

AGENCY FOR INTERNATIONAL DEVELOPMENT
 WASHINGTON, D. C. 20523
 BIBLIOGRAPHIC INPUT SHEET

FOR AID USE ONLY

1. SUBJECT CLASSIFICATION	A. PRIMARY Serials	Y-PC00-0000-0000
	B. SECONDARY Population--Family planning	

2. TITLE AND SUBTITLE
 Program for applied research on fertility regulation; progress report, July-Dec. 1978

3. AUTHOR(S)
 (101) Northwestern Univ. Medical School

4. DOCUMENT DATE 1978	5. NUMBER OF PAGES 98p.	6. ARC NUMBER ARC
--------------------------	----------------------------	----------------------

7. FUNDING AGENCY NAME AND ADDRESS
 Northwestern

8. SPECIAL NOTES (for health, Organization, Publishers, Availability)

9. ABSTRACT

10. CONTROL NUMBER PN-AAG-422	11. PRICE OF DOCUMENT
12. DESCRIPTORS Fertility Birth control Contraceptives Sterilization	13. PROJECT NUMBER 931054600
	14. CONTRACT NUMBER AID/csd-3608 Res.
	15. TYPE OF DOCUMENT

17 17

DEPT-ANNOUN, 11 -

JULY 1, 1977 - JULY 31, 1978

PA-PRG-1122

PROGRAM FOR APPLIED RESEARCH
ON FERTILITY REGULATION

SEMI-ANNUAL REPORT

JULY 1, 1978 - DECEMBER 31, 1978

Submitted to: Research Division
 Office of Population
 Development Support Bureau
 Agency for International Development
 Department of State
 Washington, D.C. 20523

Submitted by: Program for Applied Research
 on Fertility Regulation
 Northwestern University
 Medical School
 1040 Passavant Pavilion
 303 East Superior Street
 Chicago, Illinois 60611

In compliance with Contract AID/csd-3608

TABLE OF CONTENTS

	<u>Page</u>
I. REPORT SUMMARY.....	1
II. CONTRACT OBJECTIVES.....	2
III. PROGRAM ACCOMPLISHMENTS.....	3
LDC Involvement.....	3
Scientific Summary.....	5
Administrative Summary.....	6
Subcontract Negotiations.....	7
Personnel.....	13
Organization Chart.....	14
Scientific Advisory Committee.....	15
Site Visits.....	18
Consultants.....	20
Subcontracts (Capsule Summaries).....	21
IV. WORK PLAN.....	42
Anticipated Accomplishments.....	42
Procedures and Activities.....	43
Plans for LDC Involvement.....	44
V. FINANCIAL REPORTS.....	45
Summary Financial Report.....	45
Expenditures for Reporting Period.....	46
Budget Forecast.....	47
VI. APPENDIX	
Scientific Advisory Committee Minutes	
Vaginal Contraception Workshop Program	
PARFR Newsletter	

REPORT SUMMARY

Project Title and Contract Number:

Program for Applied Research on Fertility Regulation
AID/csd-3608

Principal Investigator:

John J. Sciarra, M.D., Ph.D.
Professor and Chairman
Department of Obstetrics and Gynecology
Prentice Women's Hospital and Maternity Center
333 East Superior Street
Chicago, Illinois 60611

Contractor:

Northwestern University
c/o Sponsored Projects Administration
619 Clark Street
Evanston, Illinois 60201

Contract Period:

July 1, 1975 - June 30, 1979

Reporting Period:

July 1, 1978 - December 31, 1978

Total Expenditures Through June 30, 1978: \$1,876,804.87

Total Expenditures July 1, 1978 - December 31, 1978: \$ 538,667.60

Outstanding Commitments at December 31, 1978: \$1,185,748.89

Additional Projected Expenses Through June 30, 1979: \$ 661,376.71

CONTRACT OBJECTIVES

"The contractor shall establish a [Program for Applied Research on Fertility Regulation (PARFR)] which will actively involve a panel of experts to solicit, evaluate, and assist in the development and monitoring of a series of studies which require modest funding both within the U.S. and in less developed countries. These studies will include work to develop improved means of male and female sterilization, studies of once-a-month means of fertility control, and evaluation of locally-effective male and female methods of contraception."

"...The contractor shall make available and employ its research and development facilities and personnel... (to) perform a research and development program directed toward actively pursuing a number of promising leads of goal directed research to develop a new means of fertility control."

ACCOMPLISHMENTS

PROGRAM ACCOMPLISHMENTS

3

LDC Involvement

Dr. Elizabeth B. Connell joined the PARFR staff on September 1, 1978 as our Research Project Development Coordinator. In her position, Dr. Connell is primarily responsible for foreign project development aimed at the initiation of Phase I or early Phase II clinical trials and their subsequent monitoring in less developed countries. Dr. Connell has been working with Dr. Carl Pauerstein, University of Texas, San Antonio, to develop a network of Latin American investigators and institutions that are able to assist PARFR in these clinical trials. Individual participants in this network have been identified in Chile, Colombia, Argentina, Brazil and Mexico. Drs. Connell and Pauerstein will visit, during our next reporting period, these individuals to solicit interest in collaborating in PARFR projects.

In July, 1978 Dr. Aquiles Sobrero traveled to Guatemala City, Guatemala and contacted Drs. Santiso and Galich of APROFAM to obtain local support for the PARFR Workshop. PARFR is sponsoring an International Workshop: New Developments in Vaginal Contraception, April 25-27, 1979 in Guatemala City, Guatemala. We are grateful to the United Nations Fund for Population Activities who has granted PARFR funds to invite attendees from LDCs to the Workshop. At the time of this writing, we have identified over 75 individuals from LDCs representing 27 LDC countries, 16 of which are in Latin America.

On October 4, 1978, Ms. Krier traveled from Salvador to Guatemala to confer with Dr. Santiso of APROFAM regarding their involvement in PARFR's Workshop scheduled for April, 1979. Ms. Krier also met with Mr. Scott Edmonds, AID Population Officer, and the hotel staff at the Camino Real Hotel to initiate meeting arrangements. Dr. Santiso expressed his interest, on behalf of APROFAM, to participate in clinical studies with PARFR.

Dr. Neuwirth, Dr. Richart and Ms. Krier performed a project development site visit, October 1-4, 1978 in San Salvador, El Salvador. The purpose of this site visit was to interest potential investigators in Phase I clinical trials of "Fallopian Tube Closure using Methylcyanoacrylate (MCA) Delivered through the Single Application Fertility Regulation (FEMCEPT) Device." The site visitors met with Drs. Gustavo Argueta (ADS), Ernesto Moran-Caceres (Social Security Institute), Angel Quan (Maternity Hospital), and Vernon Madrigal. All four doctors expressed interest in participating in the project.

As of this writing, clinical trials will definitely be performed at ADS (Dr. Argueta) and ISSS (Dr. Moran-Caceres). A training session is scheduled for Wednesday, March 21, 1979. Subcontracting is complete for these two institutions and we anticipate that Dr. Angel Quan of Maternity Hospital will also join the study.

The MCA-FEMCEPT project is currently in clinical trials in West Germany and Seoul, Korea. Due to technical problems with the drug, these trials have been temporarily halted. Thirty-three patients had been treated in Germany prior to this time. Dr. Sung-bong Hong (Korea University) was trained in the procedure in Germany. Due to the amount of time since Dr. Hong's training session and the subsequent unavailability of the MCA, Dr. Neuwirth will be retraining Dr. Hong in Seoul, Korea in May, 1979.

LDC Involvement (continued)

PARFR will be arranging a site visit of PARFR-86K (the MCA-FEMCEPT study) with Dr. Hong, and PARFR-97K, "Research on Instillation Techniques for Pregnancy Termination in Korea," with Dr. Moon (Yonsei University) and the 3 other investigators in the project, the week of May 7-10, 1979 in Seoul, Korea.

Dr. Danny Lewis of Southern Research Institute recently went to CIFE in Mexico City to manufacture the compound being studied under PARFR-98M, "Norethisterone Microcapsule Injectable Contraceptive Study." There has been a great delay in this project due to the fact that equipment sent to Mexico was tied up in Customs because of problems between the U.S. Embassy and Mexican Customs in regard to clearance of the equipment. The Customs problems have now been solved and the equipment released.

Dr. Fouad Hefnawi's project entitled: "Measurement of Blood Loss in Women Fitted with Copper Clad Lippes Loops" at Al-Azhar University, Cairo, Egypt, will be terminating April 30, 1979.

Professor Gamal El-Din Beheri, Cairo University, Egypt, submitted an informal proposal for the development of a reversible male sterilization procedure which was reviewed at the July 10, 1978 Scientific Advisory Committee Meeting. The Committee felt that his proposal was very similar to Dr. Zaneveld's PARFR supported project, PARFR-95N (University of Illinois) entitled: "Development and Evaluation of a Reversible Vas Deferens Blocking Device." It was recommended that the PARFR staff encourage communication between Dr. Zaneveld and Dr. Beheri since Dr. Zaneveld's shug device should be ready for human testing in a few months. Dr. Omran of IFRP recently visited PARFR in Chicago and we explained our desire to collaborate with Dr. Beheri in Egypt. On a recent trip, she represented PARFR plans to Dr. Beheri and he has indicated to her, as well as in his communications with Dr. Zaneveld, that he is interested in a collaborative effort.

Scientific Summary

During this reporting period, PARFR continued its scientific program as follows:

- (1) Staff and Scientific Advisory Committee (SAC) review of extension, formal, pilot study and informal research proposals. Please refer to the Scientific Advisory Committee section (Program Accomplishments) and SAC Minutes (Appendix) regarding specific determinations.
- (2) Staff, SAC and consultant monitoring of active research progress by review of technical reports and site visits to the following projects:
 - a. 9/12-15/78 - Dr. Gerald Zatuchni; University of Essen, West Germany and Evangelisches Krankenhaus, Cologne, West Germany (81N - Tauber and 86G - Zinser/Eldering/Baur).
 - b. 10/15/78 - Drs. Robert Chatterton and Elizabeth Connell; Columbia University, New York (89N - Gregor).
 - c. 10/16/78 - Drs. Robert Chatterton and Elizabeth Connell; New York Medical College, New York (90N - Davis).
 - d. 10/17/78 - Drs. Robert Chatterton, Elizabeth Connell and Gerald Zatuchni; Dynatech R/D Company, Cambridge, Massachusetts (91N - Wise).
 - e. 10/23/78 - Dr. Gerald Zatuchni and Ms. Diane Krier; University of Arizona, Tucson, Arizona (85N - Chvapil).
 - f. 11/21/78 - Drs. Kenneth Tung and Gerald Zatuchni; Oklahoma State University, Stillwater, Oklahoma (99N - Garner).
- (3) Preparation of manuscripts from the Northwestern University Workshop and Postgraduate Course, Pregnancy Termination: Procedures, Safety and New Developments, for publication by Harper and Row. The anticipated publication date of this volume is July 15, 1979.
- (4) The PARFR staff has been actively planning a Workshop on Intra-vaginal Contraception to be held in Guatemala, April 25-27, 1979. Foreign speakers and observers are being invited, especially those from LDCs. The Workshop Program and Abstracts are being printed in Spanish as well as English. PARFR plans to arrange for simultaneous Spanish translation of the presentations at the Workshop.
- (5) PARFR staff participated in the following medical and scientific meetings:
 - a. 7/17-20/78 WHO Task Force on Female Sterilization, Geneva, Switzerland
 - b. 8/17-19/78 Second National Conference on Safety of Fertility Control, Long Beach, California
 - c. 9/11-12/78 WHO Meeting of International Agencies Conducting Research in Fertility Control, Geneva, Switzerland
 - d. 9/24-26/78 National Abortion Federation Meeting, San Francisco, California
 - e. 10/24-27/78 APPP Meeting, San Diego, California
 - f. 11/15-18/78 AAGL Meeting, Hollywood, Florida
 - g. 12/7-8/78 IFRP IUD Advisory Committee Meeting, Washington, D.C.

PROGRAM ACCOMPLISHMENTS

Administrative Summary

In addition to the routine management of the program, the efforts of the PARFR administrative staff were chiefly directed toward:

- 1) Preparation of a newsletter for distribution in October, 1978. PARFR's own mailing list of approximately 2,000 names was used for this mailing. The list was retyped on index cards and divided into foreign and domestic categories. The list is continuously being revised.
- 2) Three Scientific Advisory Committee agendas were coordinated and mailed during this period. The first SAC meeting was July 10, 1978 and the agenda included: 5 extension proposals (PARFR 80N, 92N, 95N, P8, P9); 3 formal proposals; 2 pilot studies; 10 informal proposals; 4 PARFR initiated projects; and project monitoring, including 8 technical reports. The September 6, 1978 SAC meeting included: 2 extension requests (PARFR 79N and 91N); 7 formal proposals; 1 PARFR initiated proposal; 5 informal proposals; and project monitoring, including 2 technical reports and 1 site visit report. The December 11, 1978 SAC agenda included: 4 extension proposals (PARFR 89N, 90N, 91N and 85N); 7 formal proposals; 1 pilot study; 2 informal proposals; and project monitoring, including 5 site visit reports and 10 technical reports.
- 3) Negotiation and execution of subcontracts for 12 extended research projects (PARFR 86N, 86G, 86K, 97N, 97K, 98M, 99N, 100N, 101N, 102N, 103N, 104N). Negotiation and amendment of 17 subcontracts for continuation of previously supported research (PARFR 63B, 79N, 80N, 81N, 82N, 84N, 85N, 88N, 89N, 90N, 91N, 92N, 93N, 94N, 95N, 99N, P10) and development of 2 formal proposals from acceptable informal proposals submitted. PARFR P-12, P-13, P-14, P-15 and P-16 were all negotiated and subcontracts executed from approved pilot study proposals.
- 4) The manuscripts from the May, 1978 post-graduate course and workshop, Pregnancy Termination: Procedures, Safety, and New Developments, were submitted to Harper and Row. The completed publication is anticipated July 15, 1979.
- 5) PARFR exhibited at the Association of Planned Parenthood Physicians/Planned Parenthood Federation of America meeting in San Diego, California October 25-27, 1978. PARFR staff attending were Gerald I. Zatuchni, M.D., Elizabeth B. Connell, M.D., and Diane H. Krier.
- 6) Elizabeth B. Connell, M.D. joined the PARFR staff September 1, 1978 as Research Project Development Coordinator.
- 7) Julie M. Jaworski was hired as Secretary I on October 2, 1978 to fill the position vacated by Hazel Hagan.
- 8) Staffing in the program was modified to include the following during this reporting period:

Program Director	John J. Sciarra, M.D., Ph.D.
Director of Administration	Diane H. Krier, M.B.A.
Director of Technical Assistance	Gerald I. Zatuchni, M.D., M.Sc.
Project Coordinator	Aquiles J. Sobrero, M.D.
Research Project Development Coordinator	Elizabeth B. Connell, M.D.
Project Controller	Georgia L. Fackler
Three Full-Time Secretaries	Ruvenia Thomas
	Mary Rose Traylor
	Julie M. Jaworski

7/1/78 - 12/31/78
SUBCONTRACT NEGOTIATIONS

PROJECT #	TITLE, INVESTIGATOR, INSTITUTION	ACTION	PERIOD	FUNDING
PARFR-63B	"Development of a Reversible and Permanent Uterotubal Blocking Technique by Hysteroscopy" A.H. Hosseinian, M.D. L.J.D. Zaneveld, D.V.M., Ph.D. University of Illinois	Extension w/funds	7/1/78- 6/30/79	\$ 1,477.00
PARFR-79N	"A Method for Reversible Sterilization in the Female" C.I. Meeker, M.D. Maine Medical Center	Extension w/funds (Amend #2)	10/1/78- 9/30/79	\$ 57,537.00
PARFR-80N	"Fertility Control through Local Cervical Injection of Microencapsulated Progestins" D.W. Keller, M.D. Washington University	No-cost extension (Amend #9)	7/1/78- 7/11/78	- 0 -
PARFR-81N	"Clinical Evaluation of Intrauterine Devices Containing Epsilon Aminocaproic Acid (EACA)" P.F. Tauber, M.D. University of Essen Essen, West Germany	Extension w/funds (Amend #3)	7/1/78- 9/30/78	\$ 9,408.00
PARFR-82N	"The Measurement of Blood Loss in Women Fitted with Copper-Clad and Standard Lippes Loops in Cairo, Egypt" F. Hefnawi, M.B., M.S. Al-Azhar University Cairo, Egypt	Extension w/funds (Amend #4)	7/1/78- 4/30/79	\$ 14,960.13
PARFR-84N	"Evaluation of the Copper T IUD as a Postcoital Method of Contraception" J. Lippes, M.D. Planned Parenthood of Buffalo, Inc.	Extension w/decr. funds (Amend #1)	7/1/78- 8/15/78	(\$ 23,128.87)

PARFR-85N	"Collagen Sponge Contraceptive--Testing of Efficacy in Human Volunteers" M. Chvapil, M.D., Ph.D. University of Arizona	No-cost extension (Amend #1)	7/1/78- 12/31/78	- 0 -
		No-cost extension (Amend #2)	1/1/79- 6/30/79	- 0 -
PARFR-86N	"Phase I Clinical Trial of Fallopian Tube Closure Using Methylcyanoacrylate (MCA) Tissue Adhesive Delivered Through the Single-Application Fertility Regulation (FEMCEPT) Device" R.S. Neuwirth, M.D. St. Luke's Institute for Health Sciences	New Sub-contract	6/1/78- 5/31/79	\$ 36,602.00
PARFR-86G	(Same title as PARFR-86N) H.K. Zinser, H. Baur, M.D., G. Eldering, M.D. Bureau Mengen Cologne, West Germany	New Sub-contract	9/1/78- 8/31/79	\$ 27,159.00
PARFR-86K	(Same title as PARFR-86N) S.B. Hong, M.D. Korea University Medical College Seoul, Korea	New Sub-contract	6/1/78- 5/31/79	\$ 16,080.00
PARFR-88N	"Study to Determine the Safety and Efficacy of Copper Releasing IUDs as a Method of Postcoital Contraception" L.B. Tyrer, M.D. Planned Parenthood Federation of America, Inc.	No-cost extension (Amend #2)	7/1/78- 8/31/78	- 0 -
PARFR-89N	"Fallopian Tube Cauterization and Closure by Silver Acetate-Alginate Formulations" H.P. Gregor, Ph.D. Columbia University	Add'l funding (Amend #2)	Same	\$ 11,649.00
PARFR-89N	St. Luke's Institute for Health Sciences Animal Care Facility	Add'l funding	Same	\$ 4,350.00

PARFR-90N	"New Method for Obstructing the Vas Deferens by Direct Injection of Chemical Agents: A Non-Operative Technique of Male Sterilization" J.E. Davis, M.D. New York Medical College	No-cost extension (Amend #3)	10/1/78- 12/31/78	- 0 -
PARFR-91N	"Preparation and Evaluation of Biodegrad- able Cylindrical Implants for Fertility Control" D.L. Wise, Ph.D. Dynatech R/D Company	Extension w/funds (Amend #2)	7/1/78- 9/30/78	\$ 15,450.00
PARFR-92N	"Contraception by Induction of Mild Uterine Inflammation" D.J. Anderson, Ph.D. Medical Research Foundation of Oregon	Extension w/funds (Amend #2)	7/1/78- 6/30/79	\$ 49,963.00
PARFR-93N	"Workshop on Animal Models of Fertility and Contraception" N.A. Muckenhirn, Ph.D. National Academy of Sciences	No-cost extension (Amend #1)	7/1/78- 6/30/79	- 0 -
PARFR-94N	"Modern Modified Aldridge Procedure" W. DroegemueLLer, M.D. University of Arizona	Extension w/funds (Amend #2)	10/1/78- 12/31/79	\$ 24,317.50
PARFR-94N	University of Illinois Biologic Resources Laboratory	Separate agreement	10/1/78- 12/31/79	\$ 17,849.50

PARFR-95N	"Development & Evaluation of a Reversible Vas Deferens Blocking Device" L.J.D. Zaneveld, D.V.M., Ph.D. University of Illinois	Extension w/funds (Amend #2)	7/1/78- 9/30/78	\$ 12,488.00
		Extension w/funds (Amend #3)	10/1/78- 6/30/79	\$ 32,016.00
PARFR-97N	"Research on Instillation Techniques for Pregnancy Termination in Korea" T.M. King, M.D., Ph.D. Johns Hopkins University	New Sub-contract	8/1/78- 7/31/79	\$ 54,734.00
PARFR-97K	(Same title as PARFR-97N) Y.K. Moon, M.D. Yonsei University College of Medicine Seoul, Korea	New Sub-contract	7/1/78- 6/30/79	\$ 33,000.00
PARFR-98M	"Norethisterone Microcapsule Injectable Contraceptive Study" R. Aznar, M.D. Centro de Investigacion Sobre Fertilidad y Esterilidad Mexico City, Mexico	New Sub-contract	7/1/78- 6/30/79	\$ 34,265.00
PARFR-98M	University of Alabama in Birmingham	Separate agreement	7/1/78- 6/30/79	\$ 10,780.00
PARFR-98M	Southern Research Institute	Separate agreement	7/1/78- 6/30/79	\$ 9,579.00
PARFR-99N	"Immunoabsorbent Isolation of Specific Spermatozoal Antigens for Use as Anti-Fertility Immunogens" D.L. Garner, Ph.D. Oklahoma State University	New Sub-contract	7/1/78- 12/31/78	\$ 30,233.00
		No-cost extension (Amend #1)	1/1/79- 3/31/79	- 0 -

PARFR-100N	"Investigation of New Compounds to Terminate Pregnancy" L.J. Lerner, Ph.D. Jefferson Medical College	New Sub- contract	9/1/78- 8/31/79	\$ 66,286.00
PARFR-101N	"Metabolism and Pharmacokinetics of Ethynyl Estrogens" J.W. Goldzieher, M.D. Southwest Foundation for Research & Education	New Sub- contract	9/1/78- 2/28/79	\$ 23,994.00
PARFR-102N (P10)	"Fertility Regulation by Control of Progesterone Clearance" R.T. Chatterton, Ph.D. University of Illinois	New Sub- contract	11/1/78- 10/31/79	\$ 46,767.00
PARFR-103N	"Microencapsulation of Progesterone Antibodies" A.P. Gray, Ph.D. IIT Research Institute	New Sub- contract	11/1/78- 10/31/79	\$ 28,108.00
PARFR-104N (P9)	"A Fibrous Polymer for the Delivery of Contraceptive Steroids to the Female Reproductive Tract" D.H. Lewis, Ph.D. Southern Research Institute	New Sub- contract	11/1/78- 10/31/79	\$ 66,000.00
PARFR-P10	"Fertility Control by Control of Progesterone Clearance" R.T. Chatterton, Ph.D. University of Illinois	Extension w/funds (Amend #2)	8/1/78- 10/31/78	\$ 1,216.78
PARFR-P12	"Development of Microporous Materials for Thin Intravasal Implants" D.H. Frisch, Ph.D. Massachusetts Institute of Technology	New Sub- contract	7/1/78- 6/30/79	\$ 6,685.50

PARFR-P13	"An Evaluation of the Efficacy of Candidate Fimbrial Prosthesis in Female Rabbits and the Evaluation of Fimbrial Devices as a Reversible Technique of Female Sterilization" I. Brosens, M.D., Ph.D. Catholic University of Leuven Leuven, Belgium	New Sub- contract	5/1/78- 4/30/79	\$ 4,741.38
PARFR-P14	"The Bipolar Needle for Percutaneous Vas Obstruction" S.S. Schmidt, M.D.	New Sub- contract	7/1/78- 6/30/79	\$ 2,350.00
PARFR-P15	"Isolation of Effective Sperm Antigens for Use in Contraceptive Immunization" S. Shulman, Ph.D. New York Medical College	New Sub- contract	1/1/79- 12/31/79	\$ 7,500.00
PARFR-P16	"Investigations of a New Vaginal Barrier Contraceptive" E.W. Page, M.D. University of California School of Medicine	New Sub- contract	1/1/79- 12/31/79	\$ 6,000.00

PERSONNEL

Effort and salary expenditures of PARFR personnel for this reporting period are listed below:

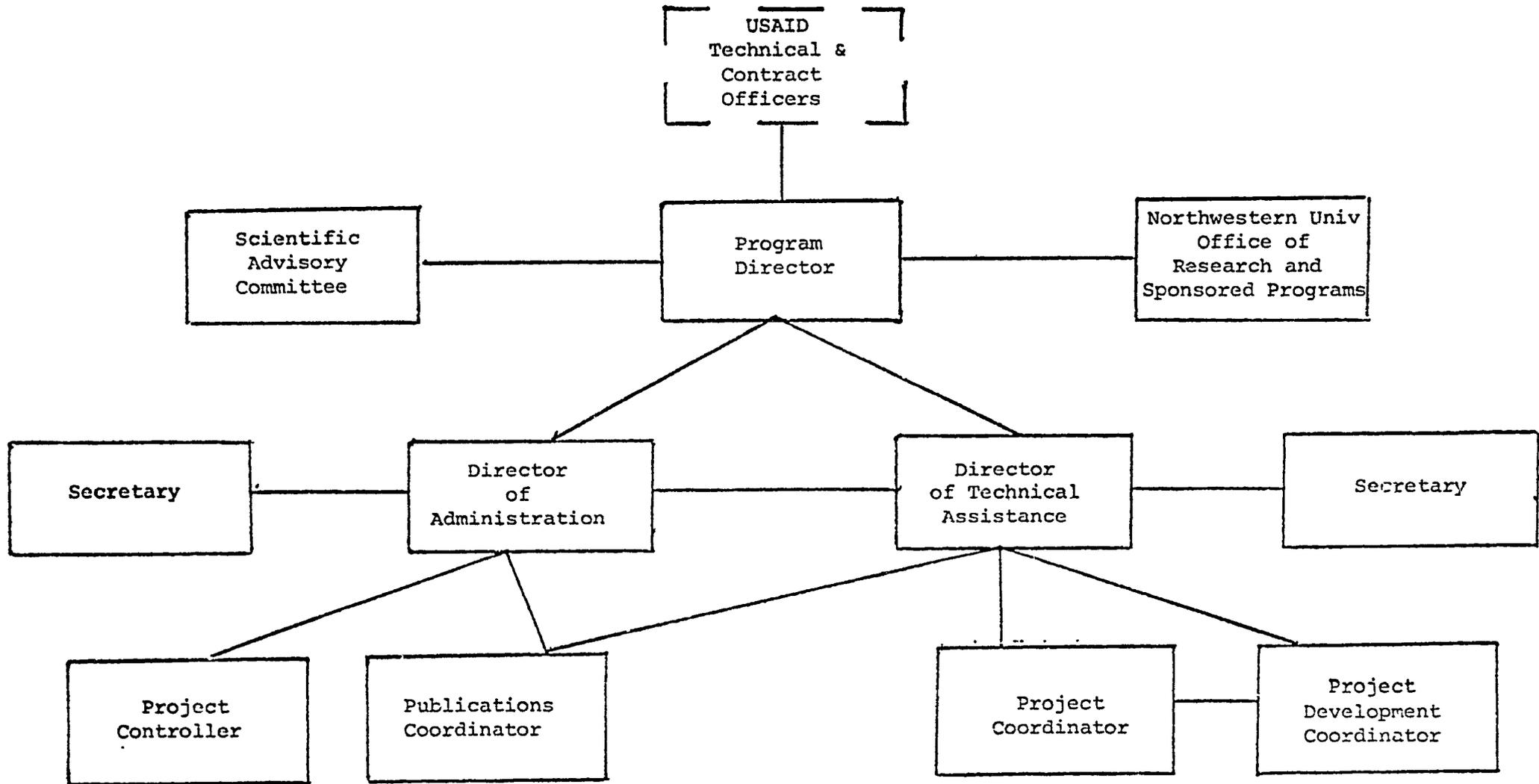
<u>Staff and Title</u>	<u>Effort In Man-Months</u>	<u>Salary</u>
John J. Sciarra, M.D., Ph.D. Director and Principal Investigator	.6	-0-
Gerald I. Zatuchni, M.D., M.Sc. Director of Technical Assistance	4.8	17,812.50
Elizabeth B. Connell, M.D. Research Development Coordinator	4.0	15,833.32
Aquiles J. Sobrero, M.D. Foreign Technical Project Coordinator	1.5	4,500.00
Diane H. Krier Director of Administration	6.0	10,500.00
Georgia L. Fackler Project Controller	6.0	7,150.00
Kelley Osborn Publications Coordinator	1.0	1,870.00
Julie M. Jaworski Secretary I	3.0	2,493.00
Ruvenia Thomas Secretary I	6.0	5,165.28
Mary Rose Traylor Secretary I	6.0	5,094.00
<u>Temporary Services</u>		
Temporary Secretary	2.5	3,406.55 *
<u>Fringe Benefits</u>	10,151.77	
<u>Indirect Costs</u>	21,419.19	

* Salary for temporary secretary has been charged to the Supplies budget line item, rather than Salaries, since this is a required procedure at Northwestern University.

Administrative Organization

The program staff is structured as indicated on the following page.

PARFR Organization



Scientific Advisory Committee

The membership of the Scientific Advisory Committee consisted of those individuals listed below during this reporting period:

John J. Sciarra, M.D., Ph.D., Chairman	Northwestern University
Nancy J. Alexander, Ph.D.	Oregon Regional Primate Research Center
Robert T. Chatterton, Ph.D.	University of Illinois
Joseph E. Davis, M.D.	New York Medical College
William Droegemueller, M.D.	University of Arizona
Edward C. Mather, D.V.M., Ph.D.	Michigan State University
Robert H. Messer, M.D.	University of New Mexico
Kamran S. Moghissi, M.D.	Wayne State University
Ralph M. Richart, M.D.	Columbia University
Susan C.M. Scrimshaw, Ph.D.	University of California
Judith L. Vaitukaitis, M.D.	Boston University
A. Albert Yuzpe, M.D.	University of Western Ontario, Canada

Dr. Scrimshaw joined the Committee during this reporting period, filling a long-standing vacancy. Her membership began with her participation in the July 1978 meeting. Dr. Connell attended her first meeting as a PARFR staff member in September, 1978.

The Scientific Advisory Committee (SAC) held three meetings during this period; July 10, 1978, in Chicago, Illinois, September 6, 1978, in Washington, D.C., and December 11, 1978, in Chicago, Illinois. Minutes of these meetings are included in the Appendix.

At these SAC meetings, the Committee reviewed Technical Reports for presently funded projects. Projects scheduled to expire during this reporting period were reviewed in depth by the Committee, who voted to extend nine subcontracts (PARFR-79N, 85N, 89N, 90N, 91N, 92N, 95N, P8, P9).

INFORMAL PROPOSALS

Seventeen informal proposals were reviewed by SAC, with resultant recommendation that three formal proposals be solicited. These projects are:

"Medicated Intrauterine Devices Releasing Prostaglandin Antagonists"
John D. Biggers, D.Sc., Ph.D., Harvard Medical School
(A formal proposal was recently received and will be included in the 3/18/79 SAC agenda.)

"A Prospective Study on the Effect of Tubal Sterilization on Menstruation and Gynecological Disorders" Gary S. Berger, M.D., University of North Carolina (A formal proposal was submitted and approved at the 12/11/78 SAC meeting.)

"The Humoral Sperm Antibody Response After Vasectomy with and without Obstruction, and its Relevance to Fertility After Vasovasostomy"
Dr. H.W.J. Hellema, Laboratory of Fertility Research,
Wilhelmina Gasthuis, Academic Hospital University, the Netherlands
(There have been several communications between PARFR and Dr. Hellema, and a formal proposal will be included in a SAC agenda when received.)

It was suggested that the author of the following informal proposal may be invited to participate in a collaborative study using Dr. Zaneveld's shug device. They are presently working towards a collaborative arrangement.

"Reversible Male Sterilization" Prof. Gamal El Din Beheri, Cairo University, Egypt

The Committee recommended funding a pilot study to test the feasibility of the following informal proposal.

"Evaluation of Acrosin-Acrolysin Inhibitors as Male Contraceptive Agents" Marion M. Bradford, Ph.D., University of Georgia

FORMAL PROPOSALS

Eighteen formal proposals were reviewed by SAC with resultant recommendation that the following ten projects be funded.

"Investigation of New Compounds to Terminate Pregnancy" Leonard J. Lerner, Ph.D., Thomas Jefferson University

"Is Sperm Antigen a Causative Agent for Atherosclerosis After Vasectomy?" Nancy J. Alexander, Ph.D., Oregon Regional Primate Research Center

"Fertility Regulation by Control of Progesterone Clearance" Robert T. Chatterton, Ph.D., University of Illinois

"Microencapsulation of Progesterone Antibodies" Allan P. Gray, Ph.D., IIT Research Institute

"A Study of a Parenterally Administered Progesterone - Cholesterol Formulation for Use as a Post-Partum Injectable Contraceptive" Harry W. Rudel, M.D., Centro de Investigacion Sobre Fertilidad y Esterilidad (C.I.F.E.)

"Development and Testing of a Cervical Dilatation System" Philip Stubblefield, M.D., Preterm Institute

"Collagen Sponge Contraceptive - Testing in Human Volunteers" M.W. Heine, M.D., Texas Tech University

"Effects of Tubal Sterilization on Menstruation: A Prospective Controlled Study" Gary S. Berger, M.D., University of North Carolina

"Ovarian Function after Tubal Sterilization" Ewa Radwanska, M.D., University of North Carolina (AID Technical Office has not approved this project since they felt it was not within PARFR's guidelines.)

"Study to Determine the Safety, Acceptability and Effectiveness of the Female Contraceptive Barrier Intra-Vaginal-Device (IVD)" Louise B. Tyrer, M.D., Planned Parenthood Federation in America

In addition, it was requested that the two following formal proposals be modified as pilot studies.

"Investigations of a New Vaginal Barrier Contraceptive" Ernest W. Page, M.D., University of California

"Development and Testing of a New Intravaginal Contraceptive Method and Device" Matthew Freund, Ph.D., Southern Illinois University

PILOT PROPOSALS

Three pilot proposals were reviewed by SAC, with resultant recommendation that one project be funded.

"Identification and Evaluation of Herbs used by Native Healers to Affect Fertility" John C. Slocumb, M.D., University of New Mexico

PARFR-INITIATED PROJECTS

The following PARFR-initiated projects received SAC approval during this reporting period:

"Comparison Among Different Ethnic Populations of the Pharmacokinetics of Ethynyl Estrogens" Joseph W. Goldzieher, Southwest Foundation for Research and Education

"Vaginal Contraceptive Capsule" Emanuel H. Bronner (A preliminary screening of the compound at the University of Illinois has been encouraging. To date, PARFR has not received a formal proposal.)

"Development of a Long-Acting Spermicidal, Vaginal Creme" C. Patrick Tharp, Ph.D., KV Pharmaceutical Company (This proposal was withdrawn by the investigator.)

SITE VISITS

Site visits were conducted on seven projects during this reporting period:

<u>Project #</u>	<u>Title of Project</u>	<u>Site Visitor</u>	<u>Date</u>
PARFR-81N	Clinical Evaluation of Intrauterine Devices Containing Epsilon Amino-Caproic Acid (EACA) Peter F. Tauber, M.D. University of Essen, West Germany	G. Zatuchni, M.D.	9/12-15/78
PARFR-85N	Collagen Sponge Contraceptive: Testing of Efficacy in Human Volunteers Milos Chvapil, M.D., Ph.D. University of Arizona	D. Krier G. Zatuchni, M.D.	10/23/78
PARFR-86G	Phase I Clinical Trial of Fallopian Tube Closure Using Methylcyanoacrylate Tissue Adhesive Delivered Through the Single Application Fertility Regulating Device Drs. Zinser, Eldering, Baur Evangelisches Krankenhaus	G. Zatuchni, M.D.	9/12-15/78
PARFR-89N	Fallopian Tube Cauterization and Closure by Silver Acetate-Alginate Formulations Harry P. Gregor, Ph.D. Columbia University	R. Chatterton, Ph.D. E. Connell, M.D.	10/15/78
PARFR-90N	New Method for Obstructing Vas Deferens by Direct Injection of Chemical Agents: A Non-operative Technique of Male Sterilization Joseph E. Davis, M.D. New York Medical College	R. Chatterton, Ph.D. E. Connell, M.D.	10/16/78
PARFR-91N	Preparation and Evaluation of Biodegradable Cylindrical Implants for Fertility Control Donald L. Wise, Ph.D. Dynatech R/D Company	R. Chatterton, Ph.D. E. Connell, M.D. G. Zatuchni, M.D.	10/17/78
PARFR-99N	Immunoabsorbent Isolation of Specific Spermatozoal Antigens for Use as Anti-fertility Immunogens Duane L. Garner, Ph.D. Oklahoma State University	K. Tung, M.D. G. Zatuchni, M.D.	11/21/78

The following project development site visits were conducted during this reporting period:

<u>Site</u>	<u>Site Visitors</u>	<u>Date</u>
Southern Illinois University Carbondale, Illinois (PARFR-P17)	R. Messer, M.D. A. Sobrero, M.D.	7/11/78
* El Salvador (PARFR-86Sa, Sb)	D. Krier R. Neuwirth, M.D. R. Richart, M.D.	10/1-4/79
* University of Texas	E. Connell, M.D.	10/7-10/78
* PARFR & IFRP Chicago and Washington, D.C.	P. Tauber, M.D.	12/3-9/78

* No consulting fees were paid for these project development site visits; only travel expenses were reimbursed by PARFR.

CONSULTANTS

The following is a list of Program Consultants, indicating their areas of expertise, contributions to the Program, and payment therefore. This list includes members of the Scientific Advisory Committee.

Consultant	Purpose	Effort	Fee
Nancy J. Alexander, Ph.D. Reproductive Physiology	SAC, 7/9-10/78	2 days	\$300.00
	SAC, 9/5-6/78	2 days	300.00
	SAC, 12/9-10/78	2 days	300.00
Robert T. Chatterton, Ph.D. Steroid Biochemistry	SAC, 7/9-10/78	2 days	300.00
	SAC, 9/5-6/78	2 days	300.00
	Site Visits (3) (10/15-17/78)	3 days	450.00
	SAC, 12/9-10/78	2 days	300.00
Joseph E. Davis, M.D. Urology	SAC, 7/9-10/78	2 days	300.00
	SAC, 9/5-6/78	2 days	300.00
	SAC, 12/9-10/78	2 days	300.00
William Droegemueller, M.D. Obstetrics and Gynecology	SAC, 7/9-10/78	2 days	300.00
	SAC, 9/5-6/78	2 days	300.00
	SAC, 12/9-10/78	2 days	300.00
Edward C. Mather, D.V.M., Ph.D. Animal Reproductive Physiology	SAC, 7/9-10/78	2 days	300.00
	SAC, 12/9-10/78	2 days	300.00
Robert H. Messer, M.D. Obstetrics and Gynecology	SAC, 7/9-10/78	2 days	300.00
	Project Development Carbondale, IL 7/11/78	1 day	150.00
	SAC, 9/5-6/78	2 days	300.00
	SAC, 12/9-10/78	2 days	300.00
Kamran S. Moghissi, M.D. Obstetrics and Gynecology Reproductive Endocrinology	SAC, 7/9-10/78	2 days	300.00
	SAC, 9/5-6/78	2 days	300.00
	SAC, 12/9-10/78	2 days	300.00
Ralph M. Richart, M.D. Obstetrics and Gynecology Pathology	SAC, 7/9-10/78	2 days	300.00
	SAC, 9/5-6/78	2 days	300.00
	SAC, 12/9-10/78	2 days	300.00
Susan C.M. Scrimshaw, Ph.D. Medical Anthropology	SAC, 7/10/78	1 day	150.00
	SAC, 9/5-6/78	2 days	300.00
	1 Review		25.00
	SAC, 12/9-10/78	2 days	300.00
Judith L. Vaitukaitis, M.D. Endocrinology	SAC, 7/9-10/78	2 days	300.00
	SAC, 9/5-6/78	2 days	300.00
	SAC, 12/9-10/78	2 days	300.00
A. Albert Yuzpe, M.D. Obstetrics and Gynecology	SAC, 7/9-10/78	2 days	300.00
	SAC, 12/10-11/78	2 days	300.00
Kenneth S.K. Tung, M.D. Immunology	Site Visit (11/21/78)	1 day	150.00

TOTAL:

9,925.00

SUBCONTRACTS

PROGRAM ACCOMPLISHMENTSSubcontracts

The following are capsule summaries of work proceeding under subcontracts during this reporting period (7/1/78 - 12/31/78).

I. SELF-ADMINISTERED METHODS

Project: PARFR-85N

Collagen Sponge Contraceptive: Testing of Efficacy in Human Volunteers

Milos Chvapil, M.D., Ph.D. -- University of Arizona

\$98,124 12/1/76 - 6/30/79

Objectives: To continue the development of the collagen sponge as an intravaginal barrier method.

Accomplishments:

Testing of the collagen sponge (CS) has been completed. Thirty-six volunteers underwent 81 sperm penetration tests (postcoital). Thirty-two of the tests were performed in control volunteers and 49 tests in those using the sponge. Among the controls, 94% exhibited the presence of motile sperm. Among the 49 sponge tests, eight examinations showed between one and three sperm per high power field (HPF): five tests showed between three and nine sperm per HPF. Of the eight positive tests, seven were done with volunteers using the 6cm CS. Only one 7cm sponge had a positive test.

The investigator feels that Phase I clinical trials for efficacy with the collagen sponge as the only contraceptive method are in order. The studies are planned to be done on a selected group of highly motivated couples at the investigator's own institution and/or at another institution. The investigator also would like support for the development of a collagen sponge impregnated with one or another spermicide. He would like to have this barrier/spermicide tested in a similar manner to the collagen sponge.

Project: PARFR-P8

Water Soluble Condom Feasibility Study

Charles Salivar -- Emko Company, St. Louis

\$5,790 7/1/77 - 6/30/78

Objectives: To develop and test a biodegradable condom made of thin polylactate/glycolate containing spermicidal drug.

PARFR-P8 (continued)

Accomplishments:

A large variety of biodegradable films have been examined with regard to their suitability for use as a spermicidal-containing condom. Several prototypes have been developed. Among the many films which have been evaluated, there is one which appears to come closest to having the desired characteristics. Negotiations are currently underway to make this material into biodegradable condoms, following which spermicidal testing will be carried out. If these are encouraging, clinical trials will be undertaken.

II. LONG-ACTING FEMALE METHODSProject: PARFR-83N

Studies to Test an Injectable Delivery System for the Sustained Release of Norethisterone

Lee R. Beck, Ph.D. -- University of Alabama
Donald R. Cowsar, Ph.D. -- Southern Research Institute

\$189,214

4/1/76 - 3/31/79

Objectives: To develop an injectable formulation for the control of fertility in women which utilizes the synthetic progestin, norethisterone, in combination with a biodegradable injectable controlled-release delivery system.

Accomplishments:

The project has been successful in developing a long-acting timed injectable contraceptive system for the continuous administration of the steroid-norethisterone (NET). The first system consists of microcapsules made of the polymer d,l-poly-lactic acid containing micronized crystals of NET dispersed homogeneously throughout the matrix with a polymer. The microspheres are small enough that a conventional needle and syringe can be utilized for the injection. Upon injection, the capsules biodegrade into lactic acid with eventual clearance by the body through the lungs and urine.

During the reporting period, work continued toward the following goals:

- 1) Continuing the examination of the biodegradation kinetics of the polymer;
- 2) Continuation of the study of factors affecting the rate of release of NET;
- 3) Developing prototype formulations for a series of injectable doses having durations of action having 1, 3, 6, and 12 months.

PARFR-83N

Accomplishments (continued)

- 4) Determination of potential mutagenicity and cytotoxicity of the polymer;
- 5) Investigation of the histology at the injection site;
- 6) Completion of the primate dose-response and release-rate studies on the 6 month system.

In another PARFR project, the investigators are participating with their Mexican colleagues in a Phase I clinical trial of the 6 month system. Investigators plan to apply for FDA-IND for a 3 month system to undergo Phase I clinical testing at the University of Alabama.

Project: PARFR-91N

Preparation and Evaluation of Biodegradable Cylindrical Implants for Fertility Control

Donald L. Wise, Ph.D. -- Dynatech R/D Company, Cambridge, MA

\$177,141 6/1/77 - 3/31/80

Objectives: To demonstrate in baboons, supported by further testing in rats, that a small biodegradable cylindrical implant releasing d-norgestrel at approximately zero-order for a period of at least twelve months is feasible.

Accomplishments:

Biodegradable cylindrical implants releasing levonorgestrel have been manufactured and implanted in baboons and small animals, in accordance with the study protocol.

A site visit of this project was done in October, 1978 and it was agreed that the investigators had completed all phases of the first portion of this project and the implants would be removed. Following this, residual steroid and polymer excretion will be monitored and the animals will be observed for the return of ovulation.

A new plan of work has been submitted to PARFR for the design of a one year implant suitable for clinical use.

Project: PARFR-104N (P9)

A Fibrous Polymer for the Delivery of Contraceptive Steroids to the Female Reproductive Tract

Danny H. Lewis, Ph.D. -- Southern Research Institute, Birmingham, AL

\$66,000 11/1/78 - 10/31/79

Objectives: To fabricate and evaluate in vitro progesterone-releasing fibers and macrospheres connected by a fiber for potential contraceptive application in women.

Accomplishments:

The selection of various fiber-forming polymers for use as the matrix for a progesterone delivery system has been accomplished. These polymers have undergone preliminary spinning of prototype steroid-loaded fibers. Extensive in vitro studies on the release of the steroid from the fibers has also been completed.

The results of the study indicate that it is possible to produce a variety of fibers loaded with significant quantities of a steroid which can provide long term release of the steroid. Loadings of 10 to 30% by weight of progesterone were achieved. Even higher loadings may be feasible utilizing the hollow fiber concept.

The investigators plan to optimize the fibrous delivery system to provide low level release of progestational agents into the female reproductive system over extended periods. Primate studies are planned once the most promising system is selected. One of the more interesting applications will be the utilization of the fiber releasing device to substitute for the inert IUD string (tail). This monofilament active tail might be utilized to improve the contraceptive efficacy of the IUD, or even to provide for cervical mucus changes due to the influence of the steroid. Other locations in the female are suggested, e.g. threaded into the fallopian tubes; or as a male application using a locally sperm suppressive drug in the fibrous delivery system.

III. MALE METHODS

Project: PARFR-99N

Immunoabsorbent Isolation of Specific Spermatozoal Antigens for use as Anti-Fertility Immunogens

Duane L. Garner, Ph.D. -- Oklahoma State University

\$30,233

7/1/78 - 3/31/79

Objectives: To develop appropriate immunoabsorbent chromatography techniques for the efficient purification of sperm-specific antigens. The specific approach involves the utilization of immunoglobins from human post-vasectomy serum which are directed toward antigens associated with certain structures of human sperm in order to form immunoabsorbence specific for these sperm antigens.

PARFR-99N (continued)**Accomplishments:**

The investigators have found that post-vasectomy sera which contains antibodies against antigens located in the equatorial segment of human sperm also recognizes a corresponding antigen in the equatorial segment of bovine sperm. Procedures have been developed for the extraction of the cross reacting antigens from bovine sperm and vascular tissue. The presence of soluble, cross reacting antigens in these extracts has been confirmed by double immunodiffusion analysis with the human equatorial segment orthoantibodies. Purified immunoglobins from human antiserum have been coupled to adarose to form an immunoabsorbent which apparently binds the equatorial segment antigens from bovine sperm extract. However, elution of the antigens from the immunoabsorbent have yet to be done. Thus far, the results suggest that some human and bovine spermatozoal antigens possess sufficient immunological similarities to allow utilization of sperm antigens isolated from non-primate species as antifertility immunogens in primates.

At the site visit, immunological expertise raised certain problems with the result of the various studies performed to date. A consultant has suggested certain lines of investigation and the investigators will prepare a revised plan of work for the next reporting period.

IV. INTRAUTERINE CONTRACEPTION

Project: PARFR-81N

Clinical Evaluation of Intrauterine Devices Containing Epsilon Aminocaproic Acid (EACA)

Peter F. Tauber, M.D. -- University of Essen, West Germany

\$53,187 5/1/76 - 6/30/78

Objectives: To determine the contraceptive efficacy and side effects of this medicated IUD; to determine actual blood loss by atomic absorption spectrophotometry of menstrual tampons collected during a control and two menstrual periods.

Accomplishments:

The protocol had called for enrollment of three groups of 60 women each using the following intrauterine devices: 1) ML-Cu 250; 2) ML-Cu 250 with EACA; and 3) plain multiload device. A number of pregnancies resulted in women using the plain multiload device and this group and device were excluded from further analysis. The other women had periodic blood loss determinations during the life of the project.

Accomplishments: (continued)

Preliminary results indicate that during the first month of use, the EACA loaded device was associated with statistically significant lower amounts of bleeding, as compared with the ML-Cu 250 device alone. Unfortunately, due to manufacturing problems, the EACA capsule eroded and disintegrated after about 30 days in utero. Thus, the bleeding analysis of both groups of IUD wearers revealed similar findings beyond the first month of the study.

The investigator has terminated all patients. He plans on selecting a new group of women once IFRP has established and manufactured an antifibrinolytic device capable of longer term intrauterine usage.

Project: PARFR-82N

Measurement of Blood Loss of Women Fitted with Copper-Clad and Standard Lippes Loops

Fouad Hefnawi, M.B., M.S. -- Al-Azhar University, Cairo, Egypt

\$74,290 . 11/1/75 - 4/30/79

Objectives: To determine the event rates, acceptability and measured blood loss in women having either a standard Lippes Loop or a copper-clad Lippes Loop.

Accomplishments:

All insertions have been completed - 100 loops and 100 copper devices. 145 women have reached their third month post-insertion follow-up; 100 have completed six months; 71 - nine months; 66 have completed their twelve month follow-up.

Preliminary results indicate that in both the copper-clad Lippes and the standard Lippes groups an increase in menstrual blood loss (MBL) was noticed in the first three post-insertion cycles, as compared to the pre-insertion values. The increase was more apparent with the copper devices. By the sixth month, the MBL in both groups were almost equal. Gradual decreases in MBL were noted at the time of the ninth and the twelfth month follow-ups. The decrease during this time was more apparent in the copper group reaching levels below the pre-insertion values.

V. POST-COITAL/POST-OVULATORY

Project: PARFR-84N

Evaluation of the Copper-T IUD as a Post-Coital Method of Contraception

Jack Lippes, M.D. -- Planned Parenthood of Buffalo, New York

\$2,569

10/1/77 - 8/15/78

Objectives: To select 100 patients from the Planned Parenthood of Buffalo Clinics requesting post-coital contraception within 96 hours of unprotected mid-cycle intercourse. These patients will have a Copper-T Intrauterine Device inserted. Various tests will be carried out, including the new, extremely sensitive beta-HCG measurements.

Accomplishments:

Copper intrauterine devices, either a Copper T or a Copper 7 were utilized in 299 women from one to seven days after unprotected coitus for the purpose of preventing pregnancy. No pregnancies were observed within the first three months after the insertions.

The investigators conclude that an IUD insertion after unprotected intercourse is a safe and effective method of preventing pregnancy. Inasmuch as some patients had IUDs inserted as late as five to seven days postcoitally, the method has a distinct advantage over other postcoital methods such as estrogen which is not effective after 48 hours. In addition, patients are able to continue with contraception by simply retaining their IUD.

Project: PARFR-88N

Study to Determine the Safety and Efficacy of Copper-Releasing IUDs as a Method of Post-Coital Contraception

Louise B. Tyrer, M.D. -- Planned Parenthood of America, Inc., New York

\$83,020

3/1/77 - 8/31/78

Objectives: To determine the effectiveness of copper-releasing IUDs in preventing intrauterine pregnancy in a population of women following unprotected mid-cycle intercourse to ascertain that in those in whom conception occurs, there is not an unacceptably high rate of extrauterine implantation.

PARFR-88N (continued)

Accomplishments:

Eighty female volunteers, aged 18-25 years, who had had one act of unprotected mid-cycle intercourse and who were interested in using the Cu-7 as a postcoital method, were enrolled in the study. At the initial visit, after signing the consent form, the patients had a Cu-7 inserted and blood was drawn to be frozen for later RIA and RRA assaying. Each patient was asked to return on day 25 of her menstrual cycle to have a second blood sample drawn. The final visit was set for approximately two weeks after the expected onset of menses for a pregnancy test and menses data recording. Serum samples were frozen and submitted at the end of the study for assay. Data were collected and analyzed to determine fertilization rate, pregnancy rate and incidence of ectopic pregnancy.

No pregnancies were observed during the study. The study results suggested that the Cu-7 IUD prevents successful implantation of a fertilized ovum when inserted within 5 days of unprotected mid-cycle coitus; this conclusion was based on positive results. The sample was too small to report any findings regarding ectopic pregnancy.

Project:

PARFR-92N

Contraception by Induction of Mild Uterine Inflammation

Deborah J. Anderson, Ph.D. -- Medical Research Foundation of Oregon

\$86,108

6/1/77 - 6/30/79

Objectives:

To determine if pregnancy can be interrupted by the induction of mild uterine inflammation.

Accomplishments:

Preliminary data indicate that glycogen, a potent leukocyte chemotactic factor, attracts large numbers of polymorphonuclear leukocytes to the uterine lumen when it is released from a biodegradable gelatin capsule. Furthermore, investigators found that insertion of glycogen releasing gelatin beads into rat uteri near the time of implantation (days 2-6 of pregnancy) causes the complete termination of pregnancy. This observation was extended to include a larger number of rats treated on various days of gestation. Histological studies on the rat uteri were also completed. Other studies have been initiated to measure release rates and the contraceptive effectiveness of chronic glycogen-releasing intrauterine devices. Preliminary studies to measure bacterial growth in uteri treated with glycogen-releasing compounds has found no bacterial growth at 2, 6, 12, 24 and 48 hours after treatment.

PARFR-92N

Accomplishments: (continued)

The investigator plans to complete these studies during the next reporting period. In cooperation with Poly-Sciences, Inc. and IFRP, the synthesis of long-term glycogen-releasing intrauterine devices should become available for testing.

Project: PARFR-97N

Research on Instillation Techniques for Pregnancy Termination in Korea

Theodore M. King, M.D., Ph.D. -- The Johns Hopkins University

\$54,734 8/1/78 - 7/31/79

PARFR-97K

Young Ki Moon, M.D. -- Yonsei University, Seoul, Korea

\$33,000 7/1/78 - 6/30/79

Objectives: To gather statistical data on the utilization of four different procedures in women undergoing midtrimester pregnancy termination in Korea.

Due to a delay in the start of this program, no results are available. The Korean PI has enlisted the support of the participating institutions, standardized the reporting procedures, and received the appropriate supplies and equipment.

The study will get underway during the next reporting period.

Project: PARFR-100N

Investigation of New Compounds to Terminate Pregnancy

Leonard J. Lerner, Ph.D. - Jefferson Medical College, Philadelphia

\$66,286 9/1/78 - 8/31/79

Objectives: To obtain new, safe and effective agents for pregnancy termination that will be easy to use and applicable to programs in lesser developed countries.

Accomplishments:

The project was delayed in its onset until the last two months of this reporting period; hence there are no results to report. However, the PI has obtained approximately 20 compounds from the Lepetit Research Laboratory in Milan, Italy which he plans to screen in the hamster and then in the rat. The investigator has also been able to obtain several other compounds from a variety of pharmaceutical companies in the United States who are willing to have the PI screen them.

Project:

PARFR-102N (P-10)

Fertility Regulation by Control of Progesterone Clearance

Robert T. Chatterton, Ph.D. -- University of Illinois

\$46,767

11/1/78 - 10/31/79

Objectives:

To devise and evaluate a progesterone absorbant that can be taken orally anytime from the time of implantation until a month after the first menstrual period for control of fertility.

Accomplishments:

Testing of the anti-progesterone anti-serum (APA) properties has continued with emphasis on the termination of the binding affinity for serum binding. Two new conjugates of 11-alpha hydroxyprogesterone have been prepared and utilized as an immunization agent in two rabbits and one sheep. Titers are expected to rise within three to four months from the initial immunization.

Assays for total serum progesterone have been finished as well as assays of bound and freed progesterone in control and antibody-treated animals.

In vitro testing of encapsulated antibodies has been started; preliminary results indicate that the entrapped antibody is accessible to radio labelled progesterone.

The findings to date have related to preparation and testing of the materials. The effect of progesterone antibody on the concentration of unbound progesterone in serum has been measured for the first time. These actual measurements reveal that the three progesterone concentrations do not change in contrast to estimates of the unbound progesterone level. The effect of the progesterone antibody on pregnancy is therefore more likely due to withdrawal of progesterone from uterine tissues in utero and not related to the concentration of free progesterone achieved in serum. Additionally, entrapment of the progesterone antibody within a polysiloxan E polymer that permits access of progesterone has been accomplished.

Project: PARFR-103N

Microencapsulation of Progesterone Antibodies

Allan P. Gray, Ph.D. -- IITTM Research Institute, Chicago

\$28,108

11/1/78 - 10/31/79

Objectives: To develop microencapsulating formulations and techniques in order to provide microcapsules in which contained progesterone antibodies will be effectively protected from degradation by digestive juices but freely accessible to endogenous progesterone.

Accomplishments:

Efforts have been directed toward establishing the applicability of, and suitable conditions for, an interfacial polymerization technique for the microencapsulation of anti-progesterone antibodies in a polyamide membrane. As the supply of APA is limited, a surrogate of homologous protein bovine gamma globulin has been used. Preliminary results indicate the successful microencapsulation of the gamma globulin. In the next reporting period the results will be confirmed and conditions improved and refined in order to provide more discreet microcapsules of more uniform size and greater stability.

This project is in support of PARFR-102N.

VI. FEMALE STERILIZATION

Project: PARFR-63B

Development of a Reversible and Permanent Uterotubal Blocking Technique by Hysteroscopy

Abdol H. Hosseinan, M.D. -- University of Chicago, Chicago Medical School

Lourens J.D. Zaneveld, D.V.M., Ph.D. -- University of Illinois

\$36,025

7/1/75 - 6/30/79

Objectives: To determine in baboons the feasibility of a utero-tubal junction blocking device inserted and/or removed by hysteroscopy. PARFR-63B is the animal work related to PARFR-87N.

Accomplishments:

In summary, 20 baboons of proven fertility had the devices implanted and no pregnancy resulted. Two baboons were hysterectomized and the pathology report indicated good tissue tolerance for the devices. One still has the device in place

Accomplishments: (continued)

for long-term follow-up. Removal of the devices was carried out in 17 baboons; all were bred to evaluate the reversibility of the sterilization technique. Two died sometime after device removal (one due to hemorrhagic cystitis and the other to acute bloat). Of the 15 remaining, 6 did not become pregnant and underwent hysterectomy; 1 still is not pregnant and undergoing further evaluation; and 8 became pregnant (53%) - only 17% less than the pregnancy rate for untreated baboons in the Biological Resource Laboratory (University of Illinois) colony. Of these pregnant animals, a total of three animals showed repeat pregnancies. Others were removed from the study on becoming pregnant.

The efficacy of the utero-tubal junction for preventing pregnancy as well as reversibility upon removal have been confirmed by the animal studies. The results indicate that Phase I clinical studies can begin.

Project: PARFR-79N

A Method for Reversible Sterilization in the Female

C. Irving Meeker, M.D. -- Maine Medical Center

\$32,370	2/1/77 - 8/31/77 (Vermont)
\$106,131	9/1/77 - 9/30/79 (Maine)
Total funding PARFR-79N: \$138,501	

Objectives: To determine whether the use of the specially designed tubal plug device is a safe, effective and reversible form of contraception.

Accomplishments:

In April, 1978, 34 animals had the tubal plugs removed and these animals have been bred a total of 313 times for an average of 9.2 breedings each. No pregnancies resulted. Two animals died of unrelated causes following surgery. Histopathologic examination revealed unremarkable tubes.

Of the 32 animals remaining in the study group, with plugs removed, the menstrual cycle data revealed the following. No pregnancies resulted in the first 12 complete cycles. Additional observation indicates only one pregnancy among the 32 animals. The investigator is concerned with the breeding techniques and this will be examined more closely in order to determine whether or not the absence of conception is due to unknown tubal damage or to inappropriate breeding.

Project: PARFR-86N

Phase I Clinical Trial of Fallopian Tube Closure Using Methylcyanoacrylate Tissue Adhesive Delivered Through the Single Application Fertility Regulating Device

Robert S. Neuwirth, M.D. -- St. Luke's Institute for Health Science
Ralph M. Richart, M.D. -- Columbia University

\$36,602 6/1/78 - 5/31/79

PARFR-86G

Professor H.K. Zinser, Hans Baur, M.D., Gerd Eldering, M.D. --
Bureau Mengen, Cologne, West Germany

\$27,159 9/1/78 - 8/31/79

PARFR-86K

Sung-bong Hong, M.D. -- Korea University

\$16,080 6/1/78 - 5/31/79

Objectives: To continue the clinical trials of tubal closure using a "blind" delivery system employing MCA tissue adhesive.

Accomplishments:

The system has been used in 33 women seeking sterilization in Cologne, West Germany. None of the patients suffered any immediate complications as a result of the procedure. Thus far, 21 patients have undergone hysterosalpingography 3-4 months following the procedure. Of these 21, 10 have been found to have bilateral tubal blockage on hysteroqram and have been permitted to go off of contraception. The failures have either selected reinjection or sterilization.

Analysis by the Population Research team of the MCA supplied revealed that the concentration of the inhibitor, phosphoric acid, was varying from ampule to ampule. Because of this, new patients were deferred at the Cologne center.

A Korean investigator at Korea University in Seoul was trained in Germany in the use of the instrument and drug. This institution will be center #2.

Drs. Richart and Neuwirth and Ms. Krier visited San Salvador and discussed at four potential testing centers there. Since that visit, two centers have entered into a subcontract arrangement for the clinical testing of the device and drug.

Project: PARFR-87N

Hysteroscopic Sterilization Technique by Using Uterotubal Junction (UTJ) Blocking Devices

Abdol H. Hosseinian, M.D. -- Reza Pahlavi Medical Center, Tehran, Iran, Chicago Medical School and Cook County Hospital

\$17,311 11/1/76 - 10/31/77

Objectives: To investigate the clinical efficacy of mechanically blocking the uterotubal junction by means of a device which could be implanted in or removed from the tubal ostium through hysteroscopy.

Accomplishments:

The investigator has obtained a modified hysteroscope from Eder Instrument Company in Chicago. The investigator has used the modified instrument in Iran in a small number of women. It is still not satisfactory.

The investigator has left Iran and is now permanently in the United States and plans to further modify the hysteroscope. His future plan calls for the involvement of two or three hysteroscopic centers, as well as his own, in the United States, to test, in a collaborative fashion, the ease and efficacy of inserting the tubal plug for fertility regulation purposes.

Project: PARFR-89N

Fallopian Tube Characterization and Closure by Silver Acetate-Alginate Formulations

Harry P. Gregor, Ph.D. -- Columbia University, New York

\$112,073 1/15/77 - 7/14/79

St. Luke's Animal Care Facility

\$63,326 11/1/77 - 7/14/79

Total funding PARFR-89N: \$175,399

Objectives: To refine the formulation of silver acetate, an insoluble calcium salt, sodium alginate, a calcium sequestering agent, and distilled water, so that it will be sufficiently fluid for administration to the fallopian tubes; to develop an improved technique for the sterilization of females which uses commercially available materials and is deliverable by a "blind" delivery system.

Accomplishments:

Working closely with his medical colleagues at St. Luke's Hospital, the investigator has been successful in developing appropriate formulations of appropriate viscosity in order for the material to be delivered "blindly" via the use of the specially designed administration system. The suspension currently being tested is stable for several hours and when injected into the fallopian tubes of rabbits and monkeys, reacts with the water present there to form a gel and release silver ions in sufficient amounts to effect cauterization and eventual tubal closure.

A site visit was carried out in October, 1978. The original objectives seem to be close to completion. Three steps must be taken in the near future if this research is to continue. First, further work must be done on the gel time of the solution. Second, it will be necessary to look at the possible toxic effects of these materials. Third, the feasibility of transfer of the research results from animals to humans must be explored, possibly using patients who are about to undergo hysterectomy.

A new plan of work has been submitted to PARFR for the accomplishment of the next stage of development.

Project: PARFR-94N

Modern Modified Aldridge Procedure

William Droegemueller, M.D. -- University of Arizona

\$62,062 12/1/77 - 12/31/79

University of Illinois Biologic Resources Laboratory

\$17,850 10/1/78 - 12/31/79

Total funding PARFR-94N: \$79,912

Objectives: To develop a means of reversible sterilization for women.

Accomplishments:

Tubal hoods made of polytetrafluoroethylene were surgically inserted in 18 baboons. None of the animals had postoperative complications. An additional two animals had been done as a pilot procedure. All 20 animals were observed for over a year and to date no pregnancies have been recognized. One animal had died of acute gastritis and postmortum examination revealed no evidence of pelvic infection and normal placement of the tubal hood.

The tubal hoods have been removed from all remaining animals and breeding will now be observed.

Project: PARFR-P11

Evaluation of Carbohexoxymethyl-2-Cyanoacrylate as a Tube-Blocking Agent

Ralph M. Richart, M.D. -- Columbia University, New York

\$5,970

2/1/78 - 6/30/79

Objectives: To determine the feasibility of carbohexoxymethyl-2-cyanoacrylate as a tube-blocking agent in primates.

Accomplishments:

The material has been supplied by Ethicon, Inc. and has been inserted in the fallopian tubes of six squirrel monkeys under direct visualization. The monkeys are being observed a period of six months in order to determine the effectiveness of the cyanoacrylate derivative for tube closure. The monkeys will be reoperated at six months and histopathology studies performed.

Project: PARFR-P13

An Evaluation of the Efficacy of Candidate Fimbrial Prosthesis in Female Rabbits and the Evaluation of Fimbrial Devices as a Reversible Technique of Female Sterilization

Ivo Brosens, M.D., Ph.D. -- Catholic University of Leuven

\$4,741

5/1/78 - 4/30/79

International Fertility Research Program

\$1,700

5/1/78 - 4/30/79

Total funding PARFR-P13: \$6,441

Objectives: To determine the efficacy of a fimbrial hood in rabbits as a reversible sterilization procedure.

Accomplishments:

Three different devices were developed by the International Fertility Research Program for this study. The first two devices were made of silastic, one of .002 inch thickness (thin) and a second of .006 inch thickness (thick). The third group was constructed from teflon.

The results indicated that the thick devices were too difficult to manipulate and at reoperation, the devices were found to be totally dislodged from the fibrium.

The four rabbits had bilateral placement of the teflon devices and these proved to be too large and appeared to attract an excessive amount of peritoneal covering. The investigators

Accomplishments: (continued)

felt that the teflon offered no advantage over the thin silastic.

Two animals had unilateral placement and 17 animals had bilateral placement of the thin silastic devices. The two unilateral placements were re-explored at 16 days and tissue obtained for scanning electronmicroscopy (SEM). No discernable differences were noted when compared with biopsies taken from the control side. In the bilaterally placed group, a simple two suture technique was utilized to anchor the device. Unfortunately the motility of the tube and fimbria tend to rock the fimbria loose from the anchor sutures. Adhesion formation has been minimal or absent, except for one animal that died of obvious infection from the surgery.

The authors plan to continue the study of the thin silastic device with an alternate fixation method. Four anchoring points will be used in six new rabbits. The original protocol for mating and control will be carried out.

Additionally, the principal investigator plans to extend the project to the primate model, obtaining the support of another institution because of the lack of primate facilities at their own.

VII. MALE STERILIZATION

Project: PARFR-90N, Np

New Method for Obstructing Vas Deferens by Direct Injection of Chemical Agents: A Non-Operative Technique of Male Sterilization

Joseph E. Davis, M.D. -- New York Medical College

\$59,305 7/1/77 - 12/31/78

Planned Parenthood Federation of America, Inc.

\$54,007 2/1/79 - 1/31/80

Objectives: to test in 100 human volunteers a direct percutaneous injection of a mixture of ethanol and formalin as a vas-occlusive agent.

Accomplishments: Twenty-seven volunteers seeking vasectomy agreed to participate in this study and underwent bilateral vas injection between October, 1977 and April, 1978. the length of time required for this group of patients to become azoospermic varied from two weeks to six months. Ten men had significantly decreased semen

Accomplishments: (continued)

analyses, although they failed to achieve azoospermia. Seven other men failed to have significant changes in the semen analyses. In none of the azoospermic men have sperm returned to the ejaculate. The group with significantly decreased sperm counts continue to show them.

All patients who did not become azoospermic have been asked either to have a repeat injection or to have a standard vasectomy performed with the removal of the section of vas judged to be the site of the injection. In addition, men who have achieved azoospermia have been asked to undergo vasectomy to obtain tissue from the injected area to evaluate the potential for reanastomosis. All of the tissue removed is being step-sectioned.

A more exact delivery system has been developed which grasps the vas through the scrotal fold and allows for multiple injections of the fixed vas.

A site visit was carried out in October, 1978 and a new work plan for future testing has been submitted to PARFR.

Project: PARFR-95N

Development and Evaluation of Reversible Vas Deferens Blocking Device

Lourens J.D. Zaneveld, D.V.M., Ph.D. -- University of Illinois

\$100,118

7/1/77 - 6/30/79

Objectives: To further test in rabbits and primates a reversible vas deferens blocking device.

Accomplishments:

As before, none of the rabbits with devices implanted ejaculated spermatozoa or impregnated female rabbits. These rabbits have had a minimal implantation period of five months. An additional six rabbits have been reversed and tested for the presence of sperm. Four of the six rabbits ejaculated sperm soon after device removal. In total so far, ten rabbits have been reversed, of which seven ejaculated sperm again for a success rate of 70%. The rate may improve over time since four of the reversals were done recently.

All twelve primates, with the exception of one, became azoospermic after having the devices implanted. The primates have remained azoospermic for four to five months except for another primate who ejaculated sperm again after two months of azoospermia. Exploratory surgery was performed on the

PARFR-95N**Accomplishments: (continued)**

animal that was never azoospermic and revealed the plug to be in place with a normal looking vas. A modified plug (a sheath placed around the vas and plug) was then utilized in this monkey.

Pending the continued good results in rabbits and in primates both with effective sperm blockage and reversal demonstrated, the investigator plans to collaborate with an Egyptian colleague in a Phase I clinical study in Egypt.

Project: PARFR-P12

Development of Microporous Materials for Thin Intravasal Implants

David H. Frisch, Ph.D. -- Massachusetts Institute of Technology

\$6,686

7/1/78 - 6/30/79

Objectives: To develop an intravasal implant and necessary delivery system in order to provide for vas deferens occlusion and simple excision for reversal should it become necessary.

Accomplishments:

Surgical tools for implanting the disks in the vas have been developed and used in dogs and one monkey. The instrument puts a tiny disk athwart the lumen of the vas. Implant materials have been examined including mylar but these were not successful in the design of the micropores in the disk. Drilling holes in stainless steel and laser drilling in diamond have also been considered, but in both of these cases the technology is too expensive. The investigator has purchased a microdrilling head and is himself adapting it to a computer controlled milling machine.

Preliminary studies of implants of solid mylar disks are ongoing in one dog and one monkey.

Project: PARFR-P14

The Bipolar Needle for Percutaneous Vas Obstruction

Stanwood S. Schmidt, M.D.

\$2,350

7/1/78 - 6/30/79

PARFR-P14 (continued)

Objectives: To determine the feasibility and effectiveness of a bipolar cautery unit to obstruct the vas deferens in male volunteers

Accomplishments:

Five volunteers have undergone experimental vasectomies. Three were observed for six months following the attempt at occluding the vas deferens under direct visualization using the bipolar cautery unit. Of the three, two have shown no reduction in sperm count and have been reoperated. Microscopic examination showed bilaterally patent lumens, with evidence that the fulgeration had occurred but that epithelial regeneration had taken place. The third patient showed sperm in his ejaculate, but in reduced numbers. The fourth patient has just reached the six month interval and still maintains a full sperm count. The fifth patient is four months postoperative and still shows a high count. The investigator feels that the bipolar cautery unit is inappropriate and does not deliver sufficient power to destroy the mucosa of the vas and some of the underlying muscle. The investigator plans to accept no further volunteers until the bipolar unit can be studied and improved.

VII. MISCELLANEOUS

Project: PARFR-101N

Metabolism and Pharmacokinetics of Ethynyl Estrogens

Joseph W. Goldzieher, M.D. -- Southwest Foundation for Research and Education

\$23,994

9/1/78 - 2/28/79

Objectives: To complete the pharmacokinetic analysis of ethynyl estradiol and mestranol. To complete the chemical analytical work and analysis of the urinary steroid conjugates of ethynyl estradiol and mestranol from U.S., Nigerian and Sri Lankan women; to complete the chemical analysis and interpretation of the free radioactive steroid metabolites in urine in these same women.

Accomplishments:

The pharmacokinetic analysis of plasma levels of ethynyl estradiol and mestranol have been completed on samples from U.S. studies and Singapore, Thailand, Sri Lanka and Nigeria. Substantial differences were observed in the

PARFR-101N

Accomplishments: (continued)

kinetics of the EE in the various localities; the origin of these differences, which might have considerable clinical significance, remains to be identified.

Chemical work on the separation and analysis of urinary radioactive conjugates in 10 women from Nigeria, Sri Lanka, and comparison U.S. population of 8 women has been completed.

Analysis of the hydrolyzed (free) steroid fractions from the urine of Nigerian, Sri Lankan and U.S. women have been completed and their chromatographic profiles completed.

WORK PLAN

WORK PLANAnticipated Accomplishments

PARFR's next six month reporting period promises even greater expansion over this and previous reporting periods. This is due to the following:

- 1) Dr. Elizabeth B. Connell's completed orientation period and her work towards the generation of proposals in LDCs.
- 2) In October, 1978, the PARFR newsletter was sent to a mailing list of over 2,000.
- 3) The participation of staff in relevant scientific meetings.
- 4) Negotiations are underway for clinical trials of the following PARFR supported developments:

Collagen Sponge - The investigator and PARFR are interested in testing the sponge in a variety of socio-cultural settings in both developed and developing countries. The SAC approved, at the December 11 meeting, a trial at Texas Tech with Dr. Wayne Heine as the principal investigator. This project has been held up due to Northwestern University Institutional Review Board's uncertainty with regard to the new DHEW requirements regarding human subjects. Hopefully this matter will be settled early in 1979.

Spermicidal Condom - Additional PARFR support will be requested to permit the small scale manufacture of a suitable number of biodegradable condoms containing spermicide to be used in clinical studies of acceptability and effectiveness. These clinical studies are anticipated to be carried out in the U.S. and in developing countries. This study has been delayed since Schering has recently bought the previous subcontractor, the Emko Company (PARFR P8). Questions have been raised with regard to patent rights.

The Utero-Tubal Junction Blocking Device - The investigator and PARFR are again working closely together on the equipment modifications required and the development of an appropriate protocol for Phase II human studies to be carried out in the United States, and possibly in Chile and Germany. Dr. Hosseinian has returned to the United States and will be submitting a formal proposal for the March 18 SAC meeting to initiate clinical trials at Cook County Hospital in Chicago.

MCA-FEMCEPT Project - In January, 1979, negotiations were completed and subcontracts were written with two Salvador institutions for the project entitled: "Phase I Clinical Trial of Fallopian Tube Closure Using Methylcyanoacrylate (MCA) as a tissue Adhesive Delivered Through the Single Application Fertility Regulation (FEMCEPT) Device."

Two other Latin American institutions, one in Salvador and one in Guatemala, may join this study during the next reporting period.

5) Publications:

- a) On February 2, 1979, Harper and Row Publishers finally made available the proceedings of the PARFR Workshop on Reversal of Sterilization. As of this writing, PARFR is in the process of mailing copies to the participants of this workshop.
- b) The proceedings of the 6th PARFR supported Workshop, PARFR-93N, entitled Animal Models for Research on Contraception and Fertility, held at the National Academy of Sciences in Washington, D.C. in May, 1978, are in the galley proof stages. The expected publication date is July 15, 1979.
- c) The manuscripts and discussion summaries for the 7th PARFR workshop, Pregnancy Termination: Procedures, Safety and New Developments, held in Nassau, Bahamas, May, 1978 have been completed and submitted to Harper and Row during this reporting period. As of this writing, the editors are reviewing galley proofs. The publication is expected to be released on July 15, 1979.
- d) PARFR is in the planning stages of its 8th workshop entitled New Developments in Vaginal Contraception to be held at the Camino Real Hotel in Guatemala City, Guatemala, April 25-27, 1979. Publication of the proceedings is anticipated and we are exploring the possibility of publishing a Spanish version of the book.
- e) Fertility Regulation Research and Development - An Update - PARFR is planning to establish a research technical information report that would review the latest R and D efforts on selected topics in a series of four to six issues per year. PARFR would select a pertinent and knowledgeable investigator to review published and unpublished studies in a specific area of fertility regulation. The selected investigator - consultant would be given adequate time and PARFR assistance to review the findings in the specified field. This material then would be submitted to PARFR for final review and editing, and subsequent publication. Each review would be about six to ten pages, prepared in a loose-leaf manner. PARFR would use its own mailing lists, domestic and foreign, and selected mailing from the Population Report series. Approximately 3,000 copies of each issue would be distributed internationally.

Procedures and Activities

- 1) The scheduled Scientific Advisory Committee Meetings for 1979 are: March 18, 1979 (New Orleans); June 4, 1979 (Chicago); September 5, 1979 (Washington, D.C.); and December 10, 1979 (Chicago).
- 2) At this writing, PARFR has exhibited at the American Fertility Society (AFS) 35th Annual Meeting in San Francisco, California, February 4-7, 1979. PARFR staff feels that exhibits at relevant meetings are a mechanism for exposure and to solicit potential projects

Procedures and Activities (continued)

and investigators. At the AFS meeting, PARFR staff met Dr. Maia (Bahia, Brazil) and Dr. M.H.H. Badraoui (Cairo, Egypt). PARFR staff also met with current PARFR investigators.

Plans for LDC Involvement

- 1) PARFR Workshop in Guatemala - PARFR will gain significant exposure in Latin America with the Guatemala Workshop, since representatives from over 15 Latin American countries are invited to participate and the PARFR staff will be on hand to discuss proposal development.
- 2) AVS Meeting in Seoul, Korea - PARFR is planning to support speakers at the AVS meeting in Seoul, Korea in May, 1979. While in Korea, Dr. Zatuchni and Ms. Krier will do a site visit of Korea University (PARFR-86K) and Yonsei University (PARFR-97K).
- 3) Refer to LDC Involvement section for more detail.

FINANCIAL

SUMMARY FINANCIAL REPORT

7/1/75 - 12/31/78

	BUDGET 7/1/75 - 6/30/79	EXPENDED 7/1/75 - 6/30/78	EXPENDED 7/1/78 - 12/31/78	EXPENDED 7/1/75 - 12/31/78
Salaries	\$ 379,353.03	\$ 214,208.73	\$ 71,630.59	\$ 285,839.32
Fringe Benefits	52,354.04	28,800.18	10,194.77	38,994.95
Indirect Costs	133,140.46	74,923.97	21,489.19	96,413.16
Supplies	113,322.18	71,572.11	15,767.53	87,339.64
Equipment	15,755.55	10,570.80	2,024.65	12,595.45
Consulting Fees	50,944.00	23,773.11	6,825.00	30,598.11
Travel	135,321.02	77,234.07	22,736.66	99,970.73
Moving Expenses	6,846.17	1,846.17	1,117.74	2,963.91
Remodeling & Maintenance	16,249.30	11,249.30	-	11,249.30
Workshop/Publications	203,404.33	94,904.33	13,750.00	108,654.33
Subcontracts	3,077,193.92	1,232,277.35	361,301.48	1,593,578.83
Pilot Studies	<u>125,347.00</u>	<u>35,444.75</u>	<u>11,829.99</u>	<u>47,274.74</u>
TOTAL	\$ 4,309,231.00	\$ 1,876,804.87	\$ 538,667.60	\$ 2,415,472.47

PARFR EXPENDITURES FOR THE PERIOD July 1, 1978 - December 31, 1978

	<u>July 1978</u>	<u>August 1978</u>	<u>September 1978</u>	<u>October 1978</u>	<u>November 1978</u>	<u>December 1978</u>	<u>Total Period</u>
Salaries - Prof.	6,129.16	6,687.50	10,814.10	12,037.49	12,360.00	10,850.00	58,878.31
Non-Prof.	<u>1,658.00</u>	<u>1,658.00</u>	<u>1,752.56</u>	<u>2,603.00</u>	<u>2,603.00</u>	<u>2,477.72</u>	<u>12,752.28</u>
Total Salaries	7,787.16	8,345.50	12,566.72	14,640.49	14,963.00	13,327.72	71,630.59
Fringe Benefits	1,090.20	1,168.37	1,797.04	2,093.59	2,139.71	1,905.86	10,194.77
Indirect Costs	2,336.15	2,503.65	3,770.02	4,392.15	4,488.90	3,998.32	21,489.19
Supplies	4,598.12	2,488.87	1,470.47	2,635.15	1,642.87	2,932.05	15,767.53
Equipment	1,568.00	-	-	325.90	-	130.75	2,024.65
Consulting Fees	100.00	2,850.00	1,550.00	1,500.00	450.00	375.00	6,825.00
Travel	3,815.85	2,924.66	2,170.58	4,525.12	6,422.00	2,878.45	22,736.66
Moving Expense	-	-	-	1,117.74	-	-	1,117.74
Remodel. & Maint.	-	-	-	-	-	-	-
Workshops/Publications	-	-	-	10,000.00	-	3,750.00	13,750.00
Subcontracts	83,944.86	36,228.73	71,098.41	29,342.21	58,260.84	82,426.43	361,301.48
Pilot Studies	<u>1,136.45</u>	<u>1,823.98</u>	<u>-</u>	<u>856.87</u>	<u>860.15</u>	<u>7,152.54</u>	<u>11,829.99</u>
Total Research	85,081.31	38,052.71	71,098.41	30,199.08	59,120.99	89,578.97	373,131.47
Total Workshop	-	-	-	10,000.00	-	3,750.00	13,750.00
Total Admin.	<u>21,295.48</u>	<u>20,281.05</u>	<u>23,324.83</u>	<u>31,230.14</u>	<u>30,106.48</u>	<u>25,548.15</u>	<u>151,786.13</u>
TOTAL	106,376.79	58,333.76	94,423.24	71,429.22	89,227.47	118,877.12	538,667.60

PARFR Budget Forecast
1/1/79 - 6/30/79

	Budget 7/1/75- 6/30/79	Expended 7/1/75- 12/31/78	Current Commits thru 6/30/79*	Add'l Exp. Projections thru 6/30/79*	Projected Balance 6/30/79
Salaries-Prof.	266,278.89	200,678.89	65,600.00	---	---
Non-Prof	113,074.14	85,160.43	15,618.00	---	12,295.71
Total Salaries	379,353.03	285,839.32	81,218.00	---	12,295.71
Fringe Benefits	52,354.04	38,994.95	11,542.67	---	1,816.42
Indirect Costs	133,140.46	96,413.16	24,215.40	---	12,511.90
Supplies	113,322.18	87,339.64	12,236.38	13,500.00	246.16
Equipment	15,755.55	12,595.45	1,368.00	1,500.00	292.10
Consulting Fees	50,944.00	30,598.11	3,300.00	8,000.00	9,045.89
Travel	135,321.02	99,970.73	3,811.21	28,000.00	3,539.08
Moving Expenses	6,846.17	2,963.91	---	---	3,882.26
Remodeling & Maint.	16,249.30	11,249.30	---	---	5,000.00
Workshops/Publ.	203,404.33	108,654.33	3,750.00	91,000.00	---
Subcontracts	3,077,193.92	1,593,578.83	1,012,594.62	495,573.00	(24,552.53)
Pilot Studies	125,347.00	47,274.74	31,712.61	23,803.71	22,555.94
Total Research	3,202,540.92	1,640,853.57	1,044,307.23	519,376.71	(1,996.59)
Total Workshop	203,404.33	108,654.33	3,750.00	91,000.00	---
Total Administration	903,285.75	665,964.57	137,691.66	51,000.00	48,629.52
TOTAL	4,309,231.00	2,415,472.47	1,185,748.89	661,376.71	46,632.93

* In Research categories only (Subcontracts & Pilot Studies), Commitments and Projections are given for the entire term of the subcontracts, most of which extend beyond 6/30/79.

APPENDIX

PARFR SCIENTIFIC ADVISORY COMMITTEE

MEETING XXV

CHICAGO, ILLINOIS
July 10, 1978

VOTING SAC MEMBERS PRESENT

John J. Sciarra, M.D., Ph.D.
Nancy J. Alexander, Ph.D.
Robert T. Chatterton, Ph.D.
Joseph E. Davis, M.D.
William Droegemueller, M.D.
Edward C. Mather, D.V.M., Ph.D.
Robert H. Messer, M.D.
Kamran S. Moghissi, M.D.
Ralph M. Richart, M.D.
Susan C. M. Scrimshaw, Ph.D.
Judith L. Vaitukaitis, M.D.
A. Albert Yuzpe, M.D.

PARFR STAFF PRESENT

Georgia L. Fackler
Diane H. Krier
Aguiles J. Sobrero, M.D.
Gerald I. Zatuchni, M.D., M.Sc.

U.S.A.I.D. MEMBERS PRESENT

J. Joseph Speidel, M.D., M.P.H.
Kate Prager

The twenty-fifth meeting of the PARFR Scientific Advisory Committee convened on Monday, July 10, 1978 at 8:00 a.m. at the Hyatt Regency O'Hare in Chicago, Illinois. Dr. John J. Sciarra presided as Chairman. Minutes of the March 29, 1978 meeting were approved with no voiced corrections.

I. ANNOUNCEMENTS

A. Susan C. M. Scrimshaw, Ph.D., Assistant Professor, Division of Population, Family and International Health, School of Public Health, UCLA, was formally introduced to the SAC Members. A copy of her C.V. was circulated.

B. The remaining SAC dates for 1978 remain the same:

September 6, 1978 -- Washington, D.C., International Inn (Thomas Circle)
December 11, 1978 -- Chicago, Illinois, O'Hare Hilton.

C. The following SAC dates were approved for 1979:

Sunday, March 18, 1979 -- New Orleans, Louisiana
Monday, June 4, 1979 -- Chicago, Illinois
Wednesday, September 5, 1979 -- Washington, D.C.
Monday, December 10, 1979 -- Chicago, Illinois

II. NEW BUSINESS

A. Extension Proposal Review

1. PARFR-80N -- David W. Keller, M.D., Washington University

"Fertility Control Through Local Cervical Injection of Microencapsulated Progestins"

Dr. Keller had requested a six month extension request with additional funding of \$34,778. Dr. Mather reported on the previous site visit of February 15, 1978 with Ms. Krier to St. Louis. At that time the investigators did not indicate that they would be requesting an extension. They stated that they had had sufficient funds to complete the latest animal studies under the current contract which terminated June 30, 1978. Dr. Mather had been the principal site visitor of this project since its inception in 1975. He reported that on numerous occasions Dr. Keller had been advised to have histopathology from the cervical injection site in the cows; but to date none have been accomplished. There have been numerous problems with the delivery system in this project and also critical problems relating to the management. He felt that the presently used dosage was too high to produce any valid results. The SAC Members voted unanimously not to extend this project.

2. PARFR-92N -- Deborah J. Anderson, Ph.D., Oregon Regional Primate Research Center

"Contraception by Induction of Mild Uterine Inflammation"

Dr. Anderson requested a year extension with additional funding of \$46,703. This PARFR funded study on the prevention or interruption of pregnancy by the induction of transient uterine leukocytosis in rats has, serendipitously, found that a single intrauterine injection of 10% glycogen terminates very early pregnancy. The investigators have examined a large number of uterine leukocytosis induction agents, and it appears that 10% glycogen is the most effective, provided it remains in the uterus for a few hours. There was considerable discussion relating to glycogen being utilized as an abortifacient in regard to bacterial infections in utero. It was suggested that bacteriologic studies be done as soon as possible. Dr. Zatuchni would relay the Committee's concerns to Dr. Anderson. SAC Members voted to extend this project.

3. PARFR-95N -- L.J.D. Zaneveld, D.V.M., Ph.D., University of Illinois at the Medical Center

"Development and Evaluation of a Reversible Vas Deferens Blocking Device"

Dr. Zaneveld requested a year extension with additional funding of \$43,818. He reported that all primates had become azoospermic

Extension Proposal Review (continued)

PARFR-95N (continued)

with the exception of one whose sperm count is presently very low. Of the six rabbits that had been reversed so far after long-term and short-term implants, five have ejaculated spermatozoa again. Dr. Zatuchni had reported that Dr. Zaneveld has made good progress with this project despite the unforeseen technical problems he originally encountered. Dr. Moghissi queried if PARFR had ever been involved in marketing of a successful development from a PARFR supported project. The discussion turned to the area of patent rights. The PARFR subcontract form has the flexibility to incorporate three different patent clauses which are negotiated during the subcontracting process. Generally, institutions that can provide technology transfer capability can request to retain the patent rights and are granted such. Nonetheless, the subcontractor grants to the government a nonexclusive, nontransferable paid up license to make use and sell each subject invention throughout the world by or on behalf of the government of the United States. The Committee voted to extend this subcontract.

4. PARFR-P8 -- Charles Salivar, The Emko Company, St. Louis, Mo.

"Water Soluble Condom Feasibility Study"

This extension requested an additional year with funding at \$39,730. Dr. Zatuchni reported that this pilot study has proceeded in an exemplary manner and has produced several promising biocompatible films that could result in a useable water soluble spermicidal condom. Mr. Ray Belsky, consultant for the project, has clearly outlined the next steps in the development of this contraceptive method. The Committee suggested that this project should go into Phase I studies in humans and that the animal testing be bypassed. SAC Members voted unanimously to extend this project.

5. PARFR-P9 -- Danny H. Lewis, Ph.D., Southern Research Institute, Birmingham, Alabama

"A Fibrous Polymer for the Delivery of Contraceptive Steroids to the Female Reproductive Tract"

Dr. Lewis requested a year extension with \$66,000 additional funding. Dr. Zatuchni reported that the investigators determined that certain polymers can be loaded with progesterone and probably other steroids and be extruded in the form of fibers. The investigator proposes to develop a fibrous polymer for the delivery of progestational agents to the female reproductive tract. Dr. Scrimshaw suggested that cultural acceptability in the developing world would be higher if an alternative, such as an injectable polymer rather than an IUD actuated tail, could be developed. Reference to the PARFR project developing an injectable, long-acting polymer-steroid was made. The Committee voted to approve the extension.

B. Formal Proposal Review

1. Leonard J. Lerner, Ph.D., Thomas Jefferson University, Philadelphia, Pennsylvania

"Investigation of New Compounds to Terminate Pregnancy"

Funding requested \$66,286. Length of project one year.

Dr. Zatuchni reported that this proposal is a well designed screening program to develop compounds exhibiting a 100% efficacy in pregnancy termination that would be orally effective when administered in very early pregnancy. Dr. Lerner through his previous connection at Lepetit Research Laboratory in Milano, Italy, will try to obtain approximately 20-30 compounds for testing and evaluation in the hamster and then in the rat. Dr. Speidel suggested that Dr. Lerner contact Dr. Csapo in St. Louis in that he is getting good results with his rat model in similar studies. There was some discussion as to the central nervous system effects of some of these known compounds. Dr. Chatterton suggested that the investigator be advised to examine injectable compounds in addition to seeking orally active derivatives. The SAC Members voted to approve this proposal.

2. Jack Lippes, M.D., Deaconess Hospital, Buffalo, New York

"An Assessment of the Efficacy of Prostaglandin Synthetase Inhibitors in Reducing IUD Associated Blood Loss"

Funding requested \$25,020. Length of project 18 months.

Dr. Lippes proposes to investigate if prostaglandin synthetase inhibitors (ibuprofen, mefenamic acid, tylenol, placebo) could decrease bleeding due to an IUD. The committee voted not to approve this formal proposal. Instead, the Committee suggested that the investigator be advised that IFRP might be interested in supporting these studies.

3. Ernest W. Paqc, M.D., University of California, School of Medicine

"Investigations of a New Vaginal Barrier Contraceptive"

Funding requested \$39,812. Length of project 18 months.

There was considerable discussion of this proposal in relation to other vaginal contraceptives under development. The general consensus was approval of this project, however, it was suggested that the proposal be modified by PARFR Staff to bring the initial costs down to the range of a pilot study. Should the initial findings with regard to efficacy be positive, PARFR should consider supporting the delivery system development.

C. Pilot Study Review

1. Theodore Braun, M.D., Ph.D., Northwestern University Med. School

"Evaluation of LH-RH Analogs as Antispermato-genic Agents
(A Pilot Model Study in Rats)"

Funding requested \$7,500. Length of project one year.

Dr. Zatuchni reported that the objective of this pilot study is to establish the effectiveness of treatment of male rats with native LH-RH and its synthetic analogs, both agonist and antagonist, on spermatogenesis. Dr. Vaitukaitis indicated that the protocol design was weak and that the fertility method proposed was not a practical form for long-term contraception. The proposal was not approved.

2. Ronnie B. Bush, Ph.D., The Chicago Medical School

"Reversal of Vas Sclerosing With the Use of Hydrocortisone"

Funding requested \$6,000. Length of project one year.

Dr. Zatuchni reported on this proposal whereby the investigators plan to evaluate the possibility of reversing male sterilization accomplished by sclerosing agents. The SAC held that the hydrocortisone could not "dissolve" fibrosis after prolonged duration. The SAC Members voted not to approve this project.

D. Informal Proposal Review

1. John D. Biggers, D.Sc., Ph.D., Harvard Medical School

"Medicated Intrauterine Devices Releasing Prostaglandin Antagonists"

Funding requested \$121,015. Length of project two years.

Dr. Biggers has seized upon the probabilities that prostaglandins are important in implantation of the fertilized ova and that prostaglandins also may be responsible for the unwanted side effects of an IUD. Dr. Biggers proposes to explore the possibility of developing an IUD that would release prostaglandin synthetase inhibitors. SAC Members voted to request a formal proposal.

2. Professor Gamal El Din Beheri, Cairo University, Egypt

"Reversible Male Sterilization"

Funding requested \$29,440. Length of project two years.

Dr. Zatuchni reported the similarity to Dr. Zaneveld's shug device study. He indicated that this informal proposal was included in the agenda as an expression of interest on the part of Professor Beheri in the development of a potentially reversible male sterilization method. Dr. Zatuchni recommended that a collaborative project be worked out between Dr. Beheri and Dr. Zaneveld in order to proceed with further animal testing on the shug device in Egypt and look forward to a Phase I clinical study in Egypt early in 1979. The Committee voted agreement with Dr. Zatuchni's suggestion.

Informal Proposal Review (continued)

The SAC voted not to request formal proposals from the following eight investigators:

1. Alan B. Dudkiewicz, Ph.D., University of Houston
"Development of an Anti-Acrosomal Enzyme Contraceptive"
Funding requested \$66,610. Length of project one year.
2. Sidney Shulman, Ph.D., New York Medical College
"Isolation of Effective Sperm Antigens for Use in Contraceptive Immunization"
Funding requested \$65,254. Length of project one year.
3. Andre Lemay, M.D., Ph.D., St. Francois d'Assise Hospital, Quebec, Canada
"LH-RH and hCG as Potential Luteolytic Agents in the Human"
Funding requested \$37,500. Length of project two years.
4. Charles H. Rodgers, Ph.D., University of Illinois
"Catechol Estrogens as Selective Inhibitors of Gonadotropin Secretion"
Funding requested \$49,300. Length of project three years.
5. Malur R. Sairam, Ph.D., Clinical Research Institute of Montreal, Quebec, Canada
"Drug Inhibition of Lutropin (LH) Action In Vivo and In Vitro"
Funding requested \$32,000. Length of project three years.
6. Fernando B. Ubaldo, Jr., M.S., Creativity Research and Development Foundation, Inc.
"Diagnostic Value of the Bioelectrical Resistance of the Human Body in Detecting Accurately the Time of Human Ovulation"
Funding requested \$7,470. Length of project one year.
7. Abubakar A. Shaikh, D.V.M., Ph.D., Southwest Foundation for Research and Education, San Antonio, Texas
"Steroid Induced Regulation of Ovulation"
Funding requested \$111,925. Length of project two years.
8. V. Daniel Castracane, Ph.D., Southwest Foundation for Research and Education, San Antonio, Texas
"Contraception by a Combination Menstrual Induction Regimen"
Funding requested \$110,829. Length of project two years.

E. PARFR-Initiated Projects

1. Joseph W. Goldzieher, M.D., Southwest Foundation for Research and Education, San Antonio, Texas

"Comparison Among Different Ethnic Populations of the Pharmacokinetics of Ethynyl Estrogens"

Funding requested \$22,000. Length of project six months.

Dr. Zatuchni reported that Dr. Goldzieher had a long-term research project to examine the metabolism of administered contraceptive steroids in women of the United States versus women in Sri Lanka and Nigeria in order to detect possible differences in the way the steroids are metabolised, and to examine the health and safety implications of such findings. The protocol had called for the obtaining of radioactive urine samples from these developing countries having them shipped frozen to the U.S. and analyses run. Unfortunately, until these arrangements could be worked out with the countries, October, 1977, Dr. Goldzieher's project ran out of time. USAID in Washington had already extended the project but because of administrative constraints could no longer continue supporting the final phases of analysis. Hence, AID Washington has asked PARFR to consider supporting the final data analyses, which Dr. Goldzieher says is about 90% completed. Dr. Goldzieher estimates that four months will be necessary involving a cost of around \$22,000. Dr. Zatuchni had asked Drs. Chatterton and Moghissi to review the preliminary findings of this research. The Committee voted to approve support for the completion of these studies.

2. Emanuel H. Bronner

"Vaginal Contraceptive Capsule"

Dr. Zatuchni had included in the agenda correspondence from Edward Callan, Dr. Bronner's attorney, relating to the contraceptive gel described in Dr. Bronner's patent. PARFR will obtain free samples, in bulk, for initial in vitro testing. Should these tests be positive, PARFR will initiate animal model studies at a suitable facility.

PARFR-Initiated Projects (continued)

3. C. Patrick Tharp, Ph.D., KV Pharmaceutical Company, St. Louis, Mo.

"Development of Prolonged Acting Spermicidal Creme Containing Nonoxynols"

Dr. Zatuchni reported that KV Pharmaceutical has had a 25 year experience in prolonged release drug formulations and manufacture. The President of the company is the inventor of the first sustained release capsule. KV has developed a unique sustained release vaginal creme which they have combined with antibiotics and other agents for severe vaginal infection problems. KV is now interested in combining their sustained release preparation with a spermicide and they have requested PARFR support for further development of such a compound and the preliminary animal and human testing. Dr. Zatuchni reported that the contact with KV Pharmaceutical Company has ramifications for other PARFR supported research. For example, the creme might be combined with the 10% glycerin as a slow matrix delivery system for Dr. Anderson's project. PARFR will support initial in vitro studies and human volunteer studies; the latter probably in cooperation with Dr. William Masters.

4. Jaime Zipper, M.D.

"Use of Quinacrine Pellets for Female Sterilization"

Dr. Zatuchni included in the agenda Dr. Zipper's report on 139 cases from January, 1977 through May, 1978. Dr. Zatuchni stated that Dr. Zipper inserts five pellets, each containing 50 mg of quinacrine, utilizing sodium penothal to dissolve the pellets; he administers these to women over three consecutive cycles. In the 139 cases reported, only one resulted in pregnancy. Dr. Zipper purports to develop a protocol whereby he can get the administration down to one dose of 500 mg of the quinacrine. Dr. Zatuchni reported that he had traced down information through the help of Drs. Oscar Davidson and Howard Tatum on the one unreported death associated with quinacrine. As it turns out, the death resulted from the paracervical block (xylocaine) and that the quinacrine was never administered. Dr. Richart had reported that in Bangkok, quinacrine had produced low tubal closure rates. He also stated that Drs. Tatum and Segal felt that quinacrine had significant central nervous system side effects such as excitation. Dr. Moghissi suggested that Dr. Zatuchni request information from FDA regarding additional tests that the FDA would require.

F. Technical Reports

The following technical reports were included in the agenda for information purposes:

1. PARFR-79N -- C. Irving Meeker, M.D., Maine Medical Center
"A Method for Reversible Sterilization in the Female"
2. PARFR-82N -- Fouad Hefnawi, M.B., M.S., Al-Azhar Univ., Egypt
"Measurement of Blood Loss in Women Fitted With Copper Clad Lippes Loops"
3. PARFR-85N -- Milos Chrapil, M.D., Ph.D., Arizona Health Sciences Ctr.
"Collagen Sponge Contraceptive - Testing of Efficacy in Human Volunteers"
4. PARFR-89N -- Harry P. Gregor, Ph.D., Columbia University, N.Y.
"Fallopian Tube Cauterization and Closure by Silver Acetate-Alginate Formulations"
5. PARFR-90N -- Joseph E. Davis, M.D., New York Medical College
"New Method for Obstructing the Vas Deferens by Direct Injection of Chemical Agents: A Non-Operative Technique of Male Sterilization"
6. PARFR-91N -- Donald L. Wise, Ph.D., Dynatech R/D Company
"Preparation and Evaluation of Biodegradable Cylindrical Implants for Fertility Control"
7. PARFR-94N -- William Droegemueller, M.D., Arizona Health Sciences Ctr.
"Modern Modified Aldridge Procedure"
8. PARFR-P10 -- Robert T. Chatterton, Ph.D., University of Illinois at the Medical Center
"Fertility Regulation by Control of Progesterone Clearance"

III. OLD BUSINESS:

A. Pending from December 7, 1977 SAC Meeting

1. Extension Proposal: PARFR-89N, Harry P. Gregor, Ph.D.
Columbia University, New York, New York
"Fallopian Tube Cauterization and Closure by Silver Acetate-Alginate Formulations"
Amendment fully executed.

2. Formal Proposal:

a. Midtrimester Abortion Study

1' PARFR-97N - Theodore M. King, M.D., Ph.D.
The Johns Hopkins Univ., Baltimore, Md.

2' PARFR-97K - Young-Ki Moon, M.D., Yonsei University
College of Medicine, Seoul, Korea

Participating: Korea Univ., Sung-bong
Hong, M.D.; Seoul National Univ., Syung
Wook Kim, M.D.; Kyung Hee Univ.,
Kap-soon Ju, M.D.

The subcontracts are in the final stages of approval and
execution.

3. Pilot Studies

a. PARFR-P12 - David H. Frisch, Ph.D., Massachusetts Institute
of Technology, Cambridge, Massachusetts

"Development of Microporous Materials for Thin Intravasal
Implants"

6/1/78 - 5/31/79 \$6,685.50

AID Contract Office approved, awaiting signed copy from MIT.

b. PARFR-P13 - Ivo Brosens, M.P., Ph.D., Willem Boeckx, M.D.
Catholic Univ. of Leuven, Leuven, Belgium

"An Evaluation of the Efficacy of Candidate Fimbrial Pros-
thesis in Female Rabbits and the Evaluation of Fimbrial
Devices as a Reversible Technique of Female Sterilization"

5/1/78 - 4/30/79 \$4,741.38

Fully executed subcontract. An agreement with IFRP totaling
\$1,700 for their involvement.

c. PARFR-P14 - Stanwood S. Schmidt, M.D., California

"The Bipolar Needle for Percutaneous Vas Obstruction"

7/1/78 - 6/30/79 \$2,350.00

Contract fully executed.

B. Updates on Determinations of the March 29, 1978 SAC Meeting

1. Extension Proposals:

PARFR-83N -- Lee R. Beck, Ph.D., University of Alabama Medical Center, Birmingham, Alabama

"Study to Test an Injectable Delivery System for the Sustained Release of Norethisterone"

Amendment #5 fully executed, extending contract to March 31, 1979.

2. Formal Proposals:

a. PARFR-98M -- Ramon Aznar, M.D., Gustavo Zamora, M.D.
Centro De Investigacion Sobre Fertilidad y Esterilidad, Mexico City, Mexico

"Norethisterone Microcapsule Injectable Contraceptive Study"

7/1/78 - 6/30/79 \$34,265 (CIFD)

Separate agreements are being negotiated with the University of Alabama for assay determinations and the Southern Research Institute for development of a polymer.

b. PARFR-99N -- Duane L. Garner, Ph.D., Oklahoma State University, Stillwater, Oklahoma

"Immunoabsorbent Isolation of Specific Spermatozoal Antigens for Use as Anti-Fertility Immunogens"

7/1/78 - 12/31/78 \$30,233

The subcontract is fully executed.

C. Administrative Update

1. The following have been administratively amended to September 30, 1978:

- a. PARFR-79N -- Meeker
- b. PARFR-90N -- Davis
- c. PARFR-91N -- Wise
- d. PARFR-94N -- Droegemueller
- e. PARFR-95N -- Zaneveld

2. PARFR-82N - Fouad Hefnawi, M.B., M.S., Al-Azhar University
Cairo, Egypt

"Measurement of Blood Loss in Women Fitted with Copper Clad Lippes Loops"

Will be amended for ten months to complete this study.

Administrative Update (continued)

3. "Phase I Clinical Trial of Fallopian Tube Closure Using Methyl-cyanocrylate (MCA) Tissue Adhesive Delivered Through the Single-Application Fertility Regulation (SAFR) Device"

PARFR-86N - Robert S. Neuwirth, M.D., St. Luke's Institute for Health Sciences; Ralph M. Richart, M.D., Columbia University

PARFR-86K - Sung-bong Hong, M.D., Korea University Medical College, Seoul, Korea

PARFR-86G - Professor H. K. Zinser, Evangelisches Krankenhaus, Cologne, Germany

The informed consent form is being revised and the subcontracts are completed for processing once this approval is received.

4. PARFR-96N - Ramaa P. Rao, M.D., Michael Reese Hospital and Medical Center, Chicago, Illinois

"Long-Term Study on the Effectiveness of an Injectable Polymer System in Producing Tubal Occlusion in Rabbits"

4/1/78 - 9/30/78 \$18,805 with a purchase order to Abcor of \$1,500.

The work under this subcontract has not begun since Abcor has not provided Michael Reese with the polymer; Abcor is awaiting outside manufacture of certain components of polymer. An amendment will be processed once Michael Reese receives the polymer to give the investigator the full time for the research.

5. Pilot Study Update

a. PARFR-P10 - Robert T. Chatterton, Ph.D., University of Illinois

"Fertility Regulation by Control of Progesterone Clearance"

Administratively amended to 10/31/78.

b. PARFR-P11 - Ralph M. Richart, M.D., Columbia University, New York, New York

"Evaluation of Carbohexoxymethyl 2 Cyanoacrylate as a Tube-Blocking Agent"

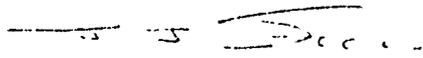
This subcontract was amended to June 30, 1979 in that there was a delay in starting.

IV. MISCELLANEOUS

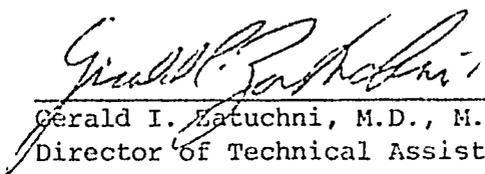
- A. Dr. Alexander gave a brief report on the NAS-sponsored Animal Models Workshop in May, 1978 in Washington, D.C.
- B. Dr. Zatuchni reported on the 1978 International Workshop and Postgraduate Course on Pregnancy Termination: Procedures, Safety and New Developments, May 23-26, 1978, Britannia Beach Hotel, Paradise Island, Nassau, Bahamas. This workshop was supported without AID funding. PARFR Staff has received excellent feed-back from speakers and participants who attended this meeting.
- C. PARFR Workshop for 1979 is proposed on Intravaginal Contraception for April 24-28, 1979 to be held in Guatemala City, Guatemala.

There being no further business the meeting adjourned at 4:15 p.m.

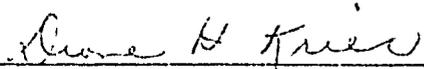
Respectfully submitted,



John J. Sciarra, M.D., Ph.D.
Program Director, Chairman, SAC



Gerald I. Zatuchni, M.D., M.Sc.
Director of Technical Assistance
PARFR



Diane H. Krier
Director of Administration
PARFR

PARFR SCIENTIFIC ADVISORY COMMITTEE

MEETING XXVI

Washington, D.C.
September 6, 1978

VOTING SAC MEMBERS PRESENT

John J. Sciarra, M.D., Ph.D.
Nancy J. Alexander, Ph.D.
Robert T. Chatterton, Ph.D.
Joseph E. Davis, M.D.
William Droegemueller, M.D.
Robert H. Messer, M.D.
Kamran S. Moghissi, M.D.
Ralph M. Richart, M.D.
Susan C. M. Scrimshaw, Ph.D.
Judith L. Vaitukaitis, M.D.

SAC MEMBERS ABSENT

Edward C. Mather, D.V.M., Ph.D.
A. Albert Yuzpe, M.D.

PARFR STAFF PRESENT

Elizabeth B. Connell, M.D.
Diane H. Krier
Aquiles J. Sobrero, M.D.
Gerald I. Zatuchni, M.D., M.Sc.

U.S.A.I.D. MEMBERS PRESENT

Miriam H. Labbok, M.D., M.P.H.
James D. Shelton, M.D., M.P.H.
J. Joseph Speidel, M.D., M.P.H.
Kate Prager, Sc.D. Candidate

The twenty-sixth meeting of the PARFR Scientific Advisory Committee convened on Wednesday, September 6, 1978 at 9:00 a.m. at the International Inn in Washington, D.C. Dr. John J. Sciarra presided as Chairman. Minutes of the July 10, 1978 meeting were approved with no voiced corrections.

I. ANNOUNCEMENTS

- A. Elizabeth B. Connell, M.D., PARFR's Research Project Development Coordinator, was formally introduced to the SAC Members. A copy of her C.V. was circulated.
- B. The remaining SAC date for 1978 is:

December 11, 1978 -- O'Hare Hilton, Chicago, Illinois.
- C. The following are SAC dates for 1979:

Sunday, March 18, 1979 -- Fairmont, New Orleans, Louisiana
Monday, June 4, 1979 -- Chicago, Illinois
Wednesday, September 5, 1979 -- Washington, D.C.
Monday, December 10, 1979 -- Chicago, Illinois

II: NEW BUSINESS

A. Extension Proposal Review

1. PARFR-79N -- C. Irving Meeker, M.D., The Maine Medical Center

"A Method for Reversible Sterilization in the Female"

Dr. Meeker requests additional funding of \$50,324 for one year to continue breeding the 32 remaining animals and to try two different types of tubal device anchors. Five of these animals still have the devices in place and 27 of the macaques have had the devices removed. Two pregnancies have occurred in the latter group. No pregnancies occurred with the devices in place. During the first year two problems arose: 1) problem with the suture material causing adhesions; and 2) a minimal degree of hydro-salpinx, proximal to the tubal device, in approximately one-third of the reoperated animals. There was considerable discussion regarding the project and in the final analysis, the Committee approved the extension request to determine the results in the breeding of the reversed animals: to do histopathological studies of the tubes in the five animals with devices in place and in those animals who do not get pregnant following device removal. It was suggested that Dr. Meeker confer with Dr. Richart regarding the histology. Dr. Zatuchni will discuss the Committee recommendations with Dr. Meeker and revise the protocol for the extension.

2. PARFR-91N -- Donald L. Wise, Ph.D., Dynatech R/D Company

"Preparation and Evaluation of Biodegradable Cylindrical Implants for Fertility Control"

Dr. Wise requests additional funding of \$66,000 for one year to continue his project monitoring, by radioactive measurement, of steroid release rates of a biodegradable implant in the animal models; pathological examination of the rats; continuing in vivo analysis of polymer hydrolysis; testing for sterilization during the manufacturing process; and development of alternative implant geometries. Dr. Zatuchni reported on the May 18, 1978 site visit to Dynatech by himself and Professor George Whitesides (MIT). The Committee raised several questions relating to Dr. Wise's proposed research regarding the release rate and whether it would be applicable to humans. It was suggested that the project be administratively extended until such time a site visit could be arranged to confer with Dr. Wise relating to the questions raised by SAC.

B. Formal Proposal Review

1. Nancy J. Alexander, Ph.D., Oregon Regional Primate Research Center

"Is Sperm Antigen a Causative Agent for Atherosclerosis After Vasectomy?"

Funding requested \$54,849. Length of project one year.

Dr. Zatuchni reported that Dr. Alexander proposes a study on the long-term safety of vasectomy through the determination of whether specific antigen-antibody complexes cause arteritis atherosclerosis and glomerulonephritis. Dr. Alexander has received NIH support for studies in these areas of investigation but there is no overlap with respect to this proposed research. Considerable discussion ensued. The Committee approved the project, but suggested that Dr. Alexander seek immunological consultation for critical review of parts of the protocol.

2. Robert T. Chatterton, Ph.D., University of Illinois at the Med. Ctr.

"Fertility Regulation by Control of Progesterone Clearance"

Funding requested \$86,436. Length of project two years.

In collaboration with: Allan P. Gray, Ph.D., IIT Research Institute

"Microencapsulation of Progesterone Antibodies"

Funding requested \$48,710. Length of project two years.

Dr. Chatterton's proposal is an outgrowth of the previously supported pilot study (PARFR-P10) which demonstrated that unprotected anti-progesterone antibodies injected intraperitoneally can significantly decrease the circulating levels of free progesterone in pseudopregnant rats and that such antibodies have good binding capacity and high stability. Dr. Chatterton now proposes to continue this work including encapsulation of the antibody that would provide oral administration, which is the companion proposal from Dr. Gray at IIT. There was discussion relating to human applicability of anti-progesterone antibody for early pregnancy termination. The Committee approved both proposals.

B. Formal Proposal Review (continued)

3. Brian M. Cohen, M.B.Ch.B., M.D., University of Tennessee Center
for Health Sciences

"An Evaluation of Cryosurgery As a Safe and Potentially Reversible
Means of Occluding the Oviduct for Purposes of Sterilization"

Funding requested \$102,634. Length of project two years.

Dr. Cohen proposes to study the efficacy and safety of using a cryosurgical apparatus via laparoscopy for tubal occlusion. This proposal was not approved due to the Committee being unable to see the benefits of such a proposed method of sterilization over currently accepted methods and that the costs of utilizing such a method in less developed countries would be prohibitive.

4. Matthew Freund, Ph.D., Southern Illinois University

"Development and Testing of a New Intravaginal Contraceptive
Method and Device"

Funding requested \$185,557. Length of project three years.

Dr. Freund proposes to develop an appropriate intravaginal contraceptive device (IVCD) and perform efficacy and safety studies in the rabbit. Dr. Freund had submitted a similar project to SAC at the March, 1977 meeting. A project development site visit was done on July 11, 1978 by Drs. Messer and Sobrero. The Committee criticized the lack of specifics in the plan of work. They approved the concept of the project, but insisted on seeing these specifics. A small study was suggested in order to stimulate Dr. Freund in establishing the feasibility of the concept.

5. Harry W. Rudel, M.D., Centro de Investigacion Sobre Fertilidad
y Esterilidad (C.I.F.E.)

"A Study of a Parenterally Administered Progesterone-Cholesterol
Formulation for Use as a Post-Partum Injectable Contraceptive"

Funding requested \$56,236. Length of project one year.

Dr. Rudel and the CIFE group propose a four-part clinical pharmacology study to develop a post-partum injectable contraceptive. Progesterone-cholesterol pellets will be prepared to deliver 2 and 4 mg of progesterone per day in a zero order release. Phase I is to be accomplished in male volunteers to determine bioavailability and tolerance of the material. Phase II will determine the anti-fertility effect of two dose levels of progesterone in women using LH and endometrial histology as indices. Plasma progesterone will also be monitored. Phase III will determine the amount of progesterone secreted in human milk using the estimated antifertility

B. Formal Proposal Review (continued)

5. Harry W. Rudel, M.D. (continued)

dose. Phase IV will evaluate a thirty day progesterone dosage form in nonlactating women for tolerance and effectiveness.

CIFE will be responsible for all phases of the study, from the manufacture of the material through the clinical studies and to the presentation of the results to the National Family Planning Board. The investigators feel that a thirty day formulation would be extremely useful and competitive with other less safe thirty day injectables now used in Mexico and other countries.

Dr. Chatterton suggested that controls receiving only cholesterol pellets must be included since daily blood sampling itself inhibits ovulation and LH surge in a significant number of subjects, up to 30-40% in his experience. Dr. Connell feels that the study should be supported in view of the problems Depo-Provera is having with FDA. The Committee voted unanimously to approve the project.

6. Philip Stubblefield, M.D., Preterm Institute

"Development and Testing of a Cervical Dilatation System"

Funding requested \$60,000. Length of project one year.

This proposal seeks support for the continuing development of a unique cervical dilatation system that would provide for controlled, safe, and uniform cervical dilatation aimed especially for use during pregnancy termination.

Preterm Institute has invested four years and much effort in attempting to develop possible approaches to a better system. The results of these investigations is a mechanical method which involves a spring driving a piston to force interleaved sheaves apart. The mechanism is activated by body temperature and/or heat. A prototype model has been manufactured and is ready for larger scale testing. Dr. Stubblefield has reported results in over 100 cases at the recent NWU Postgraduate Conference on Pregnancy Termination in May, 1978. These results indicate that non-traumatic, gentle, uniform dilatation up to 12 mm occurs in six minutes or less. Apparently the dilatation is done so gently that paracervical block may not be required.

The investigators propose to manufacture nine additional cervical dilatation devices and accessories (handle and sheath); clinically test the device in five separate abortion facilities (1000 patients); refine the present dilator based on these field results; and work towards the creation of a production model that would cost about one dollar for each application.

B. Formal Proposal Review (continued)

6. Philip Stubblefield, M.D. (continued)

Considerable discussion ensued and in the final analysis the Committee felt that the project should be approved; however, various questions were raised regarding the budget. The plan of work should be redone with PARFR Staff assistance reducing the number of devices made and the number of patients studied.

7. John Josimovich, M.D., Planned Parenthood Center, Newark, N.J.

"Phase II Study of the Female Contraceptive Barrier
Intra-Vaginal Device (IVD)"

Funding requested \$63,804.

Length of project one year.

Dr. Zatuchni reported that International Vortex Development, Ltd., is a subsidiary of Source, Inc., apparently organized for the sole purpose of development and distribution of a new intra-vaginal contraceptive. The company has spent the past several years developing polymerized forms of spermicides, and have succeeded in doing so with nonoxynol-9. The polymerized material is in the form of a small cylinder which is hydrophilic. The cylinder is inserted into the vagina by hand or by a simple applicator prior to intercourse. Theoretically, the sponge can be left in place for two to three days even with repeated intercourse. The mechanism of contraceptive action is both barrier and spermicide. Vortex, Inc. discussed the IVD with FDA; they have been advised that this contraceptive device falls in the category of a non-drug contraceptive. Vortex, Inc. seeks to determine, in a scientific manner, the actual use-effectiveness among 200 women for a period of one year. To do so they have enlisted the support of Planned Parenthood and its clinical center in Newark, New Jersey.

The Committee reacted to the poorly written proposal. Many suggestions were made, the primary one being a Phase I post-coital test for efficacy first, possibly in conjunction with Dr. Masters in St. Louis. Further discussion with FDA regarding categorization of the device is imperative. A legal review regarding public sector rights also was highly recommended. The protocol for the Phase II human study for efficacy needs much work.

C. PARFR-Initiated Proposal Review

1. C. Patrick Tharp, Ph.D., KV Pharmaceutical Company

"Development of a Long-Acting Spermicidal, Vaginal Creme"

Funding requested \$59,629. Length of project one year.

At the July 10, 1978 SAC meeting the members requested PARFR Staff to continue negotiations with KV Pharmaceutical Company aiming at their development of a long-acting spermicidal vaginal creme. After several meetings, this formal proposal is submitted to SAC.

KV is optimistic that they can further refine their secret process so that it will include FDA approved spermicidal ingredients manufactured in such a way that a long acting effect will be obtained. The PI feels confident that a minimum 24-hour effect is obtainable, but he is aiming for 72 hours. The physical properties of the creme are such that it will avoid the usual messiness of presently available products.

All the development work will be done at KV Pharmaceutical, although the in vitro spermicidal activity testing will be done on a sub-contract basis. By the end of 12 months, if not before, PARFR will be asked to support animal and human testing of the prototypes. PARFR has made some inquiries and it appears that several animal facilities would be interested in such a testing program. Additionally, initial contacts have been made with Dr. Masters (St. Louis) and other clinical investigators for possible participation in a Phase I human trial.

The Committee noted the lack of supportive scientific data in the proposal. However, the Committee approved the project with the recommendation that PARFR Staff put KV in touch with a biologist as a consultant, obtain company confidential data on the creme and review patent implications for upholding public sector rights.

D. Informal Proposal Review

1. Gary S. Berger, M.D., University of North Carolina at Chapel Hill

"A Prospective Study on the Effect of Tubal Sterilization on Menstruation and Gynecological Disorders"

Funding requested \$30,800. Length of project one year.

This proposal seeks funding support to further explore the most unique set of data on the menstrual cycle and gynecologic history of 3500 women going back about forty years. Dr. Berger has become the custodian of these data, much of it on magnetic tape through 1970. Additional data from 1971 to 1975 have been readied for inclusion on the master tape. Still more data from 1976 to 1977 have been coded, but await further data processing.

D. Informal Proposal Review (continued)

1. Gary S. Berger, M.D. (continued)

The investigator intends selecting a sample of 100 sterilized women and 100 controls. The records for each of the sterilized women will be examined for a period of three years preceeding the sterilization and three years post-op. Thus, each sterilized woman will serve as her own control with regard to menstrual cycle determinants, as well as the incidence of gynecologic disorders. Another control group of 100 nonsterilized women with similar demographic and prior contraceptive history will be compared with regard to the same parameters.

Other important questions regarding long-term use of other fertility regulation measures could be examined; e.g. restoration of fertility after prolonged intrauterine contraception, incidence of post-pill amenorrhea; occurrence of breast, uterine or hepatic tumor formation among women on long-term steroid contraception, etc. Naturally, prior to the searching of the data for these posed questions, an analysis would be necessary regarding contraceptive usage among the women in this data bank.

SAC members voted to request a formal proposal.

2. Marion M. Bradford, Ph.D., University of Georgia

"Evaluation of Acrosin-Acrolysin Inhibitors as Male Contraceptive Agents"

Funding requested \$51,315. Length of project one year.

The investigator proposes a new approach to male contraception - interference with the acrosin and acrolysin system by the administration of peptide inhibitors of these proteinases. In his laboratory, several enzyme inhibitors have been synthesized and been demonstrated to inhibit both proteinases.

The investigator proposes to use rabbits, administering the test compounds intravenously. The rabbits will be observed for sperm motility, enzyme composition of the sperm and, finally, actual mating of the experimental males using cleaved ova as the criterion for male donor fertility.

The Committee voted to request a pilot study to test feasibility.

D. Informal Proposal Review (continued)

3. Dr. H. W. J. Hellema, Laboratory of Fertility Research, Wilhelmina Gasthuis, Academic Hospital University, The Netherlands

"The Humoral Sperm Antibody Response After Vasectomy With and Without Obstruction, and Its Relevance to Fertility After Vasovasostomy"

Funding requested \$137,000. Length of project three years.

The investigators seek support to study the reversibility of a vasectomy in which the epididymal ends are not obstructed, rather implanted in the tunica or subcutaneously. The investigator's rationale for these experiments is the documented occurrence of sperm antibodies following occlusive vasectomy, which may be a factor in the inability to restore fertility among vasectomized males even after successful surgical anastomosis.

The SAC voted to request a formal proposal and suggested that PARFR Staff assist Dr. Hellema with the preparation of the proposal.

4. The SAC voted not to request a formal proposal from the following two investigators:

- a. Gary L. Curtis, Ph.D., University of Nebraska Medical Center

"Prevention of Sperm Antibody Following Vasectomy"

Funding requested \$91,227. Length of project three years.

- b. George R. Howe, Ph.D., University of Massachusetts

"The Use of Alkylating Agents as a Means of Reversible Sterilization in the Male"

Funding requested \$17,150. Length of project one year.

E. Technical Reports

The following technical reports were included in the Agenda for information purposes:

1. PARFR-83N -- Lee R. Beck, Ph.D., University of Alabama Medical Center

"Studies to Test an Injectable Delivery System for the Sustained Release of Norethisterone"

2. PARFR-84N -- Jack Lippes, M.D., Deaconess Hospital, New York

"Evaluation of the Copper T IUD as a Post-Coital Method for Contraception"

III. OLD BUSINESS: Follow-up Report

- A. All subcontracts and amendments generated via December 7, 1977 and March 29, 1978 SAC Meeting determinations are fully executed.
- B. Administrative Update from July 10, 1978 SAC Meeting:
1. Extension Proposals:
- a. PARFR-80N -- David W. Keller, M.D., Washington University
School of Medicine
- "Fertility Control Through Local Cervical Injection of
Microencapsulated Progestins"
- Amendment fully executed to extend to 7/11/78 to cover
animal charges. The principal investigator was notified
that final technical and financial reports are due by
8/31/78.
- b. PARFR-92N --Deborah J. Anderson, Ph.D., Oregon Regional
Primate Research Center
- "Contraception by Induction of Mild Uterine Inflammation"
- Amendment to 6/30/79 fully executed.
- c. PARFR-95N -- L.J.D. Zaneveld, D.V.M., Ph.D., University of
Illinois at the Medical Center
- "Development and Evaluation of a Reversible Vas Deferens
Blocking Device"
- Amendment to 6/30/79 in final stages of execution.
- d. PARFR-P8 -- Charles Salivar, The Emko Company
- "Water Soluble Condom Feasibility Study"
- Awaiting work plan changes from principal investigator before
amendment can be written.
- e. PARFR-P9 -- Danny H. Lewis, Ph.D., Southern Research Institute
- "A Fibrous Polymer for the Delivery of Contraceptive Steroids
to the Female Reproductive Tract"
- Awaiting work plan changes from principal investigator before
amendment can be written.

2. Formal Proposals:

- a. PARFR-100N -- Leonard J. Lerner, Ph.D., Thomas Jefferson University, Philadelphia, Pa.

"Investigation of New Compounds to Terminate Pregnancy"

\$66,286 9/1/78 - 8/31/79

Subcontract is fully executed.

- b. Ernest W. Page, M.D., University of California School of Medicine

"Investigations of a New Vaginal Barrier Contraceptive"

Dr. Zatuschni is working with Dr. Page to develop a pilot study.
Subcontract will be written after proposal is revised.

3. Informal Proposals:

- a. John D. Biggers, D.Sc., Ph.D., Harvard Medical School

"Medicated Intrauterine Devices Releasing Prostaglandin Antagonists"

Will be formulating a proposal upon recommendation by the Committee.
Not received to date.

4. PARFR-Initiated Project:

- a. PARFR-101N -- Joseph W. Goldzieher, M.D., Southwest Foundation for Research and Education, San Antonio, Texas

"Metabolism and Pharmacokinetics of Ethynyl Estrogens"

\$23,994 9/1/78 - 2/28/79

Subcontract is fully executed.

C. Other Administrative Matters

1. PARFR-88N -- Louise B. Tyrer, M.D., Planned Parenthood/World Populatio'

"Study to Determine the Safety-Efficacy of Copper Releasing IUDs as a Method of Post-Coital Contraception"

Administratively extended two months to 8/31/78 to allow time for completion of analysis of data and submitting a final report.

2. PARFR-96N -- Ramaa P. Rao, M.D., Michael Reese Hospital and Medical Center, Chicago, Illinois

"Long Term Study on the Effectiveness of an Injectable Polymer System in Producing Tubal Occlusion in Rabbits"

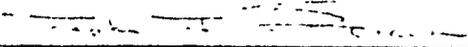
The work under this subcontract has not begun since Abcor is unable to secure a part of polymer from G.E. and Abcor is attempting to locate a different manufacturer for a suitable component. A no-cost time extension will be amended to 6/30/79.

V MISCELLANEOUS

- A. Dr. Zatuchni reported on the April 25-27 1979 PARFR Workshop on Intravaginal Contraception to be held in Guatemala City, Guatemala. A tentative program was distributed for comments from the Committee members.
- B. Dr. Connell reported on the AVS meeting to be held in May, 1979 in Seoul, Korea.

There being no further business, the meeting adjourned at 3:15 P.M.

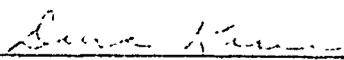
Respectfully submitted,



John J. Sciarra, M.D., Ph.D.
PARFR Program Director, Chairman SAC



Gerald I. Zatuchni, M.D., M.Sc.
Director of Technical Assistance



Diane H. Krier
Director of Administration

PARFR SCIENTIFIC ADVISORY COMMITTEE

MEETING XXVII

Chicago, Illinois
December 11, 1978

VOTING SAC MEMBERS PRESENT

John J. Sciarra, M.D., Ph.D.
Nancy J. Alexander, Ph.D.
Robert T. Chatterton, Ph.D.
Joseph E. Davis, M.D.
William Droegemueller, M.D.
Edward C. Mather, D.V.M., Ph.D.
Robert H. Messer, M.D.
Kamran S. Moghissi, M.D.
Ralph M. Richart, M.D.
Susan C. M. Scrimshaw, Ph.D.
Judith L. Vaitukaitis, M.D.
A. Albert Yuzpe, M.D.

PARFR STAFF PRESENT

Elizabeth B. Connell, M.D.
Georgia L. Fackler
Diane H. Krier
Aquiles J. Sobrero, M.D.
Gerald I. Zatuchni, M.D., M.Sc.

U.S.A.I.D. MEMBER PRESENT

Miriam H. Labbok, M.D., M.P.H.

The twenty-seventh meeting of the PARFR Scientific Advisory Committee convened on Monday, December 11, 1978 at 9:00 a.m. at the O'Hare Hilton, Chicago, Illinois. Dr. John J. Sciarra presided as Chairman. Minutes of the September 6, 1978 meeting were approved with no voiced corrections.

I. ANNOUNCEMENTS

- A. The following are SAC meeting dates for 1979:

Sunday, March 18, 1979 -- Fairmont, New Orleans, Louisiana
Monday, June 4, 1979 -- Chicago, Illinois
Wednesday, September 5, 1979 -- Washington, D. C.
Monday, December 10, 1979 -- Chicago, Illinois

- B. PARFR will have an exhibit at the American Fertility Society meeting, February 4-7, 1979 at the Hilton in San Francisco.

II. New Business

A. EXTENSION PROPOSAL REVIEW

1. PARFR 89N - Harry P. Gregor, Ph.D., Columbia University

"Fallopian Tube Cauterization and Closure by Silver Acetate-Alginate Formulations"

Funding Requested: \$29,715 Columbia + \$27,132 St. Luke's (animal work)
Period: 1/15/79 - 7/14/79 (6 months)

Dr. Connell reported on her and Dr. Chatterton's 10/15/78 site visit. The principal investigators, Drs. Gregor and Richart, presented the historical development of the project. They feel that the best formulation will be completed in six months with sufficient animal data to be able to proceed to early human trials. The previous problem of viscosity has been resolved. The only further work on the formulation is in the area of correcting the jelling time. Using the current formulation, the last four monkeys have developed bilateral tubal closure. Dr. Richart reported that Dr. Lindermann through Ethicon in Germany has been working with the Silver Acetate-Alginate formulation using a hysteroscopic delivery system. During the next six months, he and Dr. Gregor will apply for an IND with the FDA. The current thought is to develop the formulation so that it can be pumped similar to MCA and utilize the FEMCEPT device of Population Research, Inc. Drs. Gregor and Richart, with Columbia University's approval, are willing to assign patent rights to Population Research, Inc., with an exclusive license to the government. The SAC Committee voted to approve the extension request.

2. PARFR 90N - Joseph E. Davis, M.D., New York Medical College to 12/31/78
Planned Parenthood Federation of America (1/1/79-12/31/79)

"New Method for Obstructing the Vas Deferens by Direct Injection of Chemical Agents: A non-operative Technique of Male Sterilization"

Dr. Connell reported on her and Dr. Chatterton's 10/16/78 site visit. This extension request included a change in institutional support from New York Medical College to Planned Parenthood Federation of America. 27 patients have undergone this vasal occlusion procedure with a 50% success rate. Dr. Frisch at MIT developed a new vasal clamp. Hopefully, the new technology will produce a higher rate of success. The protocol changes the procedure from the hospital to Dr. Davis's office. PPFA will aid Dr. Davis in recruiting 50 volunteers. The 27 patients done during the 1st year will be followed. Some of the failures and successes will be subjected to standard vasectomy and Dr. Richart will perform a histological examination of the specimen. There was considerable discussion on the budget (\$70,611). The SAC committee voted to approve the extension request and the PARFR staff will negotiate the budget.

3. PARFR 91N - Donald L. Wise, Ph.D., Dynatech R/D Company

"Preparation and Evaluation of Biodegradable Cylindrical Implants for Fertility Control"

Funding Requested: \$66,313 Period: 2/1/79 - 1/31/80

Dr. Chatterton reported on his, Drs. Connell and Zatuchni's 10/17/78 site visit. It was recommended by the site visitors that the geometry be changed to reduce the size of the implant to release about 10 micrograms per day for 1-2 years. It was also suggested that Dr. Wise obtain biological consultation for the next year and that they be given a time framework to have something ready at the end of the year for phase I clinical trials. Dr. Zatuchni stated that the major developmental pro-

blem has been the successful manufacture of an implantable biodegradable system having a clinically unacceptable geometry. The SAC Committee approved the extension request and Dr. Vaitukaitis was asked to consult with Dr. Wise and assist in the monitoring of the project. Ms. Krier will negotiate the funding level to incorporate the period of 10/1/78 - 1/31/79, which is the wind-down time for the old protocol.

4. PARFR 85N - Milos Chvapil, M.D., Ph.D., University of Arizona
"Collagen Sponge Contraceptive - Testing of Efficacy in Human Volunteers"
Funding: Carry-over of \$62,543.93 Period: 1/1/79-6/30/79

Dr. Chvapil's technical report was included in this section in order to have continuity to the companion proposal by Dr. Heine. Dr. Zatushni reported on his and Ms. Krier's 10/23/78 site visit. The post-coital test revealed 85% negative for sperm; 5%, 1-3 sperm per high powered field (HPF); and 10%, 4-9 sperm/HPF. Considerable discussion ensued relating to the appropriateness of human trials with the collagen sponge alone vs sponge with Nonoxynol-9. Dr. Droegemueller, the clinician on the project, feels that without the spermicide there would be a high pregnancy rate. Dr. Moghissi felt that he has not yet seen a mechanical barrier that totally inhibits sperm transport. He suggested that something else (e.g. citric acid, acetic acid) be used as a spermicidal agent. Dr. Scrimshaw suggested the use of vinegar. Dr. Moghissi stated that WHO standards relating to how post-coital tests should be performed and interpreted will be published in 6 months.

B. FORMAL PROPOSAL REVIEW

1. M.W. Heine, M.D. - Texas Tech University
"Collagen Sponge Contraceptive - Testing in Human Volunteers"
Funding Requested: \$54,836 Period: One year

The discussion for this request was raised under consideration of Dr. Chvapil's technical report and his extension request at no-cost for six months for testing the collagen sponge with a spermicide.

The SAC Committee voted to approve Dr. Heine's formal proposal of testing the collagen sponge alone provided that the volunteer patients be provided an adequate informed consent; the budget be negotiated lower; and that the study be stopped if an unacceptable level of pregnancy is reached.

In regard to informed consent, no PARFR-supported project dealing with human trials can be funded without approval of adequate informed consent by the human investigation committee of the proposing institution, as well as approval by Northwestern University's Institutional Review Board according to DHEW requirements on the Protection of Human Subjects.

Ms. Krier had distributed an additional DHEW regulation which will be effective January 2, 1979. The regulation addresses the addition of compensation for complications arising from research procedures. The summary states: "The Department of Health, Education, and Welfare hereby amends the definition of informed consent in its regulations on protection of human subjects by requiring that prospective subjects be advised as to the availability or non-availability of medical treatment or compensation for physical injuries incurred as the result of participating in biomedical or behavioral research."

2. Gary S. Berger, M.D., University of North Carolina at Chapel Hill

"Effects of Tubal Sterilization on Menstruation: A Prospective Controlled Study"

Funding Requested: \$47,676 Period: One year

Dr. Berger proposes to look at the relationship of tubal sterilization to menstrual abnormalities. Dr. Berger has access to the data collected over 40 years by Dr. Treloar. He proposes that if a relationship exists in the group of 180 women that he'd be able to look at other facets to the question.

There was considerable discussion relating to PARFR's involvement in an epidemiological investigation. The SAC Committee did approve the proposal for funding in that the data base would be lost if it wasn't given support. PARFR's goal does include the safety factor of fertility regulation.

3. Ewa Radwanska, M.D., University of North Carolina at Chapel Hill

"Ovarian Function after Tubal Sterilization"

Funding Requested: \$48,141 Period: One year

Dr. Zatuchni presented the investigator's hypothesis that tubal sterilization somehow compromises ovarian vascular supply leading to luteal function changes which may be responsible for the menstrual irregularities found among some sterilized women. The SAC Committee also discussed this proposal in terms of PARFR's objectives and voted to approve for funding by a narrow margin. Dr. Labbok felt this proposal to be inappropriate to PARFR's objectives. Subsequently, Dr. Labbok informed Ms. Krier that she and Dr. Speidel will submit the proposal to Dr. Ravenholt for a determination.

4. Frederick P. Zuspan, M.D., The Ohio State University Research Foundation

"Effect of Contraceptive Steroids on the Adrenergic-Vascular System"

Funding Requested: \$275,530 Period: Three years

Dr. Zuspan's protocol proposes to determine whether oral contraceptive steroids cause vascular changes. The discussion centered around the fact that the proposed basic research would really make no difference to PARFR's "applied" goals. The SAC voted not to approve the proposal for funding in that this "safety" study really is outside the realm of PARFR's objectives.

5. Carlton A. Eddy, Ph.D., University of Texas Health Science Center at San Antonio

"Postcoital Intravaginal Prostaglandin Administration As A Contraceptive Method"

Funding Requested: \$103,212 Period: Two years

Dr. Eddy's proposal seeks to develop a new post-coital method of contraception utilizing prostaglandins. Pursuing this type of research is not within PARFR's goals because currently prostaglandins are too expensive and have a short shelf life and wouldn't be useful in the developing world. Additionally, several published studies on humans indicate several problems with using PG suppositories either post-coitally or as early abortifacients. The proposal was not approved for PARFR support.

6. Louise B. Tyrer, M.D., Planned Parenthood Federation of America

"Study to Determine the Safety, Acceptability and Effectiveness of the Female Contraceptive Barrier Intra-Vaginal-Device (IVD)"

Funding: \$62,600 Period: One Year

Dr. Connell presented a summary of the proposed protocol for testing the IVD. The SAC committee voted to approve the project for PARFR funding.

7. Ricardo H. Asch, M.D., University of Texas Health Science Center at San Antonio

"The Effects of Different Cannabis Derivatives as Inhibitors of Ovulation in the Rhesus Monkey"

Dr. Asch proposes to look at the effects of marijuana on human reproduction. Dr. Vaitukaitis pointed out that there exists conflicting data in the literature which reflects a poor selection of controls. Dr. Moghissi stated that to his knowledge, the only effect has been demonstrated in monkeys; i.e. ovulation is inhibited; however, this has caused other problems. The proposal was not approved for PARFR support.

C. PILOT STUDY REVIEW

1. John C. Slocumb, M.D., University of New Mexico

"Identification and Evaluation of Herbs used by Native Healers to Affect Fertility"

Funding Requested: \$7,700 Period: 8 months

Dr. Messer presented a summary of Dr. Slocumb's involvement with the Navaho Indians and the native Spanish Curanderos. This pilot study was approved for PARFR support.

D. INFORMAL PROPOSALS

1. James P. Koch, M.D., Boston Hospital for Women

"Exploring the Potential of the Cervical Cap"

2. Margaret Ward Orsini, Ph.D., University of Wisconsin - Madison

"The IUD in the Golden Hamster"

SAC voted not to request a formal proposal for either these projects.

E. TECHNICAL REPORTS

1. PARFR 80N - David W. Keller, M.D., Washington University

(Final) "Fertility Control through Local Cervical Injection of Microencapsulated Progestin"

2. PARFR 82N - Fouad Hefnawi, M.B., M.S., Al-Azhar University, Cairo, Egypt

"Measurement of Blood Loss in Women Fitted with Copper Clad and Standard Lippes Loops"

3. PARFR 86N - Robert S. Neuwirth, M.D., St. Luke's Institute for Health Sciences
"Phase I Clinical Trial of Fallopian Tube Closure using Methylcyanoacrylate (MCA) Tissue Adhesive Delivered Through the Single-Application Fertility Regulation (FEMCEPT) Device"

Dr. R. Richart reported on his, Dr. Neuwirth and Ms. Krier's Salvador Project Development site visit, 10/1-4/78. Four clinical sites may be instituted for human trials in Salvador by April, 1979.
4. PARFR 88N - Louise B. Tyrer, M.D., Planned Parenthood Federation of America (Final) "Study to Determine the Safety and Efficacy of Copper-Releasing IUDs as a Method of Post-Coital Contraception"
5. PARFR 92N - Deborah J. Anderson, Ph.D., Oregon Regional Primate Research Center
"Contraception by Induction of Mild Uterine Inflammation"

Dr. Alexander reported that Dr. Anderson has shown lack of impregnation in the rat model and can't speculate further until the monkey data is available in spring.
6. PARFR 95N - L.J.D. Zaneveld, D.V.M., Ph.D., University of Illinois
"Development and Evaluation of a Reversible Vas Deferens Blocking Device"

Dr. Alexander reported that in the rabbit model, short-term animals didn't develop antibodies and long-term, developed antibodies. She hasn't received monkey sera yet.
7. PARFR 97N - Theodore M. King, M.D., Ph.D., The Johns Hopkins University
PARFR 97K - Young Ki Moon, M.D., Yonsei University - Seoul, Korea
"Research on Instillation Techniques for Pregnancy Termination in Korea"
8. PARFR 99N - Duane L. Garner, Ph.D., Oklahoma State University
"Immunoabsorbent Isolation of Specific Spermatozoal Antigens for use as Anti-Fertility Immunogens"

Dr. Zasluchni reported on 11/21/78 site visit by himself and Dr. Ken Tung. Dr. Garner's contract will be extended without cost to 3/31/79 and he'll submit an extension request for review at the March SAC meeting.
9. PARFR P-12 - David H. Frisch, Ph.D., Massachusetts Institute of Technology
"Development of Microporous Materials for Thin Intravascular Implants"
10. PARFR P-14 - Stanwood S. Schmidt, M.D.
"The Bipolar Needle for Percutaneous Vas Obstruction"

III. OLD BUSINESS: Follow-up Report

- A. Pending from 7/10/78 SAC Meeting:
 1. Amendments [PARFR 80N, 92N, 95N, P-9 written as a new subcontract 104N(P-9)] from the 7/10/78 meeting have been fully executed.
 2. PARFR P-8 - Charles Salivar, The Emko Company, "Water Soluble Condom Feasibility Study"
Awaiting Resolution on Patents Issue before a subcontract can be negotiated

3. PARFR 100N - Leonard J. Lerner, Ph.D., Thomas Jefferson University, Philadelphia, PA, "Investigation of New Compounds to Terminate Pregnancy" Funding: \$66,286 - Period: 9/1/78-8/31/79. Subcontract is fully executed.
 4. PARFR P-16 - Ernest W. Page, M.D., University of California School of Medicine, "Investigations of a New Vaginal Barrier Contraceptive"
Proposal resubmitted per SAC recommendations as a Pilot Study. Requested funding of \$6,000. Period 1/1/79 - 12/31/79. Subcontract is fully executed.
 5. PARFR 101N - Joseph W. Goldzieher, M.D., Southwest Foundation for Research and Education, San Antonio, Texas, "Metabolism and Pharmacokinetics of Ethynyl Estrogens" - Funding: \$23,994 - Period: 9/1/78 - 2/28/79. Subcontract is fully executed.
- B. Administrative update from September 6, 1978 SAC Meeting:
1. PARFR 79N - C. Irving Meeker, M.D. - Maine Medical Center
"A Method for Reversible Sterilization in the Female"
Amendment to 9/30/79 is fully executed.
 2. PARFR 91N - Donald L. Wise, Ph.D. - Dynatech R/D Company
"Preparation and Evaluation of Biodegradable Cylindrical Implants for Fertility Control"
Resubmitted in this agenda for one year, request starting 2/1/79.
Current phase will be negotiated by Ms. Krier and Extension Proposal budget will be combined with this phase and all will be written as an Amendment to the current subcontract.
 3. Nancy J. Alexander, Ph.D. - Oregon Regional Primate Research Center
"Is Sperm Antigen A Causative Agent for Atherosclerosis after Vasectomy."
Subcontract will be written with a start date in Spring, '79.
 4. PARFR 102N(P-10) - Robert T. Chatterton, Ph.D. - University of Illinois at the Medical Center
"Fertility Regulation by Control of Progesterone Clearance"
Funding: \$46,767 - Period: 11/1/78 - 10/31/79. Subcontract is fully executed.
 5. PARFR 103N - Allan P. Gray, Ph.D. - IIT Research Institute
"Microencapsulation of Progesterone Antibodies"
Funding: \$28,108 - Period: 11/1/78 - 10/31/79. Subcontract is fully executed.
 6. PARFR P-17 - Matthew Freund, Ph.D. - Southern Illinois University
"Development and Testing of a New Intravaginal Contraceptive Method and Device"
Proposal rewritten as a pilot study, funding requested \$7,500; Period: 2/1/79 - 7/31/79. Subcontract submitted for AID approval.

7. Harry W. Rudel, M.D. - Centro de Investigacion Sobre Fertilidad y Esterilidad, Mexico City
"A Study of a Parenterally Administered Progesterone-Cholesterol Formulation for use as a Post-Partum Injectable Contraceptive"
Awaiting Northwestern University Institutional Review Board approval before subcontract can be written.
8. Philip Stubblefield, M.D. - Preterm Institute
"Development and Testing of a Cervical Dilatation System"
Awaiting revision of protocol.
9. John Josimovich, M.D. - Planned Parenthood Center, Newark, New Jersey
"Phase II Study of the Female Contraceptive Barrier Intra-Vaginal-Device (IVD)"
This proposal was rewritten and submitted in this agenda with Dr. Louise Tyrer (PPFA) being listed as the principal investigator.
10. PARFR P-15 - Sidney Shulman, Ph.D. New York Medical College
"Isolation of Effective Sperm Antigens for Use in Contraceptive Immunization"
Funding: \$7,500 - Period: 1/1/79 - 12/31/79. Subcontract is fully executed.

IV. MISCELLANEOUS

- A. Update on PARFR Workshop on Intravaginal Contraception: Barriers, Spermicides and Condoms, April 26 and 27, 1979, Guatemala.

Dr. Zatuchni reported that the program is nearly finalized and that we received approval for a UNFPA grant to support the attendance of 25 participants to the Workshop from developing countries.

- B. International Conference on Voluntary Sterilization, sponsored by AVS, May 7-10, 1979, Seoul, Korea.

Dr. Connell reported that the program will be finalized by the end of December and that some of PARFR's staff, consultants and investigators are on the program.

The meeting adjourned at 3:00 P.M.

Respectfully submitted:

John J. Sciarra, M.D., Ph.D.
Program Director, PARFR

Diane H. Krier
Diane H. Krier
Director of Administration, PARFR

INTERNATIONAL WORKSHOP ON NEW DEVELOPMENTS IN VAGINAL CONTRACEPTION

April 25-27, 1979
Guatemala City, Guatemala

Wednesday, April 25

REGISTRATION: 1200 - 1700 hrs.

1300 - 1700 hrs.

Manuscript and Slide Review
Editors and Authors

1900 hrs.

Reception

Thursday, April 26

0800 - 0830 hrs.

Opening Remarks

Gerald I. Zatzuchni, M.D., M.Sc.
Program for Applied Research on Fertility Regulation
Northwestern University
Chicago, Illinois, U.S.A.

Welcome

Roberto Santiso Galvez, M.D.
Executive Director, Asociacion Pro-Bienestar
de la Familia de Guatemala (APROFAM)
Guatemala City, Guatemala
Lic. Mario Coll Solares
Chairman of the Board of Directors, APROFAM
Guatemala City, Guatemala

J. Joseph Speidel, M.D., M.P.H.
Deputy Director, Office of Population
United States Agency for International Development
Washington, D.C., U.S.A.

SESSION I. THE VAGINA

Moderator: William Droegemueller, M.D.
University of Arizona
Tucson, Arizona, U.S.A.

0830 - 0850 hrs.

Non-Steroidal Vaginal Contraception: Historical Perspective

John J. Sciarra, M.D., Ph.D.
Program for Applied Research on Fertility Regulation
Northwestern University
Chicago, Illinois, U.S.A.

0850 - 0915 hrs.

The Contraceptive Aspects of the Anatomy, Morphology
and Physiology of the Vagina

Charles E. Flowers, Jr., M.D.
University of Alabama
Birmingham, Alabama, U.S.A.

0915 - 0940 hrs.

Sperm Migration in the Female Genital Tract

Kamran S. Moghissi, M.D.
Wayne State University School of Medicine
Detroit, Michigan, U.S.A.

Thursday, April 26 (continued)

SESSION I. THE VAGINA (continued)

0940 - 1000 hrs. Discussion

1000 - 1015 hrs. Coffee

SESSION II. CURRENT STATUS OF VAGINAL CONTRACEPTION

Moderator: J. Joseph Speidel, M.D., M.P.H.
United States Agency for International Development
Washington, D.C., U.S.A.

1015 - 1035 hrs. Spermicidal Agents: Effectiveness, Use, and Testing
Aguiles J. Sobrero, M.D.
Program for Applied Research on Fertility Regulation
Northwestern University
Chicago, Illinois, U.S.A.

1035 - 1055 hrs. Condoms: Manufacturing Perspectives and Use
John Quinn
Akwel Industries, Inc.
New York, New York, U.S.A.

1055 - 1115 hrs. Overview of U.S. Experience with Vaginal Contraceptives
William F. Pratt, Ph.D.
National Center for Health Statistics
Hyattsville, Maryland, U.S.A.

1115 - 1200 hrs. Discussion

1200 - 1330 hrs. Lunch

Thursday, April 26 (continued)

SESSION III. VAGINAL CONTRACEPTION RESEARCH AND DEVELOPMENT

Moderator: Nancy J. Alexander, Ph.D.
Oregon Regional Primate Research Center
Beaverton, Oregon, U.S.A.

1330 - 1350 hrs.

Research in Vaginal Contraception: An Overview
John L. McGuire, Ph.D.
Ortho Pharmaceutical Corporation
Raritan, New Jersey, U.S.A.

1350 - 1500 hrs.

Panel: Sponge Barriers

Two Years of Testing Collagen Sponge
Milos Chvapil, M.D., Ph.D.
University of Arizona
Tucson, Arizona, U.S.A.

A Clinical Appraisal of A Medicated Polyurethane
Sponge Used for Contraception
Ramon Aznar, M.D.
Centro de Investigacion sobre Fertilidad
y Esterilidad (CIFE)
Mexico City, Mexico

Preliminary Results of A Multi-Clinic Trial of
Polyurethane - Spermicide Contraceptive Sponge
Alfredo Goldsmith, M.D., M.P.H.
International Fertility Research Program
Research Triangle Park, N. Carolina, U.S.A.

Intra-vaginal Spermicidal Sponge (IVD)
Louise B. Tyrer, M.D.
Planned Parenthood Federation of America, Inc.
New York, New York, U.S.A.

Discussion

1500 - 1630 hrs.

Panel: Spermicidal Formulations

Moderator: Robert H. Messer, M.D.
University of New Mexico School of Medicine
Albuquerque, New Mexico

Experience With Barrier Methods of Contraception
in Guatemala
Luis F. Galich, M.D.
APROFAM
Guatemala City, Guatemala

Clinical Trial of a Contraceptive Foaming Tablet:
A Preliminary Report
Guillermo Lopez-Escobar, M.D.
Corporacion Centro Regional de Poblacion (CCRF)
Bogota, Colombia

Thursday, April 26 (continued)

SESSION III. VAGINAL CONTRACEPTION RESEARCH AND DEVELOPMENT (continued)

Patentex Oval: Clinical Effectiveness Studies

Levie Querido, M.D.
Stimezo Nederland
Utrecht, Holland

Effectiveness of Vaginal Foam Contraceptives:
Controversies in West Germany

Peter F. Tauber, M.D.
University of Essen
Essen, West Germany

Newer Data on the Pharmacokinetics of Norgynol-9

Milos Chvapil, M.D., Ph.D.
University of Arizona
Tucson, Arizona, U.S.A.

Vaginal Contraceptives As Prophylaxis Against Sexually
Transmissible Diseases

John C. Cutler, M.D.
University of Pittsburgh
Pittsburgh, Pennsylvania, U.S.A.

Discussion

1630 - 1645 hrs.

Coffee

1645 - 1800 hrs.

Panel: New Developments in Barrier and Spermicide Methods

Moderator: A. Albert Yuzpe, M.D.
University of Western Ontario
London Ontario, Canada

Vaginal Rings Capable of Constant Release Rate
of Spermicides

Alfredo J. Gallegos, M.D.
World Health Organization
Geneva, Switzerland

A New Disposable Vaginal Barrier as a Carrier for
a Spermicide

Harry W. Rudel, M.D.
Centro de Investigacion sobre Fertilidad
y Esterilidad
Mexico City, Mexico

Development of An Intravaginal Contraceptive Device
(IVCD) and Method

Matthew Freund, Ph.D.
Southern Illinois University
Carbondale, Illinois, U.S.A.

Spermicidal Condom and Intravaginal Spermicidal Film Insert

Raymond Belsky, B.S., EE
Women's Medical Center at Kingsbrook
Brooklyn, New York, U.S.A.

Discussion

Friday, April 27

SESSION IV. EVALUATION OF VAGINAL CONTRACEPTIVES

Moderator: John L. McGuire, Ph.D.
Ortho Pharmaceutical Corporation
Raritan, New Jersey, U.S.A.

- 0830 - 0900 hrs. Vaginal Contraception: Current FDA Status
Elizabeth B. Connell, M.D.
Program for Applied Research on Fertility Regulation
Northwestern University
Chicago, Illinois, U.S.A.
- 0900 - 0920 hrs. Preclinical Evaluation of New Vaginal Contraceptives
Do Wan Hahn, Ph.D.
Ortho Pharmaceutical Corporation
Raritan, New Jersey, U.S.A.
- 0920 - 0940 hrs. Animal Testing and New Vaginal Contraceptive Agents
Lourens J. D. Zaneveld, D.V.M., Ph.D.
University of Illinois at the Medical Center
Chicago, Illinois, U.S.A.
- 0940 - 1000 hrs. Human Testing of Intravaginal Chemical Contraceptives:
Phase I Studies
William H. Masters, M.D.
Masters & Johnson Institute
St. Louis, Missouri, U.S.A.
- 1000 - 1010 hrs. Quality Assessment of Barrier Contraceptives
Gordon W. Duncan, Ph.D.
Program for the Introduction and Adaptation of
Contraceptive Technology
Seattle, Washington, U.S.A.
- 1010 - 1045 hrs. Discussion
- 1045 - 1100 hrs. Coffee

SESSION V. CLINICAL TRIALS

Moderator: Elizabeth B. Connell, M.D.
Program for Applied Research on Fertility Regulation
Northwestern University
Chicago, Illinois, U.S.A.

- 1100 - 1120 hrs. Clinical-Effectiveness Studies of Vaginal Contraceptives
Gerald S. Bernstein, M.D., Ph.D.
Los Angeles County - U.S.C. Medical Center
Los Angeles, California, U.S.A.
- 1120 - 1135 hrs. Components of An Epidemiological System for the Surveillance
of Adverse Effects Due To Vaginal Contraceptives
Paul D. Stolley, M.D., M.P.H.
University of Pennsylvania School of Medicine
Philadelphia, Pennsylvania, U.S.A.
- 1135 - 1150 hrs. An Agenda for Vaginal Contraceptive Development
Richard J. Derman, M.D.
New York Hospital
New York, New York, U.S.A.
- 1150 - 1215 hrs. Discussion
- 1215 - 1345 hrs. Lunch

Friday, April 27

SESSION VI. INTERNATIONAL PERSPECTIVES ON VAGINAL CONTRACEPTION

1345 - 1500 hrs.

Panel: Marketing and Acceptability

Moderator: Gordon W. Perkin, M.D.
The Ford Foundation
Mexico City, Mexico

Studies on the Acceptability of Vaginal Contraceptives

Susan C. M. Scrimshaw, Ph.D.
University of California
Los Angeles, California, U.S.A.

Social Marketing of Contraceptive Products

Luis de la Macorra
PROFAM
Mexico City, Mexico

Commercial Techniques to Promote Condom Usage

Manuel Ylanan
Applied Contraceptive Technology Management
and Research Center
Makati, Philippines

Discussion

1500 - 1600 hrs.

Panel: Community-Based Distribution Programs

Moderator: Allan Rosenfield, M.D.
Columbia University
New York, New York, U.S.A.

Community-Based Distribution of Contraceptives: A
Result of the Evolution of Family Planning

Gonzalo Echeverry, M.D.
PROFAMILIA
Bogota, Colombia

Barrier Methods in Community Distribution Programs
in Guatemala

Roberto Santiso Galvez, M.D.
APROFAM
Guatemala City, Guatemala

The Condom in Rural Bangladesh

Douglas H. Huber, M.D.
Advisor, Ministry of Health and Population Control
Dacca, Bangladesh

Discussion

1600 - 1615 hrs.

Coffee

Friday, April 27

SESSION VI. INTERNATIONAL PERSPECTIVES ON VAGINAL CONTRACEPTION (continued)

1615 - 1715 hrs.

Panel: Agency Programs in Vaginal Contraception

Moderator: John J. Sciarra, M.D., Ph.D.
Program for Applied Research on Fertility Regulation
Northwestern University
Chicago, Illinois, U.S.A.

United Nations Fund for Population Activities

José Donayre, M.D.
New York, New York, U.S.A.

Research on Barrier Methods of Contraception at the
National Institute of Child Health and Human Development

Phillip A. Corfman, M.D.
Bethesda, Maryland, U.S.A.

World Health Organization

Alfredo J. Gallegos, M.D.
Geneva, Switzerland

Procurement and Use of Drugs: Managing the
Process to Advantage

Peter J. Rousselle, M.B.A.
Management Services for Health, Inc.
Boston, Massachusetts, U.S.A.

Discussion

1715 - 1730 hrs.

Concluding Remarks

Gerald I. Zatuchni, M.D., M.Sc.
Program for Applied Research on Fertility Regulation
Northwestern University
Chicago, Illinois, U.S.A.

2000 hrs.

Dinner

The Importance of Vaginal Contraception

Malcolm Potts, M.B., B.Chir., Ph.D.
International Fertility Research Program
Research Triangle Park, N. Carolina, U.S.A.

PROGRAM FOR APPLIED RESEARCH ON FERTILITY REGULATION



NORTHWESTERN UNIVERSITY

October 15, 1978

SCIENTIFIC ADVISORY COMMITTEE

John J. Sciarra, M.D., Ph.D., *Chairman*
Northwestern University
Nancy J. Alexander, Ph.D.
Oregon Regional Primate Research Center
Robert T. Chatterton, Ph.D.
University of Illinois
Joseph E. Davis, M.D.
New York Medical College
William Droegemueller, M.D.
University of Arizona
Edward C. Mather, D.V.M., Ph.D.
University of Minnesota
Robert H. Messer, M.D.
University of New Mexico
Kamran S. Moghissi, M.D.
Wayne State University
Ralph M. Richart, M.D.
Columbia University
Susan C. M. Scrimshaw, Ph.D.
University of California
Judith L. Vaitukaitis, M.D.
Boston University
A. Albert Yuzpe, M.D.
University of Western Ontario

COMMISSION FOR INTERNATIONAL DEVELOPMENT

J. Joseph Speidel, M.D., M.P.H.
Office of Population
Miriam H. Labbok, M.D., M.P.H.
Office of Population

PROGRAM STAFF

John J. Sciarra, M.D., Ph.D.
Director
Gerald I. Zatuchni, M.D., M.Sc.
Director of Technical Assistance
Elizabeth B. Connell, M.D.
Research Project Development Coordinator
Aguiles J. Sobrero, M.D.
Project Coordinator
Diane H. Krier
Director of Administration

MAILING ADDRESS

PROGRAM FOR APPLIED RESEARCH
ON FERTILITY REGULATION
1040 Passavant Pavilion
303 East Superior Street
Chicago, Illinois 60611, U.S.A.
(312) 649-2990

CABLE ADDRESS

PARFR
Chicago, Illinois

PROGRAM STAFF

Elizabeth B. Connell, M.D. recently joined the PARFR staff as Research Project Development Coordinator. Dr. Connell's primary function with PARFR will involve the initiation and monitoring of Phase I clinical trials in less developed countries.

For the past five years, Dr. Connell served as Associate Director for Health Sciences for the Rockefeller Foundation where she was involved in the funding of national and international population projects. Prior to that time, she was Associate Professor of Obstetrics and Gynecology at the Columbia University College of Physicians and Surgeons and Director of Family Life Services at Columbia's International Institute for the Study of Human Reproduction.

Dr. Connell serves on several Advisory Committees of the Food and Drug Administration and is Chairman of the Board of Advisors for the Population Resource Center. She is currently Program Chairman for the Association for Voluntary Sterilization's upcoming international meeting in Korea and is the Association's Vice President. Dr. Connell chaired the National Medical Committee of Planned Parenthood during the development of the National Standards and Guidelines and is past president of the Association of Planned Parenthood Physicians.

PARFR EXHIBIT

PARFR participates at various scientific and medical meetings with an exhibit. The exhibit features information on research projects currently sponsored by the Program and provides a convenient place for interested investigators to meet with members of the PARFR staff.

The Association of Planned Parenthood Physicians 16th Annual Meeting will be held in San Diego, California, at the Town and Country Hotel, October 25-27, 1978. PARFR staff attending the meeting are Gerald I. Zatuchni, M.D., M.Sc., Director of Technical Assistance; Elizabeth B. Connell, M.D., Research Project Development Coordinator; and Diane H. Krier, Director of Administration. PARFR will participate with an exhibit.

PARFR also plans to exhibit at the American Fertility Society's 35th Annual Meeting. This meeting will be held February 3-7, 1979 in San Francisco, California.

SCIENTIFIC WORKSHOPS AND PUBLICATIONS

PARFR organizes at least one workshop per year, bringing together leading national and international scientists and clinicians representing an array of disciplines to present their experiences and exchange ideas on topics relating to fertility regulation. Past workshops have included Hysteroscopic Sterilization; Control of Male Fertility; Advances in Female Sterilization Techniques; and Risks, Benefits, and Controversies in Fertility Control.

The proceedings of all workshops are published. Hysteroscopic Sterilization is available from Intercontinental Medical Book Corporation. Control of Male Fertility, Advances in Female Sterilization Techniques, and Risks, Benefits, and Controversies in Fertility Control are available from Harper and Row, Publishers, Inc.

Summaries of PARFR's most recent workshop activities follows.

REVERSAL OF STERILIZATION IN THE MALE AND FEMALE

San Francisco, California
December 4-6, 1977

This PARFR-sponsored workshop was attended by ninety (90) participants representing nineteen (19) countries. The objectives of this workshop were to review and criticize current sterilization procedures, present new research in reversible sterilization methods, and assess the need for development of reversal of sterilization centers.

Presentations and discussions focused on the following topics:

Vasectomy and Vasovasostomy
Female Sterilization Procedures
Microsurgery for Reversal of Female Sterilization
New Potentially Reversible Techniques for Sterilization
in Women and in Men
Program Planning

Representatives from medical equipment manufacturers were present during the workshop with exhibits of items which are useful for sterilization and sterilization procedures.

Proceedings of this workshop will be published by Harper and Row, Publishers, Inc. and should be available in December, 1978.

SYMPOSIUM ON ANIMAL MODELS FOR RESEARCH ON CONTRACEPTION AND FERTILITY

Washington, D.C.
May 8-10, 1978

The National Academy of Sciences Institute of Laboratory Animal Resources sponsored this symposium which was funded by PARFR. The purpose of the meeting was to examine environmental and physiological factors influencing the suitability of diverse species for studies of reproduction.

SYMPOSIUM ON ANIMAL MODELS (continued)

Presentations were based on the following topics:

Factors That Affect Studies of Reproduction
Comparative Aspects of Reproductive Processes
Comparison of Models for Fertility and Contraceptive Research

Techniques for animal reproduction studies and unique animal models for studies in reproduction on contraception were demonstrated during poster sessions.

The proceedings of this symposium will be published by Harper and Row, Publishers, Inc. and should be available in May, 1979.

PREGNANCY TERMINATION: PROCEDURES, SAFETY AND NEW DEVELOPMENTS

Nassau, Bahamas
May 23-26, 1978

This International Workshop and Postgraduate Course was organized by the North-western University Medical School and supported by registration fees. One hundred and seventy-four (174) participants attended, representing twenty-four (24) countries. The sessions focused upon new advances and current research in the following areas:

Theoretical and Research Considerations
Early Detection of Pregnancy
Menstrual Regulation
Informed Consent; Patient Counseling and Use of Auxiliary
Health Personnel
First Trimester Pregnancy Termination
Early Mid-Trimester Pregnancy Termination
Setting Up Pregnancy Termination Services
Late Mid-Trimester Pregnancy Termination
Special Problems in Pregnancy Termination
Impact of Legal/Illegal Abortion

Proceedings of this International Workshop and Postgraduate Course will be published by Harper and Row, Publishers, Inc. It is expected that the volume will be available in May, 1979.

FUTURE WORKSHOP PLANS

PARFR is planning a Workshop on Intravaginal Contraception to be held in Guatemala City, Guatemala, April 25-27, 1979. This international symposium will gather together a multi-disciplinary group of clinical and research investigators involved in fertility control activities. The objectives of the Workshop are to review the worldwide use of vaginal contraceptive methods and the factors influencing their use; to describe and discuss research and development of new methods of vaginal contraception; and to discuss present and new methodologies for evaluation and testing of vaginal contraceptives.

PARFR-FUNDED RESEARCH

<u>PROJECT TITLE</u>	<u>INVESTIGATOR</u>	<u>INSTITUTION</u>
Observation and Care of Animals that have Uterotubal Blocking Devices Implanted	Abdol H. Hosseinian, M.D.	University of Illinois Biological Resources Laboratory
A Method for Reversible Sterilization in the Female	C. Irving Meeker, M.D.	Maine Medical Center Portland, Maine
Clinical Evaluation of IUDs Containing Epsilon Aminocaproic Acid (EACA)	Peter F. Tauber, M.D.	University of Essen Essen, West Germany
Measurement of Blood Loss in Women Fitted with Copper Clad Lippes Loops	Fouad Hefnawi, M.B., M.S.	Al-Azhar University Cairo, Egypt
Studies to Test an Injectable Delivery System for the Sustained Release of Norethisterone	Lee R. Beck, Ph.D.	University of Alabama
Collagen Sponge Contraceptive Testing of Efficacy in Human Volunteers	Milos Chvapil, M.D., Ph.D.	University of Arizona
Phase I, Clinical Trial of Fallopian Tube Closure Using Methylcyanoacrylate (MCA) Tissue Adhesive Delivered through the Single Application Fertility Regulation (FEMCEPT) Device	Robert S. Neuwirth, M.D. Ralph M. Richart, M.D. Prof. H.K. Zinser Hans Baur, M.D. Gerd Eldering, M.D. Sung-bong Hong, M.D.	St. Luke's Institute for Health Sciences New York, New York Evangelisches Krankenhaus Cologne, West Germany Korea University Seoul, Korea
Development of A Safe and Effective Hysteroscopic Sterilization Technique by Using Uterotubal Blocking Devices	Abdol H. Hosseinian, M.D.	Reza Pahlavi Medical Center Tehran, Iran
Fallopian Tube Cauterization and Closure by Silver Acetate-Alginate Formulations	Harry P. Gregor, Ph.D.	Columbia University New York, New York
New Method for Obstructing the Vas Deferens by Direct Injection of Chemical Agents: A Non-Operative Technique of Male Sterilization	Joseph E. Davis, M.D.	New York Medical College

<u>PROJECT TITLE</u>	<u>INVESTIGATOR</u>	<u>INSTITUTION</u>
Preparation and Evaluation of Biodegradable Cylindrical Implants for Fertility Control	Donald L. Wise, Ph.D.	Dynatech R/D Company Cambridge, Massachusetts
Contraception by Induction of Mild Uterine Inflammation	Deborah J. Anderson, Ph.D.	Oregon Regional Primate Research Center
Modern Modified Aldridge Procedure	William Droegemueller, M.D.	University of Arizona
Development and Evaluation of a Reversible Vas Deferens Blocking Device	L.J.D. Zaneveld, D.V.M., Ph.D.	University of Illinois
Comparative Studies on Second Trimester Pregnancy Termination	Theodore M. King, M.D., Ph.D. Young Ki Moon, M.D.	Johns Hopkins University Baltimore, Maryland Yonsei University Seoul, Korea
Norethisterone Microcapsule Injectable Contraceptive Study	Ramon Aznar, M.D.	Centro de Investigacion Sobre Fertilidad y Esterilidad (CIFE) Mexico City, Mexico
Immunoabsorbent Isolation of Specific Spermatozoal Antigens for use as Anti-Fertility Immunogens	Duane L. Garner, Ph.D.	Oklahoma State University Stillwater, Oklahoma
Investigation of New Compounds to Terminate Pregnancy	Leonard J. Lerner, Ph.D.	Jefferson Medical College Philadelphia, Pennsylvania
Metabolism and Pharmacokinetics of Ethynyl Estrogens	Joseph W. Goldzieher, M.D.	Southwest Foundation for Research and Education San Antonio, Texas
Water Soluble Condom Feasibility Study	Charles Salivar	EMKO Company St. Louis, Missouri
A Fibrous Polymer for the Delivery of Contraceptive Steroids to the Female Reproductive Tract	Danny H. Lewis, Ph.D.	Southern Research Institute Birmingham, Alabama
Fertility Regulation by Control of Progesterone Clearance	Robert T. Chatterton, Ph.D.	University of Illinois
Evaluation of Carbohexoxymethyl 2 Cyanoacrylate as a Tubal-Blocking Agent	Ralph M. Richart, M.D.	Columbia University New York, New York
Development of Microporous Materials for Thin Intra-vascular Implants	David H. Frisch, Ph.D.	Massachusetts Institute of Technology Cambridge, Massachusetts

<u>PROJECT TITLE</u>	<u>INVESTIGATOR</u>	<u>INSTITUTION</u>
An Evaluation of the Efficacy of Candidate Fimbrial Prosthesis in Female Rabbits and The Evaluation of Fimbrial Devices as a Reversible Technique of Female Sterilization	Ivo Brosens, M.D., Ph.D.	Catholic University of Leuven Leuven, Belgium
The Bipolar Needle for Percutaneous Vas Obstruction	Standwood S. Schmidt, M.L	University of California
Is Sperm Antigen a Causative Agent for Atherosclerosis After Vasectomy?	Nancy J. Alexander, Ph.D.	Oregon Regional Primate Research Center
A Study of A Parenterally Administered Progesterone-Cholesterol Formulation For Use as a Post-Partum Injectable Contraceptive	Harry W. Rudel, M.D.	Centro de Investigacion Sobre Fertilidad y Esterilidad Mexico City, Mexico
Development and Testing of a Cervical Dilatation System	Phillip Stubblefield, M.D.	Preterm Institute Boston, Massachusetts
Microencapsulation of Progesterone Antibodies	Allan P. Gray, Ph.D.	IIT Research Institute Chicago, Illinois

REQUEST FOR INFORMAL PROPOSALS

Proposals are evaluated by the PARFR Staff and Scientific Advisory Committee. The selection involves two steps: 1) Brief informal proposals are screened and selected for conformity with PARFR's aims; 2) Selected investigators will be requested to prepare and submit formal proposals for further review. Projects selected for funding may receive maximum support of \$66,000 annually through subcontracting on a cost-reimbursable basis.

PARFR also funds short-term research projects (Pilot Studies) designed to produce preliminary results from which extended research proposals may develop. These projects may receive maximum support of \$7,500 for a period not to exceed one year, and can be submitted at any time.

Informal and formal proposals must be received at least one month prior to a Scientific Advisory Committee (SAC) Meeting to be considered at that meeting. Upcoming SAC Meeting dates and their corresponding proposal deadlines are as follows:

SAC MEETING DATES

December 11, 1978
March 18, 1979
June 4, 1979
September 5, 1979

PROPOSAL DEADLINES

November 11, 1978
February 18, 1979
May 4, 1979
August 5, 1979

GUIDELINES FOR PREPARATION OF INFORMAL PROPOSALS

Information should be limited to four or five pages.

1. Project Summary

- A. Legal name and address of the organization(s) submitting the proposal (specify collaborator, if any)
- B. Date of preparation or submission
- C. Name and telephone number of investigator(s)
- D. Title of proposed research
- E. Brief statement of the objectives, methods, location(s) and expected results of the proposed research

2. Budget

An estimate of the budget should be presented for both the life of the project and each individual year. Categories could include salaries, supplies and equipment, travel, publication costs and indirect costs. In the case of collaborative projects, appropriate allocation to each organization should be included.

3. Qualification of Principal Investigator(s)

A one page curriculum vitae of the principal investigator performing the research should be included, listing his name, present institution and previous pertinent work with emphasis on training and background relative to the proposed research program.

Three (3) copies of this information should be sent to Ms. Diane H. Krier, Director of Administration. Questions regarding preparation of proposals may be referred to Gerald I. Zatuchni, M.D., Director of Technical Assistance.

PROGRAM FOR
APPLIED RESEARCH ON
FERTILITY REGULATION
Northwestern University
1040 Passavant Pavilion
303 East Superior Street
Chicago, Illinois 60611

PLEASE HELP US UPDATE OUR MAILING LIST. USE THIS FORM TO RECORD
YOUR CHANGE OF ADDRESS OR TO ADD YOUR NAME TO OUR MAILING LIST.

NAME _____

ADDRESS _____

(CITY) (STATE, COUNTRY) (ZIP)

THIS IS TO (CHECK ONE) :

_____ ADD MY NAME TO PARFR'S MAILING LIST.

_____ CHANGE MY ADDRESS ON PARFR'S MAILING LIST.

RETURN TO: PROGRAM FOR APPLIED RESEARCH ON FERTILITY REGULATION
NORTHWESTERN UNIVERSITY
1040 PASSAVANT PAVILION
303 EAST SUPERIOR STREET
CHICAGO, ILLINOIS 60611
U.S.A.