

PIR. RAP-325
1511-35011

930 0546/53

PROGRAM FOR APPLIED RESEARCH
ON FERTILITY REGULATION

S E M I - A N N U A L R E P O R T

July 1, 1983 - December 31, 1983

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

Submitted by: Program for Applied Research on
 Fertility Regulation
 Northwestern University Medical School
 Suite 1525
 875 N. Michigan Avenue
 Chicago, Illinois 60611

In compliance with Contract AID/csd-3608,
Contract AID/DSPE-C-0035 and
Cooperative Agreement DPE-0546-A-00-1003-00

TABLE OF CONTENTS

	<u>Page</u>
I. REPORT SUMMARY	1
II. PROGRAM ACCOMPLISHMENTS	2
Scientific Summary	2
LDC Involvement/Research Funds	4
Administrative Summary	6
Subagreement Negotiations	7
Personnel	12
Scientific Advisory Committee	13
Consultants	15
III. FINANCIAL REPORTS	
Summary Financial Reports	17
Detail of Expenditures and Commitments	
Under Current Agreement	18
Expenditures for the Period	
7/1/83-12/31/83 Under Current Agreement	19
IV. RESEARCH	
Technical Reports Received	20
Summaries of Active Subagreements by AID	
Contraceptive Research Area	23
V. APPENDIX	
<u>Scientific Advisory Committee Minutes</u>	
<u>Research Frontiers in Fertility Regulation</u>	
Volume 2, Number 6, December, 1983	

REPORT SUMMARY

Project Title and Contract Number:

Program for Applied Research on Fertility Regulation
AID/csd-3608
AID/DSPE-C-0035
DPE-0546-A-00-1003-00

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 -- AID/csd-3608
July 1, 1979 - June 30, 1981 -- AID/DSPE-C-0035
July 1, 1981 - June 30, 1986 -- DPE-0546-A-00-1003-00

Reporting Period:

July 1, 1983 - December 31, 1983

Total Expenditures Through June 30, 1983:

AID/csd-3608	\$ 4,331,521.82
AID/DSPE-C-0035	3,370,727.26
DPE-0546-A-00-1003-00	<u>2,366,982.28</u>
TOTAL:	\$10,069,231.36

Total Expenditures July 1, 1983 Through December 31, 1983:

AID/csd-3608	\$ - 0 -
AID/DSPE-C-0035	- 0 -
DPE-0546-A-00-1003-00	<u>740,683.56</u>
TOTAL:	\$740,683.56

Commitments Through December 31, 1983:

DPE-0546-A-00-1003-00	\$1,391,623.59
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PROGRAM ACCOMPLISHMENTS

Scientific Summary

1. Meetings of the Scientific Advisory Committee (SAC) were held on July 22 and December 14, 1983. With PARFR staff, SAC reviewed extension, formal, pilot study and informal research proposals received during the current period. Please refer to the SAC section (Program Accomplishments) and SAC Minutes (Appendix) for specific determinations.
2. Research progress was monitored by review of technical reports and site visits to projects. During this reporting period, the following research projects were visited by PARFR staff or consultants:
 - a. 9/26-10/7/83 -- Diane Krier-Morrow, M.B.A., Helsinki, Finland; Rome, Italy; Alexandria, Egypt (PARFR-337F, 300I, 300E, 314E) [Arrangements for November, 1983 PARFR Regional Seminar.]
 - b. 10/6-9/83 -- Alfredo Goldsmith, M.D., M.P.H. and David A. Edelman, Ph.D. New York, New York (PARFR-330)
 - c. 11/9-11/83 -- John J. Sciarra, M.D., Ph.D., Paris, France (PARFR-350)
 - d. 12/18-29/83 -- Alfredo Goldsmith, M.D., M.P.H. Santiago, Chile (PARFR-341C)
3. The following meetings for the purpose of project development were held and attended by PARFR staff and consultants:
 - a. 7/5/83 -- Alfredo Goldsmith, M.D., M.P.H. Washington, D.C., Poly NET 90 Studies
 - b. 10/3/83 -- Alfredo Goldsmith, M.D., M.P.H., Gerald I. Zatuchni, M.D., M.Sc., Richard L. Dunn, Ph.D., David A. Edelman, Ph.D., Kamran S. Moghissi, M.D. and Antonio Scommegna, M.D. Chicago, Illinois, Evaluation and development of a strategy for estradiol/progesterone fibrous IUD projects.
 - c. 10/4/83 -- Alfredo Goldsmith, M.D., M.P.H., Gerald I. Zatuchni, M.D., M.Sc., Lee R. Beck, Ph.D. and Danny H. Lewis, Ph.D. Chicago, Illinois, Review of the Poly NET 90 Phase II Studies and development of a strategy for Poly NET 180.
4. Dr. Alfredo Goldsmith represented PARFR at an expert meeting on quinacrine as a tubal sclerosing agent held by Family Health International in Research Triangle Park, North Carolina in September, 1983.
5. Drs. John J. Sciarra, Gerald I. Zatuchni and Alfredo Goldsmith represented PARFR at the first annual meeting of the Society for the Advancement of Contraception held November 5-8, 1983 in Cairo, Egypt.

Scientific Summary (cont'd)

6. Volume 2, Number 6 in PARFR's research technical information report was produced and distributed. The issue, "Current Status of Research on Sperm Antigens: Potential Applications as Contraceptive Vaccines," was authored by Erwin Goldberg, Ph.D.
7. At the close of the current reporting period, the book developed from the proceedings of PARFR's 13th International Workshop was in the final stages of revision. The book, "Long-Acting Contraceptive Delivery Systems" is scheduled for publication and distribution in August, 1984.
8. At the close of the current reporting period, planning for PARFR 14th International Workshop was underway. The workshop, "Intrauterine Contraception: Advances and Future Prospects" will be held May 29 - June 1, 1984 in Chicago, Illinois.
9. An International Symposium, "Long-Acting Contraception," was held November 3-4, 1983 in Alexandria, Egypt. The meeting was attended by 247 representatives from all Egyptian medical schools, major hospitals and military health services. Faculty from Northwestern University and other U.S. and major European universities attended in addition to self-pay participants from the U.S. and neighboring African countries. The meeting was covered by representatives of the newspaper and television media.

PROGRAM ACCOMPLISHMENTS

LDC Involvement

During this report period, the following subagreements in LDCs were executed:

1. PARFR-341C -- "Phase II Poly NET 90 Injectable Study"
Horacio B. Croxatto, M.D., Centro Nacional de la Familia,
Santiago, Chile
2. PARFR-341M -- "Phase II Poly NET 90 Injectable Study"
Roberto Rivera, M.D., Instituto de Investigacion Cientifica,
Durango, Mexico

Additional funding and an extension for the following LDC subagreement was executed:

1. PARFR-328B -- "An Evaluation of an Improved Needle for Transcutaneous Vas Closure"
Marcos Paulo P. de Castro, M.D., PROPATER, Sao Paulo, Brasil

A no-cost extension for the following LDC subagreement was executed:

1. PARFR-314E -- "Uterine Measurement and Clinical Comparison Study (Wing Sound II)"
Mokhtar Topozada, M.D., The University of Alexandria,
Alexandria, Egypt

The following subagreements terminated during this report period:

1. PARFR-300E -- "Poly (lactide-co-glycolide) Norethisterone Microcapsule Study (Poly NET 90)"
Mokhtar Topozada, M.D., The University of Alexandria,
Alexandria, Egypt
2. PARFR-300M -- "Poly (lactide-co-glycolide) Norethisterone Microcapsule Study (Poly NET 90)"
Roberto Rivera, M.D., Instituto Investigacion Cientifica,
Durango, Mexico
3. PARFR-305V -- "Radio-Opaque Methylcyanoacrylate (MCA) Delivered Through Single Application (FEMCEPT) Device"
Itic Zigelboim, M.D., Maternidad "Concepcion Palacios",
Caracas, Venezuela
4. PARFR-316C -- "MCA/FEMCEPT Study"
Rene Guzman-Serani, M.D., Universidad de Austral,
Valdivia, Chile

LDC Involvement (cont'd)

5. PARFR-322V -- "Uterine Measurement-Clinical Comparison Study (Wing Sound II)"
Wiktor Szczedrin, M.D., Maternidad "Concepcion Palacios",
Caracas, Venezuela

LDC Research Funds

As of December 31, 1983, the following funds were budgeted or expended for research in LDCs:

<u>Country & PARFR #</u>	<u>Budget (Dollars)</u>	<u>Total Expenditures To Date</u>
<u>BRASIL</u>		
PARFR-318B	\$14,982	\$14,701.49
PARFR-328B	<u>14,122</u>	<u>7,060.00</u>
TOTAL BRASIL:	\$29,104	\$21,761.49
<u>CHILE</u>		
PARFR-301C	31,476	31,476.00
PARFR-310C	8,000	8,000.00
PARFR-311C	9,000	9,000.00
PARFR-316C	27,000	27,000.00
PARFR-327C	20,880	13,346.00
PARFR-341C	<u>45,419</u>	<u>- 0 -</u>
TOTAL CHILE:	\$141,775	\$88,822.00
<u>EGYPT</u>		
PARFR-300E	11,930	11,930.00
PARFR-314E	<u>5,400</u>	<u>4,500.00</u>
TOTAL EGYPT:	\$17,330	\$16,430.00
<u>MEXICO</u>		
PARFR-300M	23,056	23,056.00
PARFR-330M	28,710	4,522.00
PARFR-341M	<u>36,135</u>	<u>- 0 -</u>
TOTAL MEXICO:	\$87,901	\$27,578.00
<u>VENEZUELA</u>		
PARFR-305V	24,049	21,021.79
PARFR-322V	3,600	3,600.00
PARFR-327V	<u>19,535</u>	<u>8,060.42</u>
TOTAL VENEZUELA:	\$47,184	\$32,682.21
TOTAL LDC:	\$323,294	\$187,273.70

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. Monitoring Cooperative Agreement, DPE-0546-A-00-1003-00.
2. Coordinating and mailing the agendas for the July 22 and December 14, 1983 meetings of the Scientific Advisory Committee. The July 22nd agenda included 4 formal proposals, 1 informal proposal, 1 extension proposal, 1 pilot study proposal and 17 technical reports. The December 14th agenda included 8 formal proposals, 1 informal proposal, 1 pilot study proposal and 20 technical reports.
3. Negotiating and executing:
 - 17 New Subagreements: 339, 340, 341, 341C, 341M, 341I, 341T, 343, 344, 345, 346, 347, 348, 349, 350, 351, 352
 - 5 Additional Funding/Extension Amendments: 309, 320, 324, 325, 328B
 - 1 Additional Funding Amendment: 333T
 - 2 No Cost Extension Amendments: 314E, 330T
4. Mailing 6,000 copies of Vol. 2, Number 6 in the Research Frontiers in Fertility Regulation series.
5. Planning PARFR's 14th International Workshop "Intrauterine Contraception: Advances and Future Prospects" to be held May 29 through June 1, 1984 in Chicago, Illinois.
6. Coordinating and executing an International Symposium "Long-Acting Contraception" held November 3-4, 1983 in Alexandria, Egypt.
7. Training staff in the use of and transferring data to two micro-computers purchased during the current reporting period.

7/1/83 - 12/31/83

DPE-0546-A-00-1003-00

Subagreement Negotiations

PROJECT #	TITLE/INVESTIGATORS/INSTITUTION	ACTION	PERIOD	FUNDING
309	"Ovulation Inhibition by Anordrin" Robert T. Chatterton, Ph.D. Northwestern University Medical School Chicago, Illinois	Additional Funding/ Extension (Amendment #2)	1/1/82- 6/30/84	\$57,920 (\$148,988 total)
314E	"Uterine Measurement and Clinical Comparison Study (Wing Sound II)" Mokhtar Topozada, M.D. University of Alexandria Alexandria, Egypt	No-cost Extension (Amendment #1)	2/1/82- 1/31/84	
320	"Levonorgestrel Rods Drug Release Study" Donald L. Wise, Ph.D. Dynatech R/D Company Boston, Massachusetts	Additional Funding/ Extension (Amendment #1)	7/1/82- 3/31/84	\$17,226 (\$61,723 total)
324	"Development of a Fibrous IUD Delivery System for Estradiol/Progesterone" Richard L. Dunn, Ph.D. Southern Research Institute Birmingham, Alabama	Additional Funding/ Extension (Amendment #2)	9/1/82- 11/15/83	\$ 7,497 (\$59,562 total)
325	"Development of a Vaginal Ring Delivery System for Norgestimate" Richard L. Dunn, Ph.D. Southern Research Institute Birmingham, Alabama	Additional Funding/ Extension (Amendment #2)	9/1/82- 11/15/83	\$ 7,498 (\$57,710 total)

PROJECT #	TITLE/INVESTIGATORS/INSTITUTION	ACTION	PERIOD	FUNDING
328B	"An Evaluation of an Improved Needle for Transcutaneous Vas Closure" Marcos Paulo P. de Castro, M.D. PROPATER Sao Paulo, Brasil	Additional Funding/ Extension (Amendment #1)	12/1/82- 6/30/84	\$ 7,062 (\$14,122 total)
330T	"A Clinical Evaluation of the Bioabsorbable Subdermal Norethindrone Pellet (Phase II)" Ricardo H. Asch, M.D. The University of Texas Health Science Center San Antonio, Texas	No-Cost Extension (Amendment #1)	3/1/83- 2/28/85	
333T	"Poly-gly NET 180 Microcapsule System" Jose P. Balmaceda, M.D. and Ricardo H. Asch, M.D. The University of Texas Health Science Center San Antonio, Texas	Additional Funding (Amendment #1)	3/1/83- 2/29/84	\$ 1,848 (\$40,249 total)
339	"Efficacy of Studies in Primates with the Shug in the Absence of a Tissue Wrap" Lourens J.D. Zaneveld, D.V.M., Ph.D. Rush-Presbyterian-St. Luke's Medical Center Chicago, Illinois	New Subagreement	7/1/83- 6/30/84	\$19,446
340	"Technical Assistance in NET Microcapsule Preparation" Thomas R. Tice, Ph.D. Southern Research Institute Birmingham, Alabama	New Subagreement	7/1/83- 12/31/83	\$36,500
341	"Phase II Poly NET 90 Injectable Study" Charles E. Flowers, Jr., M.D. and Lee R. Beck, Ph.D. The University of Alabama Birmingham, Alabama	New Subagreement	12/1/83- 11/30/83	\$79,264

PROJECT #	TITLE/INVESTIGATORS/INSTITUTION	ACTION	PERIOD	FUNDING
341C	"Phase II Poly NET 90 Injectable Study" Horacio B. Croxatto, M.D. Centro Nacional de la Familia Santiago, Chile	New Subagreement	1/1/84- 12/31/85	\$45,419
341M	"Phase II Poly NET 90 Injectable Study" Roberto Rivera, M.D. Instituto de Investigacion Cientifica Durango, Mexico	New Subagreement	1/1/84- 12/31/85	\$36,135
341I	"Phase II Poly NET 90 Injectable Study" Giuseppe Benagiano, M.D. Associazione per Studio della Riproduzione Umana Roma, Italy	New Subagreement	1/1/84- 12/31/85	\$39,655
341T	"Phase II Poly NET 90 Injectable Study" Jose P. Balmaceda, M.D. The University of Texas Health Science Center San Antonio, Texas	New Subagreement	1/1/84- 12/31/85	\$85,919
343	"NIH/Biotech Levonorgestrel Microcapsules" Lee R. Beck, Ph.D. University of Alabama Birmingham, Alabama	New Subagreement	11/1/83- 10/31/84	\$46,040
344	"Percutaneous Intra Vas Injection for Male Sterilization" Ralph M. Richart, M.D. Presbyterian Hospital Obstetrics and Gynecologic Services New York, New York	New Subagreement	9/1/83- 8/31/83	\$49,668

PROJECT #	TITLE/INVESTIGATORS/INSTITUTION	ACTION	PERIOD	FUNDING
345	"Effect of the Vaginal Spermicidal Barrier Contraceptive on Sperm Transport in the Human" Gerald S. Bernstein, M.D., Ph.D. University of Southern California Medical Center Los Angeles, California	New Subagreement	10/1/83- 3/31/84	\$ 6,375
346	"Development of Controlled-Release Testosterone Microcapsules for Fertility Regulation of Males" Thomas R. Tice, Ph.D. Southern Research Institute Birmingham, Alabama	New Subagreement	10/1/83- 3/31/84	\$ 49,641
347	"Studies on the Anovulatory Potency and Side Effects on an Inhibitory Analog of LH-RH in Cynomologous Monkeys" Ricardo H. Asch, M.D. The University of Texas Health Science Center San Antonio, Texas	New Subagreement	11/1/83- 10/31/85	\$145,501
348	"Development of Improved Methods and Materials for Injecting Microencapsulated Steroids" Danny H. Lewis, Ph.D. Stolle Research and Development Corporation Birmingham, Alabama	New Subagreement	11/1/83- 6/30/84	\$ 49,995
349	"Preparation of Fibrous Estradiol/Progesterone IUDs for Phase I Clinical Trials, Continuation of PARFR-324" Richard L. Dunn, Ph.D. Southern Research Institute Birmingham, Alabama	New Subagreement	11/1/83- 4/30/84	\$ 49,994

PROJECT #	TITLE/INVESTIGATORS/INSTITUTION	ACTION	PERIOD	FUNDING
350	"An Intra Tubal Device (ITD) for Female Sterilization" Jacques Hamou, M.D. Tenon Hospital Paris, France	New Subagreement	1/1/84- 6/30/85	\$11,000
351	"Development of Methods for Female and Male Contraception Based on LH-RH Antagonist" Andrew V. Schally, Ph.D. Tulane University Medical Center New Orleans, Louisiana	New Subagreement	1/1/84- 12/31/84	\$65,163
352	"Baboon Testing of Duration of NET Fused Pellets" Lee R. Beck, Ph.D. The University of Alabama Birmingham, Alabama	New Subagreement	12/1/83- 11/30/84	\$29,420

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	\$ 3,062.34
Gerald I. Zatuchni, M.D., M.Sc. Director of Technical Assistance	5.1	\$25,549.34
Alfredo Goldsmith, M.D., M.P.H. Head, Research Project Development	5.7	28,611.32
Diane Krier-Morrow, M.B.A. Director of Administration	6.0	15,146.82
Susan Dewar Project Controller	6.0	8,789.34
Kelley Osborn Publications Coordinator	0.6	3,795.00
Ruvenia Thomas Secretary II	6.0	9,325.52
Asenath Williamson Secretary I	6.0	6,149.26
Rebecca Zaccard Secretary I (Terminated 9/9/83)	2.3	2,917.44
Josephine Harris Secretary I (Started 9/26/83)	3.3	3,102.00
<u>Fringe Benefits</u>		\$19,387.55
<u>Indirect Costs</u>		81,424.29

SCIENTIFIC ADVISORY COMMITTEE

The membership of the Scientific Advisory Committee during this reporting period consisted of the following individuals:

John J. Sciarra, M.D., Ph.D., Chairman	Northwestern University
Nancy J. Alexander, Ph.D. (last meeting 12/14)	Oregon Regional Primate Research Center
Andrzej Bartke, Ph.D. (first meeting 12/14)	The University of Texas Health Science Center at San Antonio
David A. Blake, Ph.D.	The Johns Hopkins University School of Medicine
Robert T. Chatterton, Ph.D. (last meeting 7/22)	Northwestern University
Elizabeth B. Connell, M.D. (last meeting 12/14)	Emory University School of Medicine
William Droegemueller, M.D. (first meeting 12/14)	University of North Carolina
Uwe Goebelsmann, M.D. (first meeting 12/14)	University of Southern California
Miriam H. Labbok, M.D., M.P.H.	The Johns Hopkins School of Hygiene and Public Health
Kamran S. Moghissi, M.D.	Wayne State University
Dean L. Moyer, M.D.	University of Southern California School of Medicine
Antonio Scommegna, M.D. (first meeting 12/14)	Michael Reese Hospital and Medical Center
Rochelle N. Shain, Ph.D.	The University of Texas Health Science Center at San Antonio
Aquiles J. Sobrero, M.D. (last meeting 7/22)	Northwestern University

The Committee met twice during the current reporting period, on July 22 and on December 14, 1983. Both meetings were held in Chicago, Illinois.

At the July 22nd meeting, the Committee reviewed four formal, one informal, one extension and one pilot study proposal. Seventeen technical reports were also reviewed.

All of the four formal proposals submitted were approved by the Committee. Dr. Ralph M. Richart's proposal, "A Rapid and Effective Percutaneous Intra-Vas Injection for Male Sterilization" was approved with the requirement that Dr. Richart rewrite the methodology as indicated by SAC. A limited and well-controlled Phase I clinical trial in USA centers was approved for Dr. Leonard E. Laufe's proposal "Evaluation of Fimbrial Hoods as an Alternative Method of Female Sterilization". Dr. Jacques Hamou's proposal "Hysteroscopic Delivery of an Intra Tubal Device for Female Sterilization" was approved as submitted. The proposal submitted by Dr. Thomas R. Tice, "Development of Controlled-Release Testosterone Microcapsules for Fertility Regulation of Males", was unanimously approved by the Committee, although the Committee asked to review the drug release studies in Rhesus monkeys and also postponed discussion on the type of monkey to be used for the studies until the December 14th SAC meeting.

Scientific Advisory Committee (cont'd)

The extension, informal and pilot study proposals reviewed at the meeting were not approved.

Proposals for eight formal, one informal and one pilot study were reviewed at the December 14th meeting. In addition, twenty technical reports, including eight final reports, were also reviewed.

The Committee approved Dr. Nancy J. Alexander's formal proposal "Enhancement of the Secretory Immune Response to LDH-C₄" and approved the first stage of the formal proposal "Development of an Immunocontraceptive Vaccine: Role of 23-Kd Antigen in Immunofertility and Fertility Regulation" submitted by Drs. Rajesh K. Naz and Nancy J. Alexander.

Dr. Montri Chulavatnatol's pilot study proposal "Screening of Thai Plants for Proteins (or Lectins) That Can Be of Use as New Vaginal Contraceptives" was approved with the provision that a botanist be included in the study.

The informal proposal reviewed at the meeting was not approved.

Minutes of the meetings are included in the Appendix.

CONSULTANTS

The following is a list of Program Consultants, indicating their areas of expertise, contributions to the program, and payment therefore. Included in this list of consultants are members of the Scientific Advisory Committee.

<u>Consultant</u>	<u>Purpose</u>	<u>Effort</u>	<u>Fee</u>
Nancy J. Alexander, Ph.D. Reproductive Physiology	SAC 7/22-23/83	2 days	\$ 420
	SAC 12/13-14/83	2 days	420
Andrzej Bartke, Ph.D. Obstetrics and Gynecology	SAC 7/22-23/83	2 days	420
	SAC 12/13-14/83	2 days	420
David A. Blake, Ph.D. Obstetrics and Gynecology Pharmacology	SAC 12/13-14/83	2 days	420
Elizabeth B. Connell, M.D. Obstetrics and Gynecology	SAC 7/22-23/83	2 days	420
	SAC 12/13-14/83	2 days	420
William Droegemueller, M.D. Obstetrics and Gynecology	SAC 12/13-14/83	2 days	420
Robert W. Fulks	Editorial Services 8/20-26/83	14 hours	210
Uwe Goebelsmann, M.D. Reproductive Endocrinology	SAC 12/13-14/83	2 days	420
Alan E.C. Holden Statistics/Mathematics	Statistical Analysis 11/10-12/83	3 days	300
Miriam H. Labbok, M.D., M.P.H. Epidemiology	SAC 7/22-23/83	2 days	420
	SAC 12/13-14/83	2 days	420
Kamran S. Moghissi, M.D. Obstetrics and Gynecology Reproductive Endocrinology	SAC 7/22-23/83	2 days	420
	Project Consultation 10/3/83	1 day	210
	SAC 12/13-14/83	2 days	420
Dean L. Moyer, M.D. Experimental Pathology	SAC 7/22-23/83	2 days	420
Subir Roy, M.D. Obstetrics and Gynecology, Contraceptive Development	RFFR Series, Vol. 2, No. 4 3/5-27/83	5 days	1,000
Andrew V. Schally, Ph.D. Neuroendocrinology, Nobel Prize	RFFR Series Vol. 2, No. 4 3/5-27/83	5 days	1,000
Antonio Scommegna, M.D. Obstetrics and Gynecology	Project Consultation 10/3/83	1 day	210
	SAC 12/13-14/83	2 days	420

Consultants (cont'd)

Rochelle N. Shain, Ph.D. Medical Anthropology	SAC 7/22-23/83 SAC 12/13-14/83	2 days 2 days	\$ 420 420
Judith A. Vaitukaitis, M.D. Endocrinology	Proposal Review 9/15/83	1 day	50
Donald P. Waller, Ph.D. Pharmacology	Proposal Review 11/22/83	1 day	50
Lourens J.D. Zaneveld, D.V.M, Ph.D. Biochemistry and Veterinary Medicine	Proposal Review 9/15/83	1 day	50
		TOTAL	<hr/> \$10,220

SUMMARY FINANCIAL REPORTS

This section includes:

- A. Summary of Expenditures and Commitments under AID/csd-3608, AID/DSPE-C-0035, and AID/DPE-0546-A-00-1003-00
- B. Detail of Expenditures and Commitments under AID/DPE-0546-A-00-1003-00, effective 7/1/81-6/30/86
- C. Expenditures under AID/DPE-0546-A-00-1003-00 during the period 7/1/83-12/31/83

	<u>AID/csd-3608</u> <u>(7/1/75-6/30/80)</u>	<u>AID/DSPE-C-0035</u> <u>(7/1/79-6/30/82)</u>	<u>DPE-0546-A-00-1003-00</u> <u>(7/1/81-6/30/86)</u>
Expenditures 7/1/83-12/31/83	\$ - 0 -	\$ - 0 -	\$ 740,683.56
Expenditures through 6/30/83	<u>4,331,521.82</u>	<u>3,370,727.26</u>	<u>2,366,982.28</u>
Total Expenditures	\$4,331,521.82	\$3,370,727.26	\$3,107,665.84
Total Commitments @ 12/31/83	- 0 -	- 0 -	1,391,623.59
Uncommitted Balance	<u>180,990.68</u>	<u>39,272.74</u>	<u>460,710.57</u>
Total Budget	<u>\$4,512,512.50</u>	<u>\$3,410,000.00</u>	<u>\$4,960,000.00</u>

COOPERATIVE AGREEMENT: AID/DPE-0546-A-00-1003-00
 EFFECTIVE DATES: 7/1/81-6/30/86
 TOTAL AWARD: \$12,363,280
 TOTAL AWARDED TO DATE: \$4,960,000

7/1/81 - 12/31/83

Category	Budget	%	Expenditures	Commitments	Total	
<u>Research</u>	\$2,890,338	58.3	\$1,471,932.96	\$1,044,579.37	\$2,516,512.33	55.9
<u>Workshops and Publications</u>	275,374	5.6	238,494.98	30,381.00	268,875.98	6
<u>Consultants</u>	55,400	1.1	42,818.17	4,500.00	47,318.17	1.1
<u>Travel</u>	198,584	4.0	165,169.92	18,655.48	183,825.40	4.1
<u>Salaries and Fringe Benefits</u>	745,981	15.0	570,909.85	168,441.11	739,350.96	16.4
<u>Supplies, Communications and Rent</u>	302,694	6.1	249,505.39	21,636.52	271,141.91	6
<u>Equipment</u>	25,439	.5	12,511.35		12,511.35	8
<u>Indirect Costs</u>	466,190	9.4	356,323.22	103,430.11	459,753.33	10.2
	<u>\$4,960,000</u>		<u>\$3,107,665.84</u>	<u>\$1,391,623.59</u>	<u>\$4,499,289.43</u>	

COOPERATIVE AGREEMENT: AID/DPE-0546-A-00-1003-00

EXPENDITURES FOR THE PERIOD: 7/1/83-12/31/83

<u>Category</u>	<u>Expended 7/1/81-6/30/83</u>	<u>Expended 7/1/83-12/31/83</u>	<u>Total Expended 7/1/81-12/31/83</u>
<u>Research</u>	\$1,104,718.23	\$367,214.73	\$1,471,932.96
<u>Workshops & Publications</u>	175,924.18	62,570.80	238,494.98
<u>Consultants</u>	36,995.67	5,822.50	42,818.17
<u>Travel</u>	123,596.76	41,573.16	165,169.92
<u>Salaries & Fringe Benefits</u>	446,724.89	124,184.96	570,909.85
<u>Supplies, Communications and Rent</u>	203,047.37	46,458.02	249,505.39
<u>Equipment</u>	1,076.25	11,435.10	12,511.35
<u>Indirect Costs</u>	274,898.93	81,424.29	356,323.22
TOTAL:	<u>\$2,366,982.28</u>	<u>\$740,683.56</u>	<u>\$3,107,665.84</u>

TECHNICAL REPORTS

The following technical reports were reviewed at the July 22, 1983 Scientific Advisory Committee Meeting:

<u>Project</u>	<u>Period Covered by Report</u>
PARFR-300 -- "Poly (lactide-co-glycolide) Norethisterone Microcapsule Study (Poly NET 90) - Phase I"	1/1/83-7/31/83
PARFR-300I -- "Poly (lactide-co-glycolide) Norethisterone Microcapsule Study (Poly NET 90) - Phase I"	10/1/82-5/31/83
PARFR-300T -- "Poly (lactide-co-glycolide) Norethisterone Microcapsule Study (Poly NET 90) - Phase I"	2/10/83-4/30/83
PARFR-309 -- "Ovulation Inhibition by Anordrin"	1/1/83-6/30/83
PARFR-315 -- "Immunologic Suppression of Fertility by Synthetic Antigenic Determinants of LDH-C ₄ "	2/25/83-6/22/83
PARFR-320 -- "Levonorgestrel Rods Drug Release Study"	8/1/82-5/31/83
PARFR-321 -- "Guaiacol Peroxidase Levels: Predictors of Ovulation in Women"	8/1/82-7/1/83
PARFR-324 -- "Development of a Fibrous IUD Delivery System for Estradiol/Progesterone"	1/27/83-4/20/83
PARFR-325 -- "Development of a Vaginal Ring Delivery System for Norgestimate"	2/1/83-4/30/83
PARFR-326 -- "Evaluation in Sheep of Orabase® as a Vaginal Barrier Contraceptive"	2/2/83-5/31/83
PARFR-330 -- "Clinical Evaluation and Efficacy of Bioabsorbable Subdermal Contraceptive Norethindrone Pellet Implant (Phase II)"	2/1/83-6/30/83
PARFR-331 -- "Development of an Improved Microencapsulation Process for Norethisterone"	2/1/83-6/1/83
PARFR-332 -- "Development of an Injectable Long-Acting Estradiol Formulation"	3/1/83-6/15/83
PARFR-333 -- "Poly-gly NET 180 Microcapsule System"	3/1/83-7/6/83
PARFR-333T -- "Poly-gly NET 180 Microcapsule System"	3/1/83-6/30/83

Technical Reports (continued)

<u>Project</u>	<u>Period Covered by Report</u>
PARFR-334SRI -- "Development of Controlled-Release Progesterone Microcapsules for the Regulation of Fertility During Lactation"	3/1/83-6/30/83
PARFR-337F -- "Use-Effectiveness of a Levonorgestrel Releasing Intracervical Device"	Site Visit Report
<p>The following technical reports were reviewed at the December 14, 1983 Scientific Advisory Committee Meeting:</p>	
PARFR-300 -- "Poly (lactide-co-glycolide) (FINAL) Norethisterone Microcapsule Study (Poly NET 90) - Phase I"	
PARFR-301T -- "A Clinical Evaluation of the Bioabsorbable Subdermal Contraceptive Implant - Phase I"	9/1/83-2/28/83
PARFR-307(FINAL)/ -- "Development of Sperm Enzyme 338 Inhibitors as Vaginal Contraceptives"	2/20/83-11/15/83
PARFR-309 -- "Ovulation Inhibition by Anordrin"	1/1/82-10/26/83
PARFR-320 -- "Levonorgestrel Rods Drug Release (FINAL) Study"	7/1/82-11/22/83
PARFR-323 -- "Efficacy of Quinacrine and Tetracycline (FINAL) in the Primate"	2/18/83-11/15/83
PARFR-324 -- "Development of a Fibrous IUD Delivery (FINAL) System for Estradiol/Progesterone"	9/1/82-10/25/83
PARFR-325 -- "Development of a Vaginal Ring Delivery (FINAL) System for Norgestimate"	9/1/82-11/15/83
PARFR-328B -- "An Evaluation of an Improved Needle for Transcutaneous Vas Closure"	12/1/82-11/10/83
PARFR-330 -- "Clinical Evaluation and Efficacy of Bioabsorbable Subdermal Contraceptive Norethindrone Pellet Implant (Phase II)"	2/1/83-6/30/83
PARFR-330M -- "Clinical Evaluation and Efficacy of Bioabsorbable Subdermal Contraceptive Norethindrone Pellet Implant (Phase II)"	6/1/83-10/31/83
PARFR-330T -- "Clinical Evaluation and Efficacy of the Bioabsorbable Subdermal Contraceptive Norethindrone Pellet Implant (Phase II)"	3/1/83-10/31/83

Technical Reports (continued)

<u>Project</u>	<u>Period Covered by Report</u>
PARFR-331 -- "Development of an Improved Microen- (FINAL) capsulation Process for Norethisterone"	6/30/83-9/30/83
PARFR-333 -- "Poly-gly NET 180 Microcapsule System - Phase I"	3/1/83-10/11/83
PARFR-333T -- "Poly-gly NET 180 Microcapsule System - Phase I"	7/1/83-10/31/83
PARFR-334SRI -- "Development of Controlled-Release Progesterone Microcapsules for the Regulation of Fertility During Lactation"	7/1/83-10/31/83
PARFR-334UAB -- "Pharmacokinetic Studies in Baboons Relating to PARFR-334SRI"	3/1/83-11/1/83
PARFR-339 -- "Efficacy Studies in Primates with the Shug in the Absence of a Tissue Wrap"	7/1/83-11/15/83
PARFR-314E,-- "Uterine Measurement - Clinical 311C, 313E, Comparison Study (Wing Sound II)" 322V	through 11/1/83
Nonsurgical Female Sterilization with MCA	through 11/1/83

RESEARCH

PARFR SUBAGREEMENT SUMMARIES

This section summarizes the expenses of PARFR subagreements active during the period July 1, 1983 to December 31, 1983. Summaries are categorized according to the following AID Contraceptive Research Areas:

- I. Female Sterilization
 - C. Transcervical
- II. Male Sterilization
 - B. Other
- III. Intrauterine Contraception
 - D. Other
- IV. Systemic Contraception
 - B. Injectables and Implants
 - C. Other
 - 1. Male Pharmacological Methods
- V. Barrier Contraception
 - B. Female
- VI. Miscellaneous

RESEARCH PROJECTS BY AID CONTRACEPTIVE RESEARCH AREA
 UNDER COOPERATIVE AGREEMENT AID/DPE-0546-A-00-1003-00
 7/1/83-12/31/83

I. FEMALE STERILIZATION

C. TRANSCERVICAL

<u>PARFR #</u>	<u>INSTITUTION & INVESTIGATOR(S)</u>	<u>TITLE</u>	<u>DATES</u>	<u>BUDGET</u>	<u>EXPENDITURES THIS PERIOD</u>	<u>TOTAL EXPENDITURES</u>
305V	Maternidad "Concepcion Palacios" Caracas, Venezuela Itic Zighelboim, M.D. Wiktor Szczedrin, M.D.	"Radio-Opaque Methylcyanoacrylate (MCA) Delivered Through Single Application (FEMCEPT) Device"	9/10/81- 9/9/83	\$ 24,049	\$ 2,542.86	\$21,021.79
310C	Enrique Guiloff, M.D. Santiago, Chile	"MCA/FEMCEPT Video Study"	1/1/82- 6/30/83	8,000	546.00	8,000.00
316C	Universidad de Austral de Chile Valdivia, Chile Rene Guzman-Serani, M.D.	"MCA/FEMCEPT Study"	4/1/82- 3/31/84	27,000	3,390.00	27,000.00
323	University of Illinois at the Medical Center Chicago, Illinois Lourens J.D. Zaneveld, D.V.M., Ph.D.	"Efficacy of Quinacrine and Tetracycline in the Primate"	9/1/82- 8/31/83	44,100	17,934.08	23,775.13
327C	Instituto de Obstetricia y Ginecologia de Universidad Austral de Chile Valdivia, Chile Rene Guzman-Serani, M.D.	"Time Interval MCA/FEMCEPT Study"	12/1/82- 11/30/84	20,880	10,996.00	13,346.00
327V	Maternidad "Concepcion Palacios" Caracas, Venezuela Itic Zighelboim, M.D. Wiktor Szczedrin, M.D.	"Time Interval MCA/FEMCEPT Study"	12/1/82- 11/30/84	19,535	4,020.18	8,060.42

RESEARCH PROJECTS BY AID CONTRACEPTIVE RESEARCH AREA
 UNDER COOPERATIVE AGREEMENT AID/DPE-0546-A-00-1003-00
 7/1/83-12/31/83

I. FEMALE STERILIZATION (continued)

D. OTHER

<u>PARFR #</u>	<u>INSTITUTION & INVESTIGATOR(S)</u>	<u>TITLE</u>	<u>DATES</u>	<u>BUDGET</u>	<u>EXPENDITURES THIS PERIOD</u>	<u>TOTAL EXPENDITURES</u>
350	Tenon Hospital Paris, France Jacques Hamou, M.D.	"An Intra Tubal Device (ITD) for Female Sterilization"	1/1/84- 6/30/85	\$ 11,000	\$ - 0 -	\$ - 0 -

RESEARCH PROJECTS BY AID CONTRACEPTIVE RESEARCH AREA
 UNDER COOPERATIVE AGREEMENT AID/DPE-0546-A-00-1003-00
 7/1/83-12/31/83

II. MALE STERILIZATION

B. OTHER

<u>PARFR #</u>	<u>INSTITUTION & INVESTIGATOR(S)</u>	<u>TITLE</u>	<u>DATES</u>	<u>BUDGET</u>	<u>EXPENDITURES THIS PERIOD</u>	<u>TOTAL EXPENDITURES</u>
317	University of Illinois at Chicago Lourens J.D. Zaneveld D.V.M., Ph.D.	"Electroejaculation of Primates for Shug Evaluation and LDH Immunization"	7/1/82-6/30/83	\$ 11,948	\$ 3,726.61	\$11,948.00
328B	PROPATER Sao Paulo, Brasil Marcos Paulo P. de Castro, M.D.	"An Evaluation of an Improved Needle for Transcutaneous Vas Closure"	12/1/82-6/30/84	14,122	7,060.00	7,060.00
339	Rush-Presbyterian-St. Luke's Medical Center Chicago, Illinois Lourens J.D. Zaneveld, D.V.M., Ph.D.	"Efficacy of Studies in Primates with the Shug in the Absence of a Tissue Wrap"	7/1/83-6/30/84	19,446	- 0 -	- 0 -
D-47	Medical Research Consultants Chapel Hill, North Carolina	Preparation of an Investigational Device Exemption (IDE) for the Shug Device			1,615.00	1,615.00
344	Presbyterian Hospital Obstetric and Gynecological Services New York, New York Ralph M. Richart, M.D.	"Percutaneous Intra Vas Injection for Male Sterilization"	9/1/83-8/31/83	49,668	- 0 -	- 0 -
D-32	Biologic Resources Laboratory Univ. of Illinois at Chicago	Animal maintenance - Rhesus monkeys for PARFR-317			1,637.85	9,603.91

RESEARCH PROJECTS BY AID CONTRACEPTIVE RESEARCH AREA
 UNDER COOPERATIVE AGREEMENT AID/DPE-0546-A-00-1003-00
 7/1/83-12/31/83

II. MALE STERILIZATION (continued)

B. OTHER

<u>PARFR #</u>	<u>INSTITUTION & INVESTIGATOR(S)</u>	<u>TITLE</u>	<u>DATES</u>	<u>BUDGET</u>	<u>EXPENDITURES THIS PERIOD</u>	<u>TOTAL EXPENDITURES</u>
D-50	PIACT Seattle, Washington	Testing of Needles and Power Supply of the Transcutaneous Vas System			\$ 5,000.00	\$ 5,000.00

RESEARCH PROJECTS BY AID CONTRACEPTIVE RESEARCH AREA
 UNDER COOPERATIVE AGREEMENT AID/DPE-0546-A-00-1003-00
 7/1/83-12/31/83

III. INTRAUTERINE CONTRACEPTION

D. OTHER

<u>PARFR #</u>	<u>INSTITUTION & INVESTIGATOR(S)</u>	<u>TITLE</u>	<u>DATES</u>	<u>BUDGET</u>	<u>EXPENDITURES THIS PERIOD</u>	<u>TOTAL EXPENDITURES</u>
313E	Institute of Population Studies, University of Exeter, Devon, England Robert Snowden, Ph.D.	"Uterine Measurement - Clinical Comparison Study (Wing Sound II)"	2/1/82- 1/31/84	\$ 21,600	\$ - 0 -	\$18,000.00
314E	Shatby Hospital, The University of Alexandria Alexandria, Egypt Mokhtar Topozada, M.D.	"Uterine Measurement - Clinical Comparison Study (Wing Sound II)"	2/1/82- 7/31/83	5,400	1,500.00	4,500.00
322V	Wiktor Szczedrin, M.D. Itic Zigelboim, M.D. Caracas, Venezuela	"Uterine Measurement - Clinical Comparison Study (Wing Sound II)"	9/1/82- 12/31/83	3,600	1,000.00	3,600.00
324	Southern Research Institute Birmingham, Alabama Richard L. Dunn, Ph.D.	"Development of a Fibrous IUD Delivery System for Estradiol/Progesterone	9/1/82- 11/15/83	59,562	29,197.80	59,562.00
337F	University of Helsinki Helsinki, Finland Tapani Luukkainen, M.D., Ph.D.	"Use-Effectiveness of a Levonorgestrel-Releasing Intracervical Device"	5/1/83- 4/30/84	\$ 49,665	\$ 6,018.91	\$ 6,018.91
337T	The University of Texas Health Science Center San Antonio, Texas Rochelle N. Shain, Ph.D.	"Intracervical Device Acceptability Study"	6/1/83- 5/31/85	12,502	- 0 -	- 0 -

RESEARCH PROJECTS BY AID CONTRACEPTIVE RESEARCH AREA
 UNDER COOPERATIVE AGREEMENT AID/DPE-0546-A-00-1003-00
 7/1/83-12/31/83

III. INTRAUTERINE CONTRACEPTION (continued)

D. OTHER

<u>PARFR #</u>	<u>INSTITUTION & INVESTIGATOR(S)</u>	<u>TITLE</u>	<u>DATES</u>	<u>BUDGET</u>	<u>EXPENDITURES THIS PERIOD</u>	<u>TOTAL EXPENDITURES</u>
349	Southern Research Institute Birmingham, Alabama Richard L. Dunn, Ph.D.	"Preparation of Fibrous Estradiol/Progesterone IUDs for Phase I Clinical Trials, Continuation of PARFR-324"	11/1/83-4/30/84	\$ 49,994	\$ - 0 -	\$ - 0 -
D-52	Southern Research Institute Birmingham, Alabama	Preparation of an IND for the Fibrous E/P IUD Delivery System		5,000	- 0 -	- 0 -

RESEARCH PROJECTS BY AID CONTRACEPTIVE RESEARCH AREA
 UNDER COOPERATIVE AGREEMENT AID/DPE-0546-A-00-1003-00
 7/1/83-12/31/83

IV. SYSTEMIC CONTRACEPTION

B. INJECTABLES AND IMPLANTS

<u>PARFR #</u>	<u>INSTITUTION & INVESTIGATOR(S)</u>	<u>TITLE</u>	<u>DATES</u>	<u>BUDGET</u>	<u>EXPENDITURES THIS PERIOD</u>	<u>TOTAL EXPENDITURES</u>
300	University of Alabama in Birmingham Charles E. Flowers, Jr., M.D. and Lee R. Beck, Ph.D.	"Poly (lactide-co-glycolide) Norethisterone Microcapsule Study (Phase I Poly NET 90)"	8/1/81- 7/31/83	\$ 72,984	\$ 4,708.20	\$72,984.00
300E	Shatby Hospital, Univ. of Alexandria Alexandria, Egypt Mokhtar Topozada, M.D.	"Poly (lactide-co-glycolide) Norethisterone Microcapsule Study (Phase I Poly NET 90)"	10/1/82- 9/30/83	11,930	9,980.36	11,930.00
300I	Associazione per Studio della Riproduzione Umana, Roma, Italy Giuseppe Benagiano, M.D.	"Poly (lactide-co-glycolide) Norethisterone Microcapsule Study (Phase I Poly NET 90)"	10/1/82- 9/30/83	16,642.50	2,572.40	11,313.40
300M	Instituto de Investigacion Cientifica Durango, Mexico Roberto Rivera, M.D.	"Poly (lactide-co-glycolide) Norethisterone Microcapsule Study (Phase I Poly NET 90)"	10/1/82- 9/30/83	23,056	9,762.00	23,056.00
300T	The University of Texas Health Science Center at San Antonio Jose P. Balmaceda, M.D.	"Poly (lactide-co-glycolide) Norethisterone Microcapsule Study (Phase I Poly NET 90)"	8/1/82- 7/31/83	34,784	10,024.43	34,707.55
301T	The University of Texas Health Science Center at San Antonio Ricardo H. Asch, M.D.	"A Clinical Evaluation of the Bioabsorbable Subdermal Con- traceptive Norethindrone Pellet Implant"	9/1/81- 2/28/83	\$ 45,319	\$ 684.75	\$27,459.63

RESEARCH PROJECTS BY AID CONTRACEPTIVE RESEARCH AREA
 UNDER COOPERATIVE AGREEMENT AID/DPE-0546-A-00-1003-00
 7/1/83-12/31/83

IV. SYSTEMIC CONTRACEPTION (continued)

B. INJECTABLES AND IMPLANTS

<u>PARFR #</u>	<u>INSTITUTION & INVESTIGATOR(S)</u>	<u>TITLE</u>	<u>DATES</u>	<u>BUDGET</u>	<u>EXPENDITURES THIS PERIOD</u>	<u>TOTAL EXPENDITURES</u>
319	The University of Kentucky Research Foundation Lexington, Kentucky George A. Digenis, Ph.D.	"Development of Methodology Following Microcapsule Transcervical Transport in Baboons Utilizing External Scintigraphy"	7/1/82- 7/31/83	\$ 12,666	\$ 3,934.50	\$12,666.00
320	Dynatech R/D Company Cambridge, Massachusetts Donald L. Wise, Ph.D.	"Levonorgestrel Rods - Drug Release Study"	7/1/82- 3/31/84	61,723	11,963.05	49,759.95
325	Southern Research Institute Birmingham, Alabama Richard L. Dunn, Ph.D.	"Development of a Vaginal Ring Delivery System for Norgestimate"	9/1/82- 11/15/83	57,710	15,434.45	42,275.55
330	Cornell University Medical College New York, New York Brij B. Saxena, Ph.D., D.Sc.	"A Clinical Evaluation of the Subdermal Contraceptive Norethindrone Pellet (Phase II)"	2/1/83- 6/30/84	49,995	26,110.82	26,110.82
330M	Instituto de Investigacion Cientifica Durango, Mexico Roberto Rivera, M.D.	"A Clinical Evaluation of the Subdermal Contraceptive Norethindrone Pellet (Phase II)"	4/1/83- 3/30/84	28,710	4,522.00	4,522.00
330T	The University of Texas Health Science Center San Antonio, Texas Ricardo H. Asch, M.D.	"A Clinical Evaluation of the Bioabsorbable Subdermal Norethindrone Pellet Implant (Phase II)"	3/1/83- 2/28/85	48,139	1,669.56	3,007.80

RESEARCH PROJECTS BY AID CONTRACEPTIVE RESEARCH AREA
 UNDER COOPERATIVE AGREEMENT AID/DPE-0546-A-00-1003-00
 7/1/83-12/31/83

IV. SYSTEMIC CONTRACEPTION (continued)

B. INJECTABLES AND IMPLANTS

<u>PARFR #</u>	<u>INSTITUTION & INVESTIGATOR(S)</u>	<u>TITLE</u>	<u>DATES</u>	<u>BUDGET</u>	<u>EXPENDITURES THIS PERIOD</u>	<u>TOTAL EXPENDITURES</u>
331	Stolle Research and Development Corporation Birmingham, Alabama Danny H. Lewis, Ph.D.	"Development of an Improved Microencapsulation Process for Norethisterone (Two Step)"	2/1/83- 9/30/83	\$ 56,868	\$33,659.21	\$56,868.00
332	Stolle Research and Development Corporation Birmingham, Alabama Danny H. Lewis, Ph.D.	"Development of An Injectable Long-Acting Estradiol Formulation"	3/1/83- 2/29/84	70,000	37,986.44	58,115.66
333	University of Alabama in Birmingham Charles E. Flowers, Jr., M.D. and Lee R. Beck, Ph.D.	"Poly-gly NET 180 Microcapsule System"	3/1/83- 2/29/84	47,200	21,506.50	21,506.50
333T	The University of Texas Health Science Center San Antonio, Texas Jose P. Balmaceda, M.D. Ricardo H. Asch, M.D.	"Poly-gly NET 180 Microcapsule System"	3/1/83- 2/29/84	40,249	8,228.78	12,251.47
334UAB	The University of Alabama in Birmingham Lee R. Beck, Ph.D.	"Pharmacokinetics Studies in Baboons Relating to PARFR-334SRI"	3/1/83- 2/29/84	13,699	2,876.15	2,876.15
334SRI	Southern Research Institute Birmingham, Alabama Thomas R. Tice, Ph.D.	"Development of Controlled-Release Progesterone Microcapsule"	3/1/83- 2/29/84	49,500	24,892.12	35,160.49

RESEARCH PROJECTS BY AID CONTRACEPTIVE RESEARCH AREA
 UNDER COOPERATIVE AGREEMENT AID/DPE-0546-A-00-1003-00
 7/1/83-12/31/83

IV. SYSTEMIC CONTRACEPTION (continued)

B. INJECTABLES AND IMPLANTS

<u>PARFR #</u>	<u>INSTITUTION & INVESTIGATOR(S)</u>	<u>TITLE</u>	<u>DATES</u>	<u>BUDGET</u>	<u>EXPENDITURES THIS PERIOD</u>	<u>TOTAL EXPENDITURES</u>
335	Stolle Research and Development Corporation Birmingham, Alabama Danny H. Lewis, Ph.D.	"One-Month NET Microcapsules and Six-Months Levonorgestrel Microcapsule Preparation"	5/1/83- 2/29/84	\$ 16,284	\$16,284.00	\$16,284.00
336	University of South Alabama Mobile, Alabama Walter H. Wilborn, Ph.D.	"Effects of New Synthetic Progestins on Baboon Endometrium"	6/1/83- 12/31/83	46,061	21,300.00	21,300.00
340	Southern Research Institute Birmingham, Alabama Thomas R. Tice, Ph.D.	"Technical Assistance in NET Microcapsule Preparation"	7/1/83- 12/31/83	36,500	12,618.45	12,618.45
341	University of Alabama in Birmingham Charles E. Flowers, Jr., M.D. and Lee R. Beck, Ph.D.	"Phase II Poly NET 90 Injectable Study"	12/1/83- 11/30/85	79,264	- 0 -	- 0 -
341C	Centro Nacional de la Familia Santiago, Chile Horacio B. Croxatto, M.D.	"Phase II Poly NET 90 Injectable Study"	1/1/84- 12/31/85	45,419	- 0 -	- 0 -
341M	Instituto de Investigacion Cientifica Durango, Mexico Roberto Rivera, M.D.	"Phase II Poly NET 90 Injectable Study"	1/1/84- 12/31/85	36,135	- 0 -	- 0 -

RESEARCH PROJECTS BY AID CONTRACEPTIVE RESEARCH AREA
 UNDER COOPERATIVE AGREEMENT AID/DPE-0546-A-00-1003-00
 7/1/83-12/31/83

IV. SYSTEMIC CONTRACEPTION (continued)

B. INJECTABLES AND IMPLANTS

<u>PARFR #</u>	<u>INSTITUTION & INVESTIGATOR(S)</u>	<u>TITLE</u>	<u>DATES</u>	<u>BUDGET</u>	<u>EXPENDITURES THIS PERIOD</u>	<u>TOTAL EXPENDITURES</u>
341I	Associazione per Studio della Riproduzione Umana Roma, Italy Giuseppe Benagiano, M.D.	"Phase II Poly NET 90 Injectable Study"	1/1/84- 12/31/85	\$ 39,655	\$ - 0 -	\$ - 0 -
341T	The University of Texas Health Science Center San Antonio, Texas Jose P. Balmaceda, M.D.	"Phase II Poly NET 90 Injectable Study"	1/1/84- 12/31/85	85,919	- 0 -	- 0 -
343	University of Alabama in Birmingham Lee R. Beck, Ph.D.	"NIH/Biotech Levonorgestrel Microcapsules"	11/1/83- 10/31/84	46,040	- 0 -	- 0 -
346	Southern Research Institute Birmingham, Alabama Thomas R. Tice, Ph.D.	"Development of Controlled- Release Testosterone Microcapsules for Fertility Regulation of Males"	10/1/83- 3/31/84	49,641	- 0 -	- 0 -
348	Stolle Research and Development Corporation Birmingham, Alabama Danny H. Lewis, Ph.D.	"Development of Improved Methods and Materials for Injecting Microencapsulated Steroids"	11/1/83- 6/30/84	49,995	- 0 -	- 0 -
352	University of Alabama in Birmingham Birmingham, Alabama Lee R. Beck, Ph.D.	"Baboon Testing of Duration of NET Fused Pellets"	12/1/83- 11/30/84	29,420	- 0 -	- 0 -
D-41	University of Alabama in Birmingham	RIA analysis for Poly NET Studies - PARFR-300E, 300I, 300M, 300T			- 0 -	5,446.00

RESEARCH PROJECTS BY AID CONTRACEPTIVE RESEARCH AREA
 UNDER COOPERATIVE AGREEMENT AID/DPE-0546-A-00-1003-00
 7/1/83-12/31/83

IV. SYSTEMIC CONTRACEPTION (continued)

B. INJECTABLES AND IMPLANTS

<u>PARFR #</u>	<u>INSTITUTION & INVESTIGATOR(S)</u>	<u>TITLE</u>	<u>DATES</u>	<u>BUDGET</u>	<u>EXPENDITURES THIS PERIOD</u>	<u>TOTAL EXPENDITURES</u>
D-48	Fisher Scientific Itasca, Illinois	Purchase of 1200 Pregnancy Tests and 6 Heating Blocks for Use in Poly NET 90 Studies in Chile and Mexico			\$ 2,459.70	\$ 2,459.70
D-49	Cornell University Medical Center New York, New York	RIA Analysis of NET Samples for Pellet Implant Study			3,300.00	3,300.00
D-53	Stolle Research and Development Corporation Birmingham, Alabama	Production of GMP Standard Operations Procedures and Rental of GMP Laboratory for Seven Days		\$ 8,500	- 0 -	- 0 -
D-54	Cornell University Medical Center New York, New York	Data Transcription, Pellet Manufacture, RIAs, Publication and Illustration Relating to Implant Study		3,000	3,000.00	3,000.00

RESEARCH PROJECTS BY AID CONTRACEPTIVE RESEARCH AREA
 UNDER COOPERATIVE AGREEMENT AID/DPE-0546-A-00-1003-00
 7/1/83-12/31/83

IV. SYSTEMIC CONTRACEPTION (continued)

C. OTHER

<u>PARFR #</u>	<u>INSTITUTION & INVESTIGATOR(S)</u>	<u>TITLE</u>	<u>DATES</u>	<u>BUDGET</u>	<u>EXPENDITURES THIS PERIOD</u>	<u>TOTAL EXPENDITURES</u>
309	Northwestern University Medical School Chicago, Illinois Raksha Mehta, Ph.D.	"Ovulation Inhibition by Anordrin"	1/1/82- 6/30/84	\$148,988	\$15,010.57	\$93,634.75
347	The University of Texas Health Science Center San Antonio, Texas Ricardo H. Asch, M.D.	"Studies on the Anovulatory Potency and Side Effects on an Inhibitory Analog of LH-RH in Cynomologous Monkeys"	11/1/83- 10/31/85	145,501	- 0 -	- 0 -
351	Tulane University Medical Center New Orleans, Louisiana Andrew V. Schally, Ph.D.	"Development of Methods for Female and Male Contraception Based on LH-RH Antagonist"	1/1/84- 12/31/84	65,163	- 0 -	- 0 -
D-44	Northwestern University Chicago, Illinois	Animal Purchase and Care - 12 Cynomologous Monkeys for Anordrin Study			2,232.91	2,232.91
D-45	Reproductive Endocrinology Laboratory Fund Chicago, Illinois	Publication Expenses Relating to Anordrin Study			377.99	377.99
D-51	University of Alabama in Birmingham Birmingham, Alabama	Ovulation Inhibition in 4 Baboons Using Anordrin		2,801	2,551.00	2,551.00
D-51	Reproductive Endocrinology Laboratory Fund Chicago, Illinois	Laboratory Tests and Analysis (Ovulation Inhibition by Anordrin)		3,228	- 0 -	- 0 -

RESEARCH PROJECTS BY AID CONTRACEPTIVE RESEARCH AREA
 UNDER COOPERATIVE AGREEMENT AID/DPE-0546-A-00-1003-00
 7/1/83-12/31/83

IV. SYSTEMIC CONTRACEPTION (continued)

C. OTHER

1. MALE PHARMACOLOGICAL METHODS

<u>PARFR #</u>	<u>INSTITUTION & INVESTIGATOR(S)</u>	<u>TITLE</u>	<u>DATES</u>	<u>BUDGET</u>	<u>EXPENDITURES THIS PERIOD</u>	<u>TOTAL EXPENDITURES</u>
315	Northwestern University Evanston, Illinois Erwin Goldberg, Ph.D.	"Immunologic Suppression of Fertility by Synthetic Antigenic Determinants of Dehydrogenase-C4 - Extension of PARFR-232"	3/1/82- 6/30/84	\$122,093	\$15,042.00	\$86,956.55
329	Northwestern University Evanston, Illinois Erwin Goldberg, Ph.D.	"Targeting Liposomes to the Male Reproductive Tract with Antibody LDH-4"	12/1/82- 11/30/83	10,000	5,135.84	8,710.58
D-26	Connaught Laboratories Willowdale, Ontario, Canada	Diphtheria and tetanus toxoid (and customs clearance) for PARFR-315			1,248.00	8,162.40
D-32	Biologic Resources Laboratory, University of Illinois	Animal maintenance, papio baboons for PARFR-315			12,257.68	50,205.82
D-42	Jim Burns Chicago, Illinois	Injection of baboons for PARFR-315			450.00	585.00

RESEARCH PROJECTS BY AID CONTRACEPTIVE RESEARCH AREA
 UNDER COOPERATIVE AGREEMENT AID/DPE-0546-A-00-1003-00
 7/1/83-12/31/83

V. BARRIER CONTRACEPTION

B. FEMALE

<u>PARFR #</u>	<u>INSTITUTION & INVESTIGATOR(S)</u>	<u>TITLE</u>	<u>DATES</u>	<u>BUDGET</u>	<u>EXPENDITURES THIS PERIOD</u>	<u>TOTAL EXPENDITURES</u>
326	Arthur D. Little, Inc. Cambridge, Massachusetts J.P. Polidoro, Ph.D.	"Evaluation in Sheep of Orabase® as a Barrier Contraceptive"	12/1/82- 5/31/83	\$ 29,408	\$ 833.35	\$20,954.69
338	Rush-Presbyterian-St. Luke's Chicago, Illinois Lourens J.D. Zaneveld, D.V.M., Ph.D.	"Development of Sperm Enzyme Inhibitors as Vaginal Contraceptives"	7/1/83- 6/30/84	49,768	4,486.67	4,486.67
345	University of Southern California Medical Center Los Angeles, California Gerald S. Bernstein, M.D., Ph.D.	"Effect of the Vaginal Spermicidal Barrier Contraceptive on Sperm Transport in the Human"	10/1/83- 3/31/84	6,375	- 0 -	- 0 -

RESEARCH PROJECTS BY AID CONTRACEPTIVE RESEARCH AREA
 UNDER COOPERATIVE AGREEMENT AID/DPE-0546-A-00-1003-00
 7/1/83-12/31/83

VII. MISCELLANEOUS

<u>PARFR #</u>	<u>INSTITUTION & INVESTIGATOR(S)</u>	<u>TITLE</u>	<u>DATES</u>	<u>BUDGET</u>	<u>EXPENDITURES THIS PERIOD</u>	<u>TOTAL EXPENDITURES</u>
321	The University of Illinois at Chicago Chicago, Illinois John C.M. Tsibris, M.D.	"Guaiacol Peroxidase Levels: Predictors of Ovulation in Women"	8/1/82- 7/31/83	\$ 27,391	\$ 4,952.79	\$27,036.45

PARFR SCIENTIFIC ADVISORY COMMITTEE

MEETING XXXXII

Friday, July 22, 1983

THE WESTIN HOTEL
North Michigan at Delaware
Chicago, Illinois 60611
(312) 943-7200

MINUTES

VOTING SAC MEMBERS PRESENT

John J. Sciarra, M.D., Ph.D.
Nancy J. Alexander, Ph.D.
Andrzej Bartke, Ph.D.
Robert T. Chatterton, Ph.D.
Elizabeth B. Connell, M.D.
Miriam H. Labbok, M.D., M.P.H.
Kamran S. Moghissi, M.D.
Dean L. Moyer, M.D.
Rochelle N. Shain, Ph.D.

VOTING SAC MEMBER ABSENT

Aquiles J. Sobrero, M.D.

PARFR STAFF PRESENT

Alfredo Goldsmith, M.D., M.P.H.
Diane Krier-Morrow, M.B.A.
Gerald I. Zatuchni, M.D., M.Sc.

USAID STAFF PRESENT

Jeff Spieler

The forty-second meeting of PARFR's Scientific Advisory Committee convened on Friday, July 22, 1983 at 9:00 A.M. at the Westin Hotel in Chicago, Illinois. Dr. John J. Sciarra presided as Chairman. Minutes of the October 17, 1982 meeting were approved.

I. ANNOUNCEMENTS

- A. Dr. A. Bartke, the University of Texas Health Science Center at San Antonio, is introduced to the Committee as a new member.
- B. Dr. Robert Chatterton is thanked for his years of contribution to the PARFR program. Dr. Aquiles Sobrero was unable to attend this, his last SAC meeting.
- C. Future SAC meeting dates:
 - December 14, 1983 (Wednesday) -- Hyatt Regency O'Hare
Chicago, Illinois
 - April 3, 1984 (Tuesday) -- New Orleans, Louisiana
(prior to AFS)

II. NEW BUSINESS

A. EXTENSION PROPOSAL

1. PARFR-319 -- George A. Digenis, Ph.D., The University of Kentucky, Lexington
"Development of Methodology for Following Microcapsule Transcervical Transport in Baboons Utilizing External Scintigraphy"
Funding Requested: \$111,155 Length of Project: Two Years

The Committee reviewed the technical report and extension proposal request and decided that the technique developed by Dr. Digenis, inspite of some laboratory artifacts, is a technique with valuable potential for studies of transport mechanisms in the female reproductive tract. However, at this stage, the proposed study is too basic and not relevant to PARFR's immediate objectives. In addition, the private drug company previously interested in the development, decided not to pursue this approach of a microsphere vaginal delivery contraceptive formulation.

B. FORMAL PROPOSALS

1. Thomas R. Tice, Ph.D., Southern Research Institute, Birmingham, Alabama
"Development of Controlled-Release Testosterone Microcapsules for Fertility Regulation of Males"
Funding Requested: \$49,641 Length of Project: One Year

In addition to the staff review of this proposal, the Committee reviewed Dr. Emil Steinberger's independent review. The Committee unanimously encouraged implementation of this concept. However, they requested to review the drug release study in Rhesus monkeys since the amount that should be administered to monkeys would probably be significantly lower than the anticipated human dose, to correct for differences in body weight. The discussion on the type of animal to be used for the drug release studies (castrated male or female Rhesus monkeys) was postponed until the Dec. 14, 1983 Scientific Advisory Committee meeting (when Dr. Asch submits his proposal).

2. Ralph M. Richart, M.D., Presbyterian Hospital in the city of New York
"A Rapid and Effective Percutaneous Intra-Vas Injection for Male Sterilization"
Funding Requested: \$59,951 Length of Project: One Year

PARFR's technical staff informed the Committee that the PI had submitted a pilot proposal which was reviewed in-house and independently by Dr. Nancy Alexander and approved for implementation. However, due to the importance of the area, AID technical staff requested a formal proposal which was reviewed and approved by SAC provided that Dr. Richart rewrite the methodology section clearly indicating the number of animals to be used in each experiment and the criteria of selecting the best formulation for the final studies in the laboratory animal. PARFR staff members, with the concurrence of the Committee, will request the PI to eliminate from this proposal all tasks relating to the development of a modified, improved vas clamp.

B. FORMAL PROPOSALS (continued)

3. Leonard E. Lafe, M.D., The University of Texas Health Science Center
at San Antonio

"Evaluation of Fimbrial Hoods as an Alternate Method of Female
Sterilization"

Funding Requested: \$4,308.70 -- UTHSC
\$3,960.00 -- Cabot

Length of Project: One Year

PARFR's technical staff reminded the Committee that this proposal is the outcome of development projects initiated by PARFR with a small pilot subcontract (PARFR-P13) to the University of Leuven and then three years of extensive animal studies at the University of Texas Health Science Center at San Antonio [PARFR-217(111N)]. All these projects lead to the development of the tubal hood device that now belongs to the private sector. In spite of the fact that PARFR technical staff and SAC members agree that such a female sterilization technique will have a limited use in the main stream of the family planning program, they recognize that such a technique, if perfected, could be very important for the Moslem society; hence a limited and very well controlled Phase I clinical trial in U.S.A. centers was approved. Initiation of such studies is dependent on obtaining an approved FDA IDE.

4. Jacques Hamou, M.D., Tenon Hospital, University of Paris, France
"Hysteroscopic Delivery of an Intra-Tubal Device for Female
Sterilization"

Funding Requested: \$11,000

Length of Project: One Year

Dr. Sciarra and PARFR's technical staff had the opportunity to see the film presented by Dr. Hamou at the April, 1983 AFS meeting in San Francisco. In this film, Dr. Hamou showed his new hysteroscope and improved tubal plug used for female sterilization. The technique and device have the potential to solve the majority of the problems encountered by other researchers in this area such as Hosseinian and Brundin. PARFR's technical staff approached the PI and developed the protocol for prospective data collection for 100 cases. The Committee approved the proposal.

C. INFORMAL PROPOSAL

1. Thomas S. Moulding, M.D., University of Colorado School of Medicine,
Denver, Colorado

"Transcervical Oviduct Occlusion by Thermal Liquid Coagulation"

Funding Requested: \$130,302

Length of Project: Three Years

A similar proposal was reviewed and not approved by PARFR's SAC in September, 1977. The Committee questioned the safety of the procedure in that technique failure could cause a major complication. Also, PARFR and other organizations have developed viable techniques for transcervical sterilization. Most of these techniques are in clinical trials or soon to be. The Committee felt that it was inappropriate for PARFR to launch such a project at this time in that there are no advantages over current methods with proven safety and effectiveness.

42

D. PILOT STUDY PROPOSAL

1. Lindsay F. Hofman, Ph.D., Virginia Mason Research Center, Seattle, Washington
"Ovulatory Time Determined by Measurement of Hormones in Saliva"
Funding Requested: \$7,500 -- Pilot Study Length of Project: Two Years
\$35,164 -- Extended Research

The Committee voted unanimously not to approve this project. They felt that salivary determinations (already studied by WHO and others) of 17-OH-progesterone are not likely to provide information which is not readily available from urinary measurements. The probability of developing a simple, reliable and self-administered test appears to be unacceptably low.

E. TECHNICAL REPORT REVIEW

PARFR-300 -- Charles E. Flowers, Jr., M.D. and Lee R. Beck, Ph.D.,
University of Alabama in Birmingham
"Poly (lactide-co-glycolide) Norethisterone Microcapsule Study
(Poly NET-90)"

PARFR-300I -- Giuseppe Benagiano, M.D., Associazione Per Studio della
Riproduziorone Umana, Rome, Italy
"Poly (lactide-co-glycolide) Norethisterone Microcapsule Study
(Poly NET-90)"

PARFR-300T -- Jose P. Balmaceda, M.D., The University of Texas Health
Science Center at San Antonio
"Poly (lactide-co-glycolide) Norethisterone Microcapsule Study
(Poly NET-90)"

PARFR-331 -- Danny H. Lewis, Ph.D. and Lee R. Beck, Ph.D., Stolle Research
and Development Corporation, Birmingham, Alabama
"Development of an Improved Microencapsulation Process for
Norethisterone (Two-Step)"

PARFR-333 -- Charles E. Flowers, Jr., M.D. and Lee R. Beck, Ph.D.,
University of Alabama in Birmingham
"Poly-gly NET 180 Microcapsule System"

PARFR-333T -- Jose P. Balmaceda, M.D. and Ricardo H. Asch, M.D., The
University of Texas Health Science Center at San Antonio
"Poly-gly NET 180 Microcapsule System"

The SAC Committee was informed about negotiations between PARFR, FDA, Stolle, SRI, AID/W, Ortho and FHI in relation to the entire strategy of the Poly NET Delivery Systems. It was agreed by AID/W that PARFR's responsibility will end after completion of Phase II clinical studies. Responsibilities for Phase III and NDA application will be implemented by other organizations. It was also decided that the system that will be pursued more aggressively will be the 90-Day System. A pert chart was prepared by Dr. F. Greenslade and a protocol for the Phase II clinical trial was prepared by Dr. Goldsmith

E. TECHNICAL REPORT REVIEW (continued)

PARFR-300, 300I, 300T, 331, 333, 333T (continued)

and presented to SAC. In addition, the outcome of the July 20th investigators meeting on the 90-day protocol was shared with SAC members. Contracts were prepared by PARFR's administrative staff and actual study initiation depends on SRI delivering the Poly NET syringes for distribution to the 5 centers. The Phase II protocol for the Poly NET 180 will be written by PARFR staff and submitted to the FDA in the early Fall.

PARFR-309 -- Raksha Mehta, Ph.D. and Robert T. Chatterton, Ph.D.,
Northwestern University Medical School, Chicago, Illinois
"Ovulation Inhibition by Anordrin"

The Committee reviewed the technical report and the recommendation of the AID evaluation team. SAC concurs that there would be advantages to conduct a bioavailability and drug release study in China in human volunteers if arrangements can be made through WHO. However, plans should be made in order to continue the experiment at Northwestern University and duplicate some of them in another monkey species and be ready to implement the FDA required toxicology studies if the data from China is promising or if the study cannot be conducted in Chinese women in a reasonable period of time. Dr. Raksha Mehta resigned as of June 30, 1983; Dr. Chatterton will continue as sole PI.

PARFR-315 -- Erwin Goldberg, Ph.D., Northwestern University, Evanston,
Illinois
"Immunologic Suppression of Fertility by Synthetic Determinants of Lactate Dehydrogenase-C₄, Extension of PARFR-232"

The technical report was reviewed in conjunction with AID's evaluation team recommendations related to this project, Drs. Alexander and Goldberg's trip report to India and a cable from USA Embassy in India related to the immunological aspects incorporated in the recently signed Indo-American Scientific agreement. PARFR staff will explore the feasibility of additional studies in the LDH-X area in India and the feasibility of organizing a task force on immunology.

PARFR-320 -- Donald L. Wise, Ph.D., Dynatech R/D Company, Cambridge,
Massachusetts
"Levonorgestrel Rods Drug Release Study"

PARFR was able to obtain from NIH, at no cost to PARFR, the performance of the small animal (rabbit) drug release study. Data should be available for the next SAC meeting in which the following two alternatives will be discussed: human drug release studies in Wales or FDA IND submission.

PARFR-321 -- John C.M. Tsibris, M.D., University of Illinois College of
Medicine, Chicago, Illinois
"Guaiacol Peroxidase Levels: Predictors of Ovulation in Women"

The preliminary data was reviewed and a formal proposal was requested for consideration at the December 14, 1983 SAC meeting.

44

E. TECHNICAL REPORT REVIEW (continued)

PARFR-324 -- Richard L. Dunn, Ph.D., Southern Research Institute,
Birmingham, Alabama
"Development of a Fibrous IUD Delivery System for Estradiol/
Progesterone"

The release rate with the Estradiol fibers were reviewed and a special meeting will be held in early Fall with Dr. Moghissi's participation in order to review the data in detail, formulate a strategy for continuation of the E & P vector and preparing the clinical component of the IND to be submitted in winter to the FDA.

PARFR-325 -- Richard L. Dunn, Ph.D., Southern Research Institute,
Birmingham, Alabama
"Development of a Vaginal Ring Delivery System for Norgestimate"

The problems with construction of a coaxial ring were reviewed. Even though the PI was successful in the development of a triaxial ring releasing Norgestimate, this project will be tabled due to lack of present interest by Ortho in pursuing such a delivery system until NDA for oral formulation is obtained.

PARFR-326 -- Andrew Sivak, Ph.D. (Replaced J.P. Polidoro, effective
April, 1983), Arthur D. Little, Inc., Cambridge, Massachusetts
"Evaluation in Sheep of Orabase® as a Barrier Contraceptive"

The final technical report was reviewed and the project will not be continued due to the fact that it will take considerable time and funding to prepare an Orabase plus nonoxynol contraceptive that will have a similar effectiveness rate to those spermicides and vaginal sponges that are currently being used.

PARFR-330 -- Brij B. Saxena, Ph.D., D.Sc., Cornell University Medical
College, New York, New York
"A Clinical Evaluation of the Subdermal Norethindrone Pellet
(Phase II)"

Preliminary data was reviewed and depending on the outcome of this Phase II and PARFR staff site visit to be conducted in early Fall, this long-acting steroidal delivery system could be ready to be transferred to another agency for further Phase III clinical studies.

PARFR-332 -- Danny H. Lewis, Ph.D. and Lee R. Beck, Ph.D., Stolle Research
and Development Corporation, Birmingham, Alabama
"Development of an Injectable Long-Acting Estradiol Formulation"

The preliminary report was reviewed and SAC requested that the PI should, in his next technical report, address the eventual clinical use of such a delivery system, emphasizing ethynil estradiol in the upcoming PARFR-supported baboon drug release studies.

45

E. TECHNICAL REPORT REVIEW (continued)

PARFR-334SRI -- Thomas R. Tice, Ph.D., Southern Research Institute,
Birmingham, Alabama
"Development of Controlled-Release Progesterone Microcapsule"

Several release rate curves were reported. The most promising one is the 75% loaded microcapsule. Discussion is underway with Johns Hopkins and the Catholic University in Santiago, Chile for a Phase I clinical trial to be initiated once an IND application is approved by FDA.

PARFR-337F -- Tapani Luukkainen, M.D., Ph.D., University of Helsinki,
Finland
"Use-Effectiveness of a Levonorgestrel-Releasing Intracervical Device"

Rochelle Shain reported on her site visit to perfect the questionnaire. She interviewed 10 women. The patients seemed to like the ICD and were not too upset by the spotting in the first month. Dr. Moghissi suggested a limited study with Dr. Luukkainen's ICD in a "squatting" population to measure the expulsion rate, once sufficient safety data is obtained in Finland.

III. ADMINISTRATIVE

- A. The following subagreement is executed on projects reviewed and approved at the March 28, 1983 SAC meeting:
1. PARFR-338 -- L.J.D. Zaneveld, D.V.M., Ph.D., Rush-Presbyterian-St. Luke's
Medical Center, Chicago, Illinois
"Development of Sperm Enzyme Inhibitors as Vaginal Contraceptives"
Funding Period: 7/1/83-6/30/84 Amount Funded: \$49,768
- B. Amendments to subagreements for projects reviewed and approved at the March 28, 1983 SAC meeting:
1. Amendment #2 to PARFR-315 -- Erwin Goldberg, Ph.D., Northwestern Univer-
sity, Evanston, Illinois
"Immunologic Suppression of Fertility by Synthetic Antigenic
Determinants of Lactate Dehydrogenase-C₄"
Extended to: 6/30/84 Additional Funding: \$45,904
 2. Amendment #2 to PARFR-309 -- Robert T. Chatterton, Ph.D., Northwestern
University, Chicago, Illinois
"Ovulation Inhibition by Anordrin"
Extended to: 6/30/84 Additional Funding: \$57,920
 3. Amendment #1 to PARFR-328B -- Marcos Paulo P. de Castro, M.D., PRO-PATER,
Sao Paulo, Brasil
"An Evaluation of an Improved Needle for Transcutaneous Vas Closure"
Extended to: 6/30/84 Additional Funding: \$7,062

46

IV. MISCELLANEOUS

- A. PARFR Workshop on "Contraceptive Drug Delivery Systems" was held May 31 - June 3, 1983 at the Royal Orleans Hotel, New Orleans. One-hundred and fifteen (115) individuals attended representing 16 countries.
- B. The interim report of the evaluation of the PARFR program was included on the Agenda for SAC discussion. The site visit "TEAM" included: Michael J.K. Harper, Ph.D., Sc.D. (Chairman), David Archer, M.D., D.J. Patanelli, Ph.D. and J. Spieler. The site visit consisted of Dr. Patanelli's attending the March 28, 1983 SAC meeting; Dr. Archer's attending the PARFR Workshop on "Long-Acting Contraceptive Delivery Systems" in New Orleans, May 31 - June 3, 1983; a site visit of SRI, Stolle and UAB in Birmingham, Alabama, June 13-14, 1983 and a site visit to PARFR including scientific presentations on PARFR supported research by Drs. Chatterton, Goldberg and Zaneveld, on June 15-17, 1983. The evaluation was requested by PARFR's funding agency, the United States Agency for International Development and the evaluation was supported by the National Science Foundation.

SAC made the following comments relating to recommendations in the Team's written report. The following numbers coincide with the numbered recommendations:

3. SAC agrees with the Team that an individual could be appointed to SAC for an initial probationary term of one year during which time his/her performance, interest and expertise can be evaluated. If satisfactory, the member would then be appointed for another two years. Under special circumstances, appointments could be extended.
4. SAC generally agrees with the Team recommendation that SAC members should not be receiving funds from PARFR at the time of appointment nor be eligible for funding while serving on SAC. However, exceptions must be taken into account when the PI or the project is unique, and or if a SAC member is requested by PARFR to be part of a multi-centered clinical trial.
5. SAC does not agree with the Team recommendation that SAC areas of expertise should be broadened with individual experts such as a biostatistician, polymer chemist, etc. If those areas are needed, PARFR's staff should hire a consultant for a special task, as they have done in the past.
6. SAC does not agree with the Team recommendation that SAC members absent themselves from discussion concerning projects originating from their own institution, when they are not the PI. However, they should continue to abstain from voting on projects submitted by their home institution.
7. SAC unanimously recommends that Dr. Sciarra continue as chairman of SAC with full voting privileges.

IV. MISCELLANEOUS (continued)

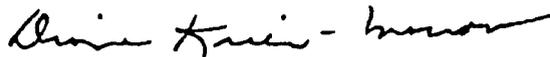
8. SAC agrees in part with the Team recommendation regarding the style of PARFR staff proposal written review; however, SAC also recognizes that PARFR staff are individuals with their own area of expertise and they are entitled to their own recommendations for funding or not funding a particular project.
9. SAC agrees with the Team regarding SAC involvement in strategy review. PARFR staff will present a priority list of projects for discussion in the December 14, 1983 SAC.
13. SAC fully agrees with the Team and staff recommendation that the unnecessary of double IRB approvals for studies conducted at DHHS approved institutions.
19. See 9.
23. SAC recognized the issue of young investigators and congratulated PARFR staff for continuing to identify new centers and investigators inspite of the reduction of core funding of such donor agencies like Rockefeller, Ford and IDRC.
28. SAC concurs with the Team in congratulating all PARFR staff on the excellent job they are doing.

There being no further business, the meeting adjourned at 3:00 P.M.

Respectfully submitted,



John J. Sciarra, M.D., Ph.D.
Program Director, PARFR
Chairman, Scientific Advisory Committee



Diane Krier-Morrow, M.B.A.
Director of Administration, PARFR

PARFR SCIENTIFIC ADVISORY COMMITTEE

MEETING XXXXIII

Wednesday, December 14, 1983

HYATT REGENCY O'HARE
Rosemont, Illinois
(312) 696-1234

MINUTES

VOTING SAC MEMBERS PRESENT

John J. Sciarra, M.D., Ph.D.
Nancy J. Alexander, Ph.D.
Andrzej Bartke, Ph.D.
David A. Blake, Ph.D.
Elizabeth B. Connell, M.D.
William Droegemueller, M.D.
Uwe Goebelsmann, M.D.
Miriam H. Labbok, M.D., M.P.H.
Kamran S. Moghissi, M.D.
Antonio Scommegna, M.D.
Rochelle N. Shain, Ph.D.

VOTING SAC MEMBER ABSENT

Dean L. Moyer, M.D.

PARFR STAFF PRESENT

Alfredo Goldsmith, M.D., M.P.H.
Diane Krier-Morrow, M.B.A.
Gerald I. Zatuchni, M.D., M.Sc.

USAID STAFF PRESENT

Jeff Spieler
Laneta Dorflinger, Ph.D.

I. ANNOUNCEMENT

- A. Drs. Droegemueller, Goebelsmann and Scommegna were introduced to the Committee as new members. Dr. Laneta Dorflinger, a fellow in the Research Division, Office of Population, AID was introduced.
- B. PARFR's International Workshop on Intrauterine Contraception: Advances and Future Prospects will be held in Chicago, Illinois, May 29 - June 1, 1984.
- C. PARFR's Regional Symposium on Long-Acting Contraception was held in Alexandria, Egypt on November 3 and 4, 1983 with 247 in attendance.
- D. Future SAC dates: Wednesday, April 11, 1984 -- Chicago, Illinois
Monday, July 30, 1984 -- Washington, D.C.

II. NEW BUSINESS

A. FORMAL PROPOSALS

Lourens J.D. Zaneveld, D.V.M., Ph.D., Rush-Presbyterian-St. Luke's
Medical Center, Chicago, Illinois
"Development of an Acrosin Inhibitor-Releasing Device for Vaginal
Application"

Funding Requested: 1st Year -- \$69,702; 2nd Year -- \$70,064
2nd Year -- Additional Primate Cost -- \$21,000
Length of Project: Two Years

PARFR's Technical Staff explained to the Committee that the Agenda contained two proposals because the first one, which concentrated on a vaginal ring release system, was reviewed by the Staff and felt that a long-term delivery system was not the next step in this development. The PI was requested to rewrite the proposal concentrating on a true pre-phase I study which is also included in the agenda. Both Committee and Staff reviewed in depth the revised proposal and decided to table their decision until the April 11, 1984 SAC meeting, in order to allow time for a project development site visit and another reworked proposal. The project development site visit should contain experts in not only toxicology but also in the in vivo testing of sperm acrosin inhibitors.

Richard L. Dunn, Ph.D., Southern Research Institute, Birmingham, Alabama
"Development of a Vaginal Delivery System for Sodium Tetracycl
Sulfate, an Acrosin Inhibitor"

Funding Requested: \$75,000 Length of Project: One Year

Due to PARFR long-term involvement (i.e. Zaneveld above) with some sperm acrosin inhibitors and the lack of private sector interest with the proposed compound, the Committee felt that a new avenue of research in this area should not be funded at this time until all methodological problems are resolved, which hopefully will be done by Zaneveld and colleagues in the near future. The PI will be requested to provide the Eli Lilly toxicological data in order to re-review this project when pertinent.

John C.M. Tsibris, Ph.D., University of Illinois College of Medicine,
Chicago, Illinois

"Guaiacol Peroxidase Levels: Predictors of Ovulation in Women"
Funding Requested: 1st Year -- \$157,997 Length of Project: Three Years
2nd Year -- \$104,037
3rd Year -- \$115,558

The Committee decided that the information obtained up until now is encouraging; however, the proposal was not approved as written. The PI will be requested to present to the April 11, 1984 SAC meeting, a revised proposal with a reduced budget mainly dealing with guaiacol peroxidase measurement in a selected group of women with follow-up for at least 6 months.

A. FORMAL PROPOSALS (cont'd)

C. Irving Meeker, M.D. and Wilfred Roth, Ph.D., Maine Medical Center,
Portland, Maine

"A Tubal Plug and Clip Method for Female Sterilization; Safety and
Efficacy Studies"

Funding Requested: 1st Year -- \$31,069 Length of Project: Two Years
2nd Year -- \$37,509

The proposal was reviewed and SAC members agreed with PARFR Technical Staff that no action can be taken until FDA replies to the IDE submission. PARFR Staff and a consultant will assist Dr. Meeker with the clinical aspects of the IDE.

Tapani Luukkainen, M.D., Ph.D., University of Helsinki, Finland

"Levonorgestrel-Releasing Intracervical Device During Lactation"
Funding Requested: \$48,890 Length of Project: One Year

The Committee decided to table this proposal until a comprehensive technical report of the interval levonorgestrel ICD (PARFR-337F) is received and evaluated. The PI will be requested to submit a report for the April 11, 1984 SAC meeting.

PARFR-315 Erwin Goldberg, Ph.D., Northwestern University, Evanston,
Illinois

"Immunologic Suppression of Fertility by Synthetic Antigenic
Determinants of Lactate Dehydrogenase-C₄"

Funding Requested: 1/1/84-6/30/84 -- \$22,274
7/1/84-6/30/85 -- \$68,095

Length of Project: 18 Months

The proposal was rejected as proposed. The following suggestions were made: (1) the present primates should be mated immediately or following another booster injection of the peptide. (2) Prior to mating and during the various mating attempts, continue measuring blood levels of antibodies to LDH-C₄. (3) Serum sample from the experimental and controlled group should be submitted to Dr. Alexander for a blind study to detect antibodies.

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

Erwin Goldberg, Ph.D., Northwestern University, Evanston, Illinois

"Enhancement of the Secretary Immune Response to LDH-C₄"

Funding Requested: \$39,388 -- Oregon Regional Primate Research Center
\$11,500 -- Northwestern University

Length of Project: One Year

The proposal was approved.

51

D. TECHNICAL REPORT REVIEW (cont'd)

PARFR-301T -- Ricardo H. Asch, M.D., The University of Texas Health Science Center at San Antonio
"A Clinical Evaluation of the Bioabsorbable Subdermal Contraceptive Norethindrone Pellet Implant"

PARFR-330 -- Brij B. Saxena, Ph.D., D.Sc., Cornell University Medical College, New York, New York
"A Clinical Evaluation of the Subdermal Norethindrone Pellet (Phase II)"

PARFR-330M -- Roberto Rivera, M.D., Instituto de Investigacion Cientifica, Durango, Mexico
"A Clinical Evaluation of the Subdermal Norethindrone Pellet (Phase II)"

PARFR-330T -- Ricardo H. Asch, M.D., The University of Texas Health Science Center at San Antonio
"A Clinical Evaluation of the Bioabsorbable Subdermal Contraceptive Norethindrone Pellet Implant (Phase II)"

Outcome of PARFR site visit (10/7/83) and FDA site visit (Cornell) were reported. Negotiations with the private sector will take place in January, 1984. No further financial input of PARFR is expected until a comprehensive report on the multi-center, Phase II clinical trials can be evaluated.

PARFR-307 (FINAL) -- Lourens J.D. Zaneveld, D.V.M., Ph.D., University of Illinois at the Medical Center, Chicago, Illinois
PARFR-338 -- Rush-Presbyterian-St. Luke's Medical Center, Chicago, Illinois
"Development of Sperm Enzyme Inhibitors as Vaginal Contraceptives"

This technical report was discussed with the proposal.

PARFR-309 -- Robert T. Chatterton, Ph.D., Northwestern University Medical School, Chicago, Illinois
"Ovulation Inhibition by Anordrin"

Outcome of discussions with WHO were presented. In the next SAC meeting, the Phase I clinical protocol will be discussed. PARFR will probably fund, if approved, another center outside of China (supported by W.J).

PARFR-320 (FINAL) -- Donald L. Wise, Ph.D., Dynatech R/D Company, Cambridge, Massachusetts
"Levonorgestrel Rods Drug Release Study"

Based on NIH animal release studies, the project was terminated.

D. TECHNICAL REPORT REVIEW (cont'd)

PARFR-323 (FINAL) -- Lourens J.D. Zaneveld, D.V.M., Ph.D., University of Illinois at the Medical Center, Chicago
"Efficacy of Quinacrine and Tetracycline in the Primate"

The technical report was not reviewed by SAC since the histopathology data was unavailable.

PARFR-324 (FINAL) -- Richard L. Dunn, Ph.D., Southern Research Institute, Birmingham, Alabama
"Development of a Fibrous IUD Delivery System for Estradiol/Progesterone"

Drs. Scommegna and Moghissi reviewed the project in-depth on October 3, 1983 and approved the clinical protocol prepared by PARFR Staff. An IND will be prepared and submitted to FDA in Spring, 1984.

PARFR-325 (FINAL) -- Richard L. Dunn, Ph.D., Southern Research Institute, Birmingham, Alabama
"Development of a Vaginal Ring Delivery System for Norgestimate"

Study was terminated because of lack of private sector interest in delivering Norgestimate through the vaginal route.

PARFR-328B -- Marcos Paulo P. de Castro, M.D., PROPATER, Sao Paulo, Brasil
"An Evaluation of an Improved Needle for Transcutaneous Vas Closure"

PARFR will request an independent appraisal of this project by Dr. Michael Free.

PARFR-333 -- Charles E. Flowers, Jr., M.D. and Lee R. Beck, Ph.D., The University of Alabama in Birmingham
"Poly-gly NET 180 Microcapsule System"

PARFR-333T -- Jose P. Balmaceda, M.D. and Ricardo H. Asch, M.D., The University of Texas Health Science Center at San Antonio
"Poly-gly NET 180 Microcapsule System"

The Phase I study is progressing according to schedule. The final technical report is expected for the next agenda.

D. TECHNICAL REPORT REVIEW (cont'd)

PARFR-334SRI -- Thomas R. Tice, Ph.D., Southern Research Institute,
Birmingham, Alabama
"Development of Controlled-Release Progesterone Microcapsule"

PARFR-334UAB -- Lee R. Beck, Ph.D., The University of Alabama in Birmingham
"Pharmacokinetic Studies in Baboons Relating to PARFR-334SRI"

Based on the preliminary data, an IND will be prepared for submission to the FDA in Spring, 1984.

PARFR-339 -- Lourens J.D. Zaneveld, D.V.M., Ph.D., Rush-Presbyterian-St.
Luke's Medical Center, Chicago, Illinois
"Efficacy of Studies in Primates with the Shug in the Absence of a Tissue Wrap"

The preliminary outcome of the IDE submission to FDA was discussed. The PI will submit a proposal to consider the long-term toxicity studies requested by FDA for the next SAC meeting.

COLLAGEN SPONGE

A final technical report was reviewed.

WING SOUND II (HASSON)

Dr. Hasson will be requested to work with FHI (the computer facility) in order to prepare a report for the next SAC meeting.

Nonsurgical Female Sterilization with MCA

No studies with the new, improved radio-opaque MCA (Version III) will be initiated until the toxicology and pre-hysterectomy data is received.

III. MISCELLANEOUS

A. The following subagreements are executed on projects reviewed and approved at the July 22, 1983 SAC meeting:

1. PARFR-346 -- Thomas R. Tice, Ph.D., Southern Research Institute,
Birmingham, Alabama
"Development of Controlled-Released Testosterone Microcapsules for Fertility Regulation of Males"
Funding Period: 10/1/83-3/31/84 Amount Funded: \$49,641

55

III. MISCELLANEOUS (cont'd)

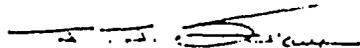
2. PARFR-344 -- Ralph M. Richart, M.D., Presbyterian Hospital, Obstetrics and Gynecological Services, New York, New York
"Percutaneous Intra Vas Injection for Male Sterilization"
Funding Period: 9/1/83-8/31/84 Amount Funded: \$49,668

 3. PARFR-350 -- Jacques Hamou, M.D., Tenon Hospital, University of Paris, France
"An Intra Tubal Device (ITD) for Female Sterilization"
Funding Period: 1/1/84-6/30/84 Amount Funded: \$11,000
- B. The following subagreements are executed on projects reviewed and approved at the March 28, 1983 SAC meeting:
1. PARFR-351 -- Andrew V. Schally, Ph.D., The Tulane University School of Medicine, New Orleans, Louisiana
"Development of Methods for Female and Male Contraception Based on LH-RH Antagonist"
Funding Period: 1/1/84-12/31/84 Amount Funded: \$65,153

 2. PARFR-347 -- Ricardo H. Asch, M.D., The University of Texas Health Science Center at San Antonio
"Studies on the Anovulatory Potency and Side Effects of an Inhibitory Analog of LH-RH in Cynomologous Monkeys"
Funding Period: 11/1/83-10/31/85 Amount Funded: \$145,501
- C. Dr. Sciarra requested that suggestions for topics for PARFR's 1985 Workshop be submitted in writing.
- D. A priority list of PARFR-supported projects, mentioned at the last meeting, was distributed for review and discussion.
- E. Dr. Sciarra thanked Drs. Alexander and Connell for their many years of PARFR/SAC participation.

There being no further business, the meeting adjourned at 3:30 P.M.

Respectfully submitted,



John J. Sciarra, M.D., Ph.D.
Program Director, PARFR
Chairman, Scientific Advisory Committee



Diane Krier-Morrow, M.B.A.
Director of Administration, PARFR

RESEARCH FRONTIERS IN FERTILITY REGULATION , VOLUME 2, NUMBER 6
December 1983

Available as PN-AAQ-257