomized selection with the investigators and patients "blinded" for use of agent or placebo. The patient will be entered into the study after treatment and proof of cure carried out in accord with the Allegheny County Health Department standards.

The clinic (research) staff will fully manage the patient, secure informed consent, and will carry out follow-up at monthly intervals including review of patient contact history, preparation use, pattern of partners, etc., and will provide new supplies and any other relevant care or referral. Intensive care will be provided as needed by any patient problems. The pattern of repeat infections or freedom therefrom will indicate the response to the agent or placebo.

3. Research Proposal

a) Introduction

All vaginal contraceptive products currently approved by the F.D.A. will be subjected to laboratory evaluation to determine the in vitro effectiveness against *N. gonorrhoea* and *C. trachomatis*.

The procedure used for *N. gonorrhoea* will be that utilized in the previous study of vaginal contraceptives as prophylaxis against gonorrhoea. Similar procedures, based upon this experience, will be developed for testing their effectiveness on *C. trachomatis*.

All manufacturers will be requested to supply samples of the base without the spermicidal agent(s), and these will be subjected to the same testing procedures. Since, in the previous study, varying degrees and patterns of germicidal properties were found in all preparations tested, it is expected that similar findings will be observed in testing *C. trachomatis*. Thus, in order to select a placebo it will be necessary to identify those bases which are minimally lethal so that one can be selected which has the same physical characteristics and packaging potential as the preparation selected for study.

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and not to divulge the code to the investigator until completion of the study. The patients will be selected from the population attending the Allegheny County Health Department V.D. clinics. At present all females are cultured for gonorrhea by cervical culture. Routine testing of all females for C. trachtomotis will be instituted. All females, 21 years of age and over, found positive, will be treated using standard A.C.H.D. protocol, and checked for proof of cure. The usual procedures to provide therapy to their contacts will be followed.

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4. The period of performance is calculated to be as follows:

Phase 1: 6 months

- a) Laboratory tests carried out to select product for testing.
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procedures for patient management developed, tested and standardized.

Phase 2: 18 months

- a) Clinical trial initiated.
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- a) Data Analysis
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Principal Investigators: Cutler, Singh, Dixon, Sarandrid, Balisky

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G. Review of Work of Other Investigators

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The experience in studies on the population group at high risk of STD's highlights the relationship of social and behavioral habits and attitudes and the resultant problem in carrying out scientifically rigid studies in the group. However, the experiences of the past in the use of prophylaxis as an important element of VD control, as well as the indication of effectiveness of various preparations as shown by the studies of recent investigators using varying preparations and experimental design offer strong evidence of the importance of continuing this research approach with experimental designs which may recognize and overcome criticism of past studies yet deal realistically with the social and behavioral beliefs and patterns of behavior of the group.

H. Facilities and Equipment

The clinical and laboratory studies will be carried out in the facilities of the Allegheny County Health Department. The laboratory serves the needs of a population of _____ while the VD clinic serves primarily an area of approximately _____ population. The quality of service and experience of the official agency VD services may perhaps be summarized by the fact that the STD rates (specific) of Allegheny County rank _____ in the last of _____ SMSA's of more than 1 million population.

The case load of the clinic is as follows:

In order to provide chamydial testing services, the laboratory will require

The additional research operation of the VD clinic will require

The Graduate School of Public Health will use existing resources.

will be taken to determine whether or not you are free from disease and you will be given a new supply of the preparation for your use. As discussed with you in the initial briefing, it will be necessary for you to keep a record of your sexual contacts and the use of the preparation given you. Should you have health problems requiring treatment, possibly acquiring another disease during the course of the study, this will be determined during your regular visits and you will be treated. Should you have any symptoms at any time, such as lower abdominal pain between visits, you should come to the clinic during clinic hours. If something serious occurs outside clinic hours, you should call the emergency number _____ and arrange to be seen.

At the end of 6 months you will receive the last of your monthly examinations and the study will have been completed as well as any needed treatment.

You will be expected to come to the clinic during the regular clinic hours unless in the case of an emergency you will be seen by a member of the Allegheny County Health Department VD staff which includes those involved in the study who will carry out the examinations, review your history and progress with you, and provide you with the necessary supplies.

In order to cover any costs you may incur, such as travel or care of member(s) of your family, etc., you will receive \$2.00 for transportation and \$5.00 for related costs for each visit. Should there be any needed treatment for disease or conditions related to the use of the preparation, this will be provided to you at no cost.

In view of the fact that the preparations being studied have been on the market for a number of years for contraceptive purposes, and in view of the fact that you are not at greater risk of infection, it is safe to say you are undergoing no additional risks by taking part in the study and you will benefit by the close observation at monthly intervals which will ensure your freedom of disease or treating you when disease is discovered. As a consequence of your participation in the study your health should be better.

As is the usual case in the Allegheny County Health Department VD Clinic, no member of your family or other person(s) will be informed of your treatment or participation in this study.

It should be understood that, if you have any concern about this study as time goes on, you are free to withdraw at any time. Should you so decide, you will not be contacted further and your responsibility will end. It should also be pointed out that in the event of physical injury or illness resulting from the research procedure, no monetary compensation will be made, but any immediate medical emergency treatment necessary will be made available without charge.

The only possible ill-effects that you or your partner may experience are occasional symptoms of irritation of the genitalia. If such should occur, you are to report to the clinic where appropriate treatment will be given.

I certify that I have read the preceeding and understand its contents. Any questions I have concerning this research have been or will be answered by Dr. _____. A copy of this consent form will be given to me. My signature below testifies that I freely agree to participate in this experimental study.

Date _____

Participant's Signature _____



GRADUATE SCHOOL OF PUBLIC HEALTH
UNIVERSITY OF PITTSBURGH ■ PITTSBURGH, PENNSYLVANIA 15213

Dr. Cutler

POPULATION DIVISION

I appreciate your taking time out of your schedule to attend the experimental design review of the Pro-Con field studies to be held in Pittsburgh, December 16, 1971.

Enclosed you will find a brief summary of the Pro-Con Project we are now engaged in along with a copy of our planned experimental design, and an agenda.

You will note that we plan to begin at 9:30am in room A-313, Graduate School of Public Health, University of Pittsburgh, 5th Avenue and DeSoto Street, Pittsburgh, Pa. 15213, and hope to finish by 3:00pm to allow time for most to return home that afternoon or early evening.

The purpose of the workshop is to review our planned experimental design and discuss possible alternatives with A.I.D. and F.D.A. representatives to be sure that the study will enable us to provide a claim of prophylaxis for a contraceptive or other compound and thus satisfy requirements for F.D.A. approval.

If you plan to arrive the night of December 15, I will be glad to make arrangements for you in a convenient hotel, the Webster Hall. If there is any other way we can be of assistance with your plans, please let me know.

The airport bus to the Webster Hall departs on the hour up to 8:00pm and requires about 45 minutes. If this is inconvenient, you should take the regular bus to the William Penn Hotel and then go by taxi to the Hotel Webster Hall or to the Graduate School of Public Health which is close by. Arrangements will be made to provide transportation between the Graduate School of Public Health and the Hotel.

Sincerely,

John C. Cutler

John C. Cutler, M.D.
Director, Population Division

JCC/rr

Enclosures

AGENDA
Experimental Design Workshop
University of Pittsburgh
Graduate School of Public Health
5th and DeSoto Street
Pittsburgh, Pa. 15213
(412) 683-1620, ext. 2377

December 16, 1971
9:30 am to 3:00pm

- I. Pro-Con Project
 - A. Objectives
 - B. Past Studies
 - C. Current Status
 - D. Future
 - E. Experimental Design of Field Trial
- II. Alternative Experimental Designs
 - A. Prostitutes
 - B. Direct Infection
 - 1. problems
 - 2. strong points
 - 3. weak points
- III. Lunch
- IV. Open Discussion
 - A. Recidivist Design
 - B. Prostitute Design
 - C. Direct Infection
 - D. Other
- V. Recommendation of Work Shop

PROJECT FOR THE DEVELOPMENT OF A COMBINED AGENT FOR
DISEASE PROPHYLAXES AND CONTRACEPTION

University of Pittsburgh
Graduate School of Public Health

J.C. Cutler, M.D.
Director, Population Division
Project Director

B. Singh, Ph.D, D.V.M.
Research Associate
Department of Epidemiology and Microbiology

H.M.D. Utidjian, M.D.
Assistant Professor
Department of Epidemiology and Microbiology

Date of Grant, June 30, 1970

Name of Grant: Development of a Combined Agent for
Disease Prophylaxes and Contraception

Grantor: Agency for International Development

Contract Number: AID/csd-2822

CONTRACEPTIVE PROPHYLACTIC PROJECT SUMMARY

After W. W. II, penicillin, the condom, and public health programs helped decrease the venereal disease rates. In fact, there ensued a serious decline in medical and public interest. We are again faced with rapidly rising rates of venereal disease throughout the world. These rates combined with steadily rising numbers of unwanted and casual pregnancies presents one of the major world-wide public health problems today.

In view of this problem, it is felt that an intra-vaginal precoital preparation offering protection to the female from venereal disease and pregnancy and to the male from venereal disease would significantly complement existing contraceptive and venereal disease control techniques. Such a preparation which could be used alone or in conjunction with other contraceptive agents, which would not require medical prescription or intervention, and which would be readily available regardless of age or sex would appeal to a large number of the sexually active and promiscuous population, whose major concern is self-protection. This preparation could be promoted effectively for wide distribution and could be incorporated into the VD programs and other public health programs with a high probability of utilization.

Although prophylactic treatment is accepted in many parts of the world, in recent years little systematic evaluation of mechanical, chemical or antibiotic agents as a means of preventing venereal disease has been made. It is hypothesized, however, that a dual purpose intra-vaginal agent can be developed by combining substances which are effective as local prophylactics against syphilis and gonorrhoea with substances that are effective as intra-vaginal contraceptives.

We plan to expedite such a study via a 3-stage program.

Stage 1.

Laboratory screening and quantitative testing, in vitro and in vivo, of a number of compounds against T. pallidum and in vitro against N. gonorrhoeae. Gonococcicidal effects will be tested in the conventional manner of bacterial sensitivity testing. A simple slide immobilization test will be used to test compounds for spirocheticidal effects. Promising compounds will then be tested in vivo, using the rabbit as an experimental model, in a manner approximating human prophylaxis. These compounds will also be tested in vitro for spermaticidal efficacy.

Stage 2.

Field efficacy trials will be conducted at several geographic locations in which AID is involved in the local health programs. The preparations will be introduced and promoted through existing VD control programs. Efficacy of the preparation will then be measured by its ability to reduce the re-infection rates in recidivist patients. The contraceptive efficacy will also be evaluated.

Stage 3.

Selected products found promising as a result of the efficacy trials shall be further tested by incorporation into existing contraceptive or population planning programs, conducted by such agencies as Pathfinder Fund, the Population Council and the Planned Parenthood/World Population.