

BIOMEDICAL RESEARCH PROJECTS

Funded or Monitored by

**Research Division
Office of Population
Bureau for Development Support
Agency for International Development**

FY 1980-1981

Prepared: June 1981

INTRODUCTION

The Office of Population serves the developing world with aid and activities for family planning. In order to achieve the goal of filling the unmet need for family planning, a primary purpose must be to make fully available those modern methods which are in use today. It is evident, however, that the available technology for contraception is not yet ideal.

As an adjunct to service delivery, the Research Division funds projects to develop new and improved means of contraception and to test the safety and efficacy of existing means in LDC settings. These projects are oriented towards field needs and technology transfer. They comprise about 3% of the total population budget.

This booklet contains synopses of the biomedical studies funded or monitored by the Research Division in FY 1980-1981. However, each AID-funded project (or "funding mechanism") may result in many individual studies. The table of contents is an outline of the subject areas covered. Each synopsis includes the study title, a contact person for detailed information, the mechanism through which AID funds the project, a brief project description, and approximate dates. Results to date are also given.

The following abbreviations are used for funding mechanisms:

IFRP - International Fertility Research Program

PARFR - Program for Applied Research on Fertility Regulation

STFM - Simplified Techniques of Fertility Management

ICCR - Population Council

TABLE OF CONTENTS

	Pages
I. FEMALE STERILIZATION	
A. Laparoscopy	1-2
B. Minilaparotomy	3
C. Transcervical	4-6
D. Reversible	7
E. Other	8-9
II. MALE STERILIZATION	
A. Vasectomy	10
B. Other	11-12
III. INTRAUTERINE CONTRACEPTION	
A. Postpartum - Postabortal	13-14
B. Medicated Devices	15
C. Other	16-17
IV. SYSTEMIC CONTRACEPTION (Male and Female)	
A. Oral Steroids	18-19
B. Injectables and Implants	20-22
C. Other	23-25
V. BARRIER CONTRACEPTION	26-28
VI. PREGNANCY TESTS	29
VII. EPIDEMIOLOGIC EVALUATION	30

I. FEMALE STERILIZATION

A. Laparoscopy

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Laparoscopy: Rocket Spring-loaded Clip vs Tubal Ring	Beth Dixon	Leuven, Belgium Plymouth, England	IFRP	Prospective clinical trial with 500 patients to evaluate complication and failure rates of the Rocket clip and tubal ring methods of tubal occlusion via laparoscopy. Methods were randomly assigned. Hypothesis: there are no differences between the two methods with respect to complication and pregnancy rates. Up to 12-month follow-up.	2/76	9/80	Clip: Surgical difficulties, 13.3%; surgical complications 1.7%. Tubal Ring: Surgical difficulties, 10.1%; surgical complications, 5.6%. No pregnancies reported for either technique.
Laparoscopic thermo-coagulation	Beth Dixon	Leiden, Netherlands	IFRP	Prospective clinical trial with 400 patients to evaluate the complication and failure rates of the thermocoagulation method of tubal occlusion. Up to 12-month follow-up.	12/76	5/80	Surgical difficulties: 5.6% interval patients, 3.2% postabortion patients. Surgical complications; 2.8% interval, 3.2% post-abortion Three (2.1%) pregnancies reported among interval patients more than 12 months poststerilization.
Laparoscopy vs Minilaparotomy: Rocket Spring-loaded Clip	Beth Dixon	Winchester, England	IFRP	Prospective clinical trial with 200 patients to evaluate the complication rates of laparoscopy and minilaparotomy procedures, using the Rocket Clip for tubal occlusions. Procedures randomly assigned. Hypothesis: there are no differences between the two procedures with respect to complication rates.	12/76	9/80	Laparoscopy: Surgical difficulties, 11.1%; complications 20%; pregnancy, 1.0% at 6 mos. Minilap: surgical difficulties, 9.1%; complications, 1.0%; pregnancy, 1.06% at 6 months.

I. FEMALE STERILIZATION
A. Laparoscopy

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Suprapubic endoscopy: Tubal ring, laprocator (laparoscope) equipment Evaluation	Beth Dixon	Cairo, Egypt Manila, Philippines Kuala Lumpur, Malaysia Baroda, India	IFRP	Prospective clinical trial with 1200 patients to evaluate the durability of the laprocator system and the complication rate associated with suprapubic endoscopy.	6/78		Admissions not complete. Preliminary analysis on 21 cases indicate 44.5% difficulties at surgery, mostly visualizing & grasping tubes and entering the peritoneum. Surgical injuries occurred in 8.7% of the patients, mostly tubal injury. Two-thirds of the women reported pelvic pain.
Open laparoscopy: Tubal ring, Laprocator (laparoscope) Equipment Evaluation	Beth Dixon	San Salvador, El Salvador (2 centers) Bandung, Indonesia Bombay, India	IFRP	Prospective clinical trial with 1200 patients to evaluate the durability of the laprocator system and the complication rate associated with the use of room air insufflation.	6/78		Admissions not complete. At one clinic, surgical difficulties were reported for 4.2% of the cases and surgical complications for 11.1%. Two-thirds of the women complained of pelvic pain. There were no major complications at early follow-up.

I. FEMALE STERILIZATION
 B. Minilaparotomy

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Tubal Ring vs Pomeroy Ligation	Beth Dixon	San Salvador, El Salvador Manila, Philippines Taipei, Taiwan Kuala Lumpur, Malaysia Dacca, Bangladesh (2 centers)	IFRP	Prospective clinical trial with 1200 patients to evaluate the complication and failure rates of the ring and Pomeroy methods of tubal occlusion via minilaparotomy. Methods are randomly assigned. Hypothesis: there are no differences between the two methods with respect to complication and pregnancy rates. Up to 12-month follow-up.	4/76		Long-term follow-up continuing. Tubal Ring: Surgical difficulties, 16.8%; surgical complications, 1.5%; Pomeroy: surgical difficulties, 19.8%; surgical complications, 1.0%. Pregnancy rates were the same for each technique, with 1 pregnancy at 6 months for each group.
Tubal Ring vs Rocket Spring-loaded Clip	Beth Dixon	Santiago, Chile Cairo, Egypt San Salvador, El Salvador San Jose, Costa Rica	IFRP	Prospective clinical trial with 800 patients to evaluate and complication and failure rates of the ring and Rocket clip methods of tubal occlusion via minilaparotomy. Methods are randomly assigned. Hypothesis: there are no differences between the two methods with respect to complication and pregnancy rates. Up to 24-month follow-up.	10/77		Admissions not complete. At one clinic, surgical difficulties were reported for 29.3% of the tubal ring cases and 24.3% of the Rocket clip cases. No surgical complications were reported for either procedure. Eleven technical failures, 10 with the ring and one with the clip, occurred. Ring failures were due to obesity, adhesions, thick tubes, and ovarian cysts. The clip failure was due to bilateral abscess. Surgical injuries occurred in 9.3% of ring patients and 2.9% of clip patients. No pregnancies were reported 6 months poststerilization.

I. FEMALE STERILIZATION
C. Transcervical

4.

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Evaluation of Quinacrine Hydrochloride Slurry	Lynda Cole	Santiago, Chile	IFRP	Prospective study of 200 patients to evaluate the effectiveness and complication rates with quinacrine slurries instilled transvaginally at admission and one and six months after the first instillation.	8/74		Results indicate 2.0% transient toxic psychosis and a 12-month gross lifetable pregnancy rate of 9.1 per 100 women. Follow-up continues.
Evaluation of Quinacrine Hydrochloride Pellets	Lynda Cole	Santiago, Chile Valdivia, Chile Baroda, India	IFRP	Prospective clinical trial of 650 patients to evaluate the effectiveness and complication rates associated with quinacrine pellets inserted transvaginally at admission and one and two months after the first insertion.	1/77		Preliminary results indicate no serious complications and a 12-month gross lifetable pregnancy rate of 1.5 per 100 women. Follow-up continues.
Data Collection and Analysis for MCA/FEMCEPT Clinical Trials	Ralph M. Richart	Columbia University New York, USA	PARFR	To determine the safety and efficacy of the single application Fertility Regulation (FEMCEPT) Device for the delivery of methylcyanoacrylate (MCA) to the fallopian tubes.	7/79	6/81	Approximately 80% of women show bilateral tubal blockage and no pregnancies reported thus far. Several approaches to improve closure rate being explored.
Phase I Clinical Trial of Fallopian Tube Closure using Methylcyanoacrylate (MCA) Tissue Adhesive delivered through the single-application fertility regulation (FEMCEPT) device	Hans Bauer	Bureau Mengen Cologne, West Germany	PARFR	(see above)	9/79	8/80	(see above)

I. FEMALE STERILIZATION

C. Transcervical

5.

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Phase I Clinical Trial of Fallopian Tube Closure using Methylcyanoacrylate (MCA) tissue adhesive delivered through the single-application fertility regulation (FEMCEPT) device	Sung-bong Hong	Korea University College of Medicine Seoul, Korea	PARFR	To determine the safety and efficacy of the single application Fertility Regulation (FEMCEPT) Device for the delivery of methylcyanoacrylate (MCA) to the fallopian tubes.	5/80	8/82	Approximately 80% of women show bilateral tubal blockage and no pregnancies reported thus far. Several approaches to improve closure rate being explored.
Phase I Clinical Trial of Fallopian Tube Closure using Methylcyanoacrylate (MCA) tissue adhesive delivered through the single-application fertility regulation (FEMCEPT) device	Ruben A. Apelo	JFMH Comprehensive Family Planning Center, Manila, Philippines	PARFR	(see above)	10/79	9/81	(see above)
Clinical trial of fallopian tube closure using MCA	Elsimar Metzker Coutinho	Maternidade Climerio de Oliveira, Salvador, Bahia, Brazil	PARFR	(see above)	9/80	9/81	(see above)
Chemical sterilization in the Cebus Appella monkeys	Renzo Antonini Filho	Centro de Estudos de Reproducao Humana de Botucatu, Botucatu, Sao Paulo, Brazil	PARFR	To evaluate transcervical blind delivery systems in the Cebus monkey.	5/80	5/81	Silver acetate unsatisfactory. Other vectors pending.

I. FEMALE STERILIZATION
C. Transcervical

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
A Fibrous Polymer for Delivery of Quinacrine to the Human Reproductive Tract	Richard L. Dunn	Southern Research Institute Birmingham, Alabama USA	PARFR	To develop a fibrous polymer to deliver quinacrine for non-surgical female sterilization.	9/80	3/81	First order release fiber developed.
Uterine Synechiae Produced by Cryosurgery	William Droegemueller	University of Arizona	Arizona	To develop a non-surgical method of female sterilization using cryosurgery.	1973		Results encouraging in prehisterectomy studies using liquid nitrogen.

I. FEMALE STERILIZATION

E. Other

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Topical Anesthesia Applied to the Fallopian Tubes	Beth Dixon	San Salvador, El Salvador Bangkok, Thailand	IFRP	Prospective clinical trial with 800 patients to evaluate the pain associated with or without the application of a topical anesthesia to the tubes during sterilization in tubal ring occlusion. Topical anesthesia or no topical anesthesia randomly was assigned to patients. Hypothesis: the use of topical anesthesia makes no difference in incidence and intensity of patient pain.	6/78		Results not yet available. Admissions not complete.
Evaluation of Various Procedures and Tubal Occlusion Methods	Beth Dixon	Townsville, Australia Valdivia, Chile Alexandria, Egypt Assuit, Egypt Cairo, Egypt (3 cntrs) San Salvador El Salvador (2 cntrs) Bandung, Indonesia Jakarta, Indonesia Ujung Pandang Indonesia Tehran, Iran Daegu, Korea Kwangju, Korea Pusan, Korea Seoul, Korea (3 cntrs) Ibadan, Nigeria Karachi, Pakistan Lahore, Pakistan Manila, Philippines Khartoum, Sudan Philadelphia, PA USA	IFRP	Multicenter prospective clinical trials with 10,350 patients to establish baseline data on the complication rates associated with various procedures and tubal occlusion methods for postpartum, postabortion and non-recently-pregnant patients. Up to 12-month follow-up.	6/74		Postoperative complication rates ranged from 2.9% to 12.9% in the various clinic locations. Admissions not complete for all clinic locations.

I. FEMALE STERILIZATION

E. Other

PROJECT STATUS

9.

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Comparison of Optic Visor versus Surgical Microscope for Reconstruction of the Fallopian Tube	John Rock	Baltimore	STFM	To determine which method will prove more effective and less expensive for tubal sterilization reversal.	7/79		No clear difference as yet.
Histopathologic Study of Female Sterilization Failures	Timothy Parmley	Baltimore	STFM	To elucidate possible mechanisms of female sterilization failure and to develop a hypothesis to improve efficacy.	7/79		Recanalization appears frequently to be related to endometriosis followed by fistulae formation. Leaving at least 4cm of proximal tubal segments might minimize this problem.

II. MALE STERILIZATION
A. Vasectomy

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Ligation and Excision	Beth Dixon	Cebu City, Philippines San Salvador El Salvador Dhiwala, Sri Lanka	IFRP	Prospective clinical trial with 2400 patients to evaluate the complication and failure rates associated with the ligation and excision technique of vas occlusion. Semen tests were performed to determine sterility.	12/76		Admissions not complete.
Surveillance of Health Effects of Vasectomy	Stephen Mumford	Oakland, California San Francisco, California	IFRP	To evaluate the relationship between prior vasectomy and a number of illnesses requiring vasectomy. Study includes vasectomized men and controls who had multiphasic health check-ups at the Kaiser-Permanente Medical Center.	7/1/80		Not yet available.

II. MALE STERILIZATION
B. Other

11.

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Development and Evaluation of a Reversible Vas Deferens Blocking Device	Lourens J.D. Zaneveld	University of Illinois at the Medical Center Chicago, Illinois	PARFR	To test in rabbits and primates a reversible vas deferens blocking device.	10/79	12/80	Inconclusive as yet.
New Method for Obstructing the Vas Deferens by Direct Injection of Chemical Agents: A Non-Operative Technique of Male Sterilization	Joseph E. Davis	Joseph E. Davis, M.D. New York, New York	PARFR	To determine the effectiveness and safety of a non-surgical technique for achieving male sterilization by injecting a sclerosing solution of 4 percent formaldehyde in alcohol percutaneously into two separate areas of the vas deferens.	9/80	8/81	Approximately 70 percent effective on one injection.
A Multi-Site Evaluation in Developed and Developing Countries of a Technique and Equipment for Transcutaneous Closure of the Vas Deferens by Electro Coagulation	Edwin L. Adair	Medical Dynamics, Inc. Englewood, Colorado USA	PARFR	To determine the effectiveness and safety of a transcutaneous vas closure technique using a bipolar electrical source.	9/80	8/81	Technical problems to date.
A Multi-Site Evaluation in Developed and Developing Countries of a Technique and Equipment for Transcutaneous Closure of the Vas Deferens by Electro Coagulation	Jose Freitas-Melo	Maternidade Climerio de Oliveira, Salvador Bahia, Brazil	PARFR	(as above)	9/80	9/81	(as above)

II. MALE STERILIZATION

B. Other

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
A Multi-Site Evaluation in Developed and Developing Countries of a Technique and Equipment for Transcutaneous Closure of the Vas Deferens by Electro Coagulation	Marcos Paulo P. de Castro	Propater Sao Paulo, Brazil	PARFR	To determine the effectiveness and safety of a transcutaneous vas closure technique using a bipolar electrical source.	9/80	9/81	Technical problems to date.
Is Sperm Antigen a Causative Agent for Atherosclerosis After Vasectomy	Nancy J. Alexander	Medical Research Foundation of Oregon Portland, Oregon	PARFR	To further define the role, if any, of immune complexes in atherosclerosis and glomerulonephritis.	7/80	12/80	Immune complexes appear important in this process in the rabbit.
Percutaneous Injection of Monoethanolamine Oleate as a Vas Deferens Sclerosing Agent	Marcos Paulo P de Castro	Centro de Reproducao Humana Sao Paulo, Brazil	PARFR	See title.	1/80	6/80	Ineffective.
Efficacy Testing of Frisch Intra-vasal Implants	Nancy J. Alexander	Medical Research Foundation of Oregon Portland, Oregon USA	PARFR	To determine the efficacy in cynomolgus monkeys of the micro-porous intra-vasal implants developed by Dr. David Frisch (MIT) under PARFR-P12.	11/79	10/80	Ineffective

III. INTRAUTERINE CONTRACEPTION
A. Postpartum-Postabortal

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Clinical Trials of the Delta Loop and Delta-T	Lynda Cole	Padang, Indonesia Jakarta, Indonesia Townsville, Australia Assuit, Egypt Manila, Philippines (2 centers) Kuala Lumpur, Malaysia (2 cntrs) Arica, Chile Mexico City, Mexico Cebu City, Philippines Dartford, England Taipei, Taiwan San Jose, Costa Rica Santiago, Chile Ankara, Turkey Zagazig, Egypt Bandung, Indonesia San Luis Potosi, Mexico Cairo, Egypt Hershey, USA Valencia, Spain Valdivia, Chile Gent, Belgium David, Panama Lima, Peru Seoul, Korea (2 cntrs) Dacca, Bangladesh Rio Claro, Brazil Salvador, Brazil Campinas, Brazil Bello Horizontal, Brazil	IFRP	The Delta Loop and Delta-T are compared with their non-sutured counterparts and with each other in a 12,000 case clinical trial. Timing of insertion (immediate vs. early) and type of insertion (hand vs. inserter) are also evaluated. Most studies are comparative, with IUDs or type of insertion randomly allocated to subjects.	5/79		Preliminary results show the Delta devices have a lower expulsion rate than their non-modified counterparts. The Delta T has a lower expulsion rate than the Delta Loop. Devices are more likely to be retained when inserted by hand and in the immediate postpartum period.

III. INTRAUTERINE CONTRACEPTION
B. Medicated Devices

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Local Effects of a Levonorgestrel-Releasing Intrauterine Device on the Endometrium and on the Genital Organs in the Human	David Edelman	Helsinki, Finland	IFRP	Study will further assess the safety of levonorgestrel-releasing IUDs. Endometrial biopsies will be obtained from 50 women who have used this IUD for 6-60 months and who elect to have it removed. Biopsies will also be obtained from women using copper-bearing IUDs.	10/1/80		Not yet available.
Levonorgestrel Concentrations in Target Tissues of Women Who Have a Levonorgestrel-Releasing IUD Inserted	David Edelman	Helsinki, Finland	IFRP	Concentrations of levonorgestrel in the endometrium, fallopian tubes, ovaries and subcutaneous fat will be evaluated in 20 women who have a scheduled hysterectomy 4-8 weeks following the insertion of a levonorgestrel-releasing IUD. This information will be useful in the assessment of the safety of the levonorgestrel releasing IUD.	12/1/81		Not yet available.
Evaluation of a Levonorgestrel-Releasing IUD	Lynda Cole	Uppsala, Sweden Bahia, Brazil Campinas, Brazil	IFRP	The project will evaluate the performance and safety of a levonorgestrel-releasing IUD compared to the TCu380Ag IUD. The comparative trial will be coordinated through the Population Council. A total of 550 insertions of each type of IUD will be performed.	11/1/80		Not yet available.
Clinical Trial of Lippes Loop with Trasylol	Lynda Cole	Essen, Germany Santiago, Chile	IFRP	The blood loss associated with the release of Trasylol from Lippes Loops is to be analyzed relative to the blood loss associated with the standard Lippes Loop. Devices are randomly allocated in a trial of 200 women.	6/79		The medicated IUDs have a higher expulsion rate than the nonmedicated devices. Complaints of intermenstrual spotting and bleeding were similar for the two IUDs. Blood loss data results are not yet available.

III. INTRAUTERINE CONTRACEPTION
C. Other

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Clinical Trials of Interval Insertions of Various IUDs	Lynda Cole	Cairo, Egypt Dacca, Bangladesh Rio de Janeiro, Brazil Khartoum, Sudan Bandung, Indonesia Ljubljana, Yugoslavia Santiago, Chile Rijeka, Yugoslavia	IFRP	In order to obtain baseline information for trials of new or improved devices, prospective and retrospective studies of the performance of various devices in common use are being performed. The trials number 6,551 women using the Lippes Loop, Copper T, Copper 7, the Soonawala device, the Finland T, and the Multiload.	4/75		These trials have provided a large amount of information on the performance of Standard IUDs. These data provide the IFRP with a baseline against which the performance of experimental IUDs can be evaluated.
Clinical Trials of Endometrial Aspiration Prior to IUD Insertion	Lynda Cole	Alexandria, Egypt Cairo, Egypt	IFRP	It was hypothesized that endometrial aspiration prior to IUD insertion would reduce the intermenstrual bleeding that normally follows insertion. A trial of 1,080 insertions was undertaken to test this hypothesis by comparing cases who received endometrial aspiration with those who did not. The cases receiving endometrial aspiration were chosen randomly.	4/75		Preliminary results indicate that devices inserted with and without prior endometrial aspiration performed similarly with respect to rates of removals for bleeding and bleeding related complaints.
Clinical Trials of the Nylon Wound T	Lynda Cole	Ljubljana, Yugoslavia San Juan, Puerto Rico	IFRP	The performance of the Nylon Wound T is compared with the copper wound T in a 400 case trial in order to determine if the copper contributes to the effectiveness of an IUD more than the increase in surface area of the copper. Devices are randomly assigned.	10/79		Results not yet available.

III. INTRAUTERINE CONTRACEPTION
C. Other

17.

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Clinical Trials of the TCU 380 Ag	Lynda Cole	Rejika, Yugoslavia Belgrade, Yugoslavia Manila, Philippines Panama City, Panama San Jose, Costa Rica Arica, Chile Mehalla-Kubra, Egypt Winchester, England	IFRP	The performance of the TCU 380Ag is compared with the Multiload Cu 375 or the Cu7 in a 2400 case clinical trial. Devices are randomly allocated.	3/80		Results not yet available.
Clinical Trial Evaluating the TCU 200 B with and without strings	Lynda Cole	Guatemala City, Guatemala Paris, France	IFRP	Incidence of PID will be compared for women with IUDs inserted with and without strings in an effort to determine the role of the IUD string in the increased risk of pelvic infection associated with IUD use. IUDs with or without strings are randomly allocated to subjects.	9/80		Results not yet available.
Graphic Assessment of Uterine Shape	Harrith M. Hasson	Harrith M. Hasson, M.D. Chicago, Illinois	PARFR	To determine the reliability of a new intrauterine measuring device that can provide a basis for more appropriate IUD fitting.	10/79	9/80	Excellent correlation between measured and computed fundal transverse dimensions and uterine angles. Further clinical studies planned.

IV. SYSTEMIC CONTRACEPTION
A. Oral Steroids

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Comparative Studies of High Estrogen Dose vs. Low Estrogen Dose Combined Oral Contraceptives	Winston Liao	Khartoum, Sudan Bangkok, Thailand Cebu City, Philippines Dacca, Bangladesh Sao Paulo, Brazil	IFRP	Prospective clinical trials with random allocation of patients to combined oral contraceptives containing 50µg or 35µg estrogen. Ongoing studies include 3000 patients. Data also collected on symptoms to determine their frequency associated with oral contraceptive use and their effects on discontinuation.	8/76		Admissions not complete. Results from one completed study of Neogynon vs. Lo-ovral show no pregnancies during the six-month study period. Total discontinuation rates were 9.7 per 100 women after 1651 woman-months of use for Neogynon and 6.0 per 100 women after 1952 woman-months of use for Lo-ovral. Preliminary data from an ongoing study of Norinyl vs. Nordette show no pregnancies and six-month discontinuation rates of 28.8 per 100 after 447 woman-months of use.
Comparative Studies of Two or More Low Estrogen Dose Combined Oral Contraceptives	Winston Liao	Assiut, Egypt Buenos Aires, Argentina Kelantan, Malaysia	IFRP	Prospective clinical trials with random allocation of patients to various combined oral contraceptives containing 35 µg estrogen. Ongoing studies include 900 patients. Data also collected on symptoms to determine their frequency associated with oral contraceptive use and their effects on discontinuation.	4/1/80		Admissions not complete. Preliminary data from one ongoing study of Brevicon vs. Lo-ovral show no pregnancies and six-month discontinuation rates of 10.3 per 100 women after 1423 woman-months of use for Brevicon and 2.0 per 100 women after 1421 woman-months of use for Lo-ovral.
Crossover Studies of High-to-Low-Dose Combined Oral Contraceptives	Winston Liao	Seattle, Washington Calcutta, India San Salvador, El Salvador Bangdung, Indonesia Khartoum, Sudan	IFRP	Prospective clinical trials with random allocation of patients to treatment groups. Each woman was changed from a 50µg estrogen dose combined oral contraceptive to a 35µg estrogen dose. Ongoing studies include 1350 patients. Data also collected on symptoms to determine their frequency associated with oral contraceptive use before and after crossover and their effects on discontinuation.	3/76		Admissions not complete. Preliminary data from one ongoing crossover study of Norinyl to Norinyl, Brevicon, and Nordette indicate a six-month pregnancy rate of 0.6 per 100 women and a total discontinuation rate of 42.4 per 100 women after 1570 woman-months of use for Norinyl. The majority of those discontinuing use reported non-medical reasons while only one-third gave a medical reason.

IV. SYSTEMIC CONTRACEPTION
A. Oral Steroids

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Clinical Trials of Progestogen-Only Oral Contraceptive in Lactating women	Winston Liao	Bombay, India Kuala Lumpur, Malaysia Cairo, Egypt Buenos Aires, Argentina	IFRP	To evaluate the side effects and effects on infants of breast-feeding women, women will be asked to choose between the use of a progestogen-only oral contraceptive and a nonhormonal contraceptive. One thousand women will be enrolled in each group. Women and their infants will be followed-up monthly for nine (9) months.	7/79		Insufficient data available for analysis of crossover effects. Studies in progress. Preliminary analysis of data from centers in Malaysia and India indicate no pregnancies have occurred among 317 cases. Of the 26 women who have discontinued, 22 did so by the third month following admission.

IV. SYSTEMIC CONTRACEPTION
B. Injectables and Implants

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUN. MECHANISM	DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Depo Provera Study	Winston Liao	Bandung, Indonesia	IFRP	The purpose is to examine: 1) bleeding patterns and drug-related side effects of 100 women administered Depo Provera (Medroxy-progesterone Acetate) and (2) the time of return of normal menstrual cycles following discontinuation of Depo Provera injections.	5/77		Results not yet available.
Health Survey of Depo-Provera Users	Pouru Bhiwandiwala	Bandung, Indonesia	IFRP	Depo-Provera has been offered as a method of fertility control since 1968 at the Hasan Sadikin Hospital, Bandung, and approximately 1000 women have used this method. These women are being contacted by social workers and interviewed at their homes. The women are offered an option to attend the hospital for a complete medical check-up and investigations. A control group of 300 volunteers will undergo the same interview and examination. The purpose of this project is to collect information on the side effects, if any, associated with Depo-Provera use among current and previous acceptors, based on the history, physical examination and investigation findings. The study will also determine reasons for discontinuation of Depo-Provera among previous users.	4/1/79		Study is ongoing and results not yet available.

IV. SYSTEMIC CONTRACEPTION
 B. Injectables and Implants

PROJECT STATUS

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Baboon Studies to Evaluate Non-Biodegradable Medicated Fibers for the Controlled-Release of Contraceptive Steroids Related to Research Supported Under PARFR-206 SRI	Lee R. Beck	University of Alabama in Birmingham Alabama USA	PARFR	To evaluate, <u>in vivo</u> , progesterone-releasing fibers as potential systems for contraception in the female.	11/79	10/80	The major accomplishments have been the measurement of the basic mechanical properties of steroid loaded fibers, the determination of the <u>in vivo</u> release characteristics of the fibers, the evaluation of a prototype fibrous contraceptive system in baboons, and the establishment of a correlation between the <u>in vitro</u> release characteristics and the <u>in vivo</u> effects upon the baboon endometrium.
Studies to Test an Injectable Delivery System for the Sustained Release of Norethisterone	Lee R. Beck	University of Alabama Birmingham, Alabama USA	PARFR	To develop and perfect a small particulate injectable system for the programmed delivery of the contraceptive steroid norethisterone.	4/80	3/81	Successful development of polymeric microspheres that provide 6- and 3-month durations of NET release. Acceptable NET release profiles have been demonstrated in baboons for both the 3- and 6-month system and Phase I human trials on the 6-month system are nearing completion.
Optimization of an Injectable Microcapsule Formulation for the 90-day delivery of Norethisterone	Danny W. Lewis	Southern Research Institute Birmingham, Alabama USA	PARFR	(see above)	4/80	3/81	(see above)

IV. SYSTEMIC CONTRACEPTION
 B. Injectables and Implants

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Preparation of Norethisterone Microcapsules	Danny W. Lewis	Southern Research Institute Birmingham, Alabama USA	PARFR	To develop and perfect a small particulate injectable system for the programmed delivery of the contraceptive steroid norethisterone.	4/80	3/81	Successful development of polymeric microspheres that provide 6- and 3-month durations of NET release. Acceptable NET release profiles have been demonstrated in baboons for both the 3- and 6- month system and Phase I human trials on the 6-month system are nearing completion.
Preparation of Norethisterone Microcapsules	Roberto Rivera	Instituto de Investigacion Cientifica Durango, Mexico	PARFR	(see above)	12/80	2/81	(see above)
A Clinical Evaluation of the Subdermal Contraceptive Norethindrone Pellet	B. Saxena and Gopi N. Gupta	The Cornell University Medical College New York, NY	PARFR	To prepare fused norethindrone pellets for Phase I clinical studies on 10 female volunteers. These studies are for the purposes of determining absorption and elimination of the contraceptive and measuring endocrine parameters during the menstrual cycles.	1/81	12/81	No results as yet.
Antifertility Effects of Luteinizing Hormone Releasing Hormone Analogue in the Female Rhesus Monkey	Ricardo H. Asch	The University of Texas Health Science Center San Antonio, Texas	PARFR	To provide information on luteolytic action of LH-RH analogue in normally cycling female Rhesus monkeys.	11/79	10/80	D-Trp-6-LH-RH induced luteolysis in regularly cycling rhesus monkeys when administered early during the lute phase. When administered during the mid-luteal phase or later, it failed to induce changes in corpus luteum function. Administration of human chorionic gonadotropin (hCG) overcame the effect of the agonist.

IV. SYSTEMIC CONTRACEPTION
C. Other

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
The Association Between Contraceptive Methods and Negative Health Outcomes	Winston Liao	Atlanta, Georgia USA	IFRP	Purpose of study is to evaluate the feasibility of conducting a case-cohort study to determine if women who have used Depo-Provera are at an increased risk of severe adverse effects compared to women who have used other contraceptive methods.	4/80		Not yet available.
Effect of LH-RH Agonist on Ovulation and Corpus Luteum Function in Women	Hugo Maia, Jr.	Maternidade Climerio de Oliveria Salvador, Bahia Brazil	PARFR	To determine in female volunteers the effects of LH-RH agonist on ovulation and subsequent corpus luteum function.	8/79	11/80	The initial results of this investigation suggest that high doses of LH-RH are effective in suppressing progesterone production by the corpus luteum. The ideal time for LH-RH administration is at midcycle right after ovulation and before the corpus luteum is completely formed.
Fertility Regulation by Control of Progesterone Clearance	Robert T. Chatterton	Northwestern University Evanston, Illinois USA	PARFR	To test the hypothesis that clearance of progesterone can be sufficiently increased by oral administration of encapsulated antiprogesterone antibodies to bring about involution of the endometrium.	9/79	12/80	Antiserum specific for progesterone (APA) has been produced. Encapsulation in polysiloxane prevents release of APA, but allows entry and binding of progesterone. Preparation of a more highly encapsulated form of APA for oral administration has begun.
Microencapsulation of Progesterone Antibodies	Kurt Gutfreund	IIT Research Institute Chicago, Illinois USA	PARFR	(see above)	11/79	10/80	(see above)

IV. SYSTEMIC CONTRACEPTION

C. Other

24.

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Induction of Luteolysis and Ovulation Inhibition by LRF Analogues	Samuel S.C. Yen	University of California San Diego, La Jolla, California USA	PARFR	To determine, in female volunteers, the efficacy of super analogs of LRF agonist to cause a luteolytic effect or ovulation inhibition.	11/80	10/81	LRF-Ag was administered at an appropriate time of the luteal phase to make evaluation of the luteolytic effect possible. Preliminary clinical impressions suggest that luteolysis occurred as indicated by the onset of menses within 6 days. In no subject was ovulation disturbed in any of the treatment or recovery cycles. When hCG (100 IU or 5000 IU) was added to the LRF-Ag treatment, the onset of menses was only delayed by 2-6 days.
Studies of LHRH Analogs	Harold Nash	Population Council Sweden, Brazil, etc.	ICCR	Various studies of LHRH Analogs including ovulation inhibition and insufficient luteal phase approaches.	9/80		Results pending.
Study of a Plant Product "Gossypol" as a Reversible Contraceptive in Male Rabbits	M.C. Chang	Worcester Foundation for Experimental Biology Shrewsbury, Mass. USA	PARFR	To study, in laboratory animals, the efficacy and toxicity of Gossypol.	1/80	12/80	Variable toxicity and effectiveness in rats, hamsters and rabbits.
Prostaglandin Levels in the Human Follicular Fluid in Relation to the Moment of Ovulation	Hugo Maia	Maternidade Climerio de Oliveira Salvador, Bahia Brazil	PARFR	To study the role of prostaglandins in ovulation and to assess prostaglandin inhibitors for antioviulatory effect.	12/80	8/81	No results to date.

IV. SYSTEMIC CONTRACEPTION
C. Other

25.

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Immunologic Suppression of Fertility by a Synthetic Antigenic Determinant of Lactate Dehydrogenase C4	Erwin Goldberg	Northwestern University Evanston, Illinois USA	PARFR	To determine if an antigenic fragment of lactate dehydrogenase C ₄ , a sperm specific isozyme, is capable of stimulating antibodies in rabbits with the peptide-carrier conjugate.	12/79	7/81	Antisera developed. Further results pending.
Prostaglandin Antagonists as Local Anti-Fertility Agents	Antonio Scommegna	Michael Reese Hospital and Medical Center Chicago, Illinois USA	PARFR	To develop an intrauterine device that would release a prostaglandin antagonist in order to improve the contraceptive efficacy of an IUD, and to reduce the side effects of pain and bleeding secondary to an IUD.	8/80	1/81	Results pending.
Vaginal Ring	Harold Nash Pop Council	Los Angeles, Sweden, Denmark, Finland, Brazil, Chile, Dominican Republic, Nigeria, Israel	ICCR	Large multi-country field trial comparing vaginal ring containing estradiol and levonorgestrel to analogous oral contraceptive. Study also underway comparing physiological effects of vaginal rings with those of different combinations of oral contraceptives.	10/77	9/81	One year results of comparative study give encouragement that the ring method can be highly effective. No pattern of adverse side effects has emerged. Clinical pharmacology studies indicate possible safety margin over pill except in area of effects on lipoproteins. Significance of lipoprotein effects being investigated.

V. BARRIER CONTRACEPTION

26.

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Development of Collagen Sponge Containing Spermicide	Milos Chvapil	The University of Arizona Health Sciences Center Tucson, Arizona USA	PARFR	(see below)	3/80	2/81	(see below)
Collagen Sponge Contraceptive - Testing of Efficacy in Human Volunteers	M.W. Heine	Texas Tech University Lubbock, Texas USA	PARFR	To determine the safety, acceptability and effectiveness of a collagen sponge contraceptive.	9/79	12/80	Disappointing results both with and without nonoxynol-9. Plan further studies with better patient selection criteria.
The Study of the Intravaginal Insert (IVI) Acceptability and Side Effects	Mohamed M. Ahmad	The University of Texas Health Science Center San Antonio, Texas USA	PARFR	To determine and assess the safety, acceptability and effectiveness of a new barrier contraceptive, the intravaginal insert (IVI). The IVI is a polyester vaginal plus to which nonoxynol-9 is added. During coitus it is released in spermicidally-effective quantities into the vagina.	7/80	6/81	Results pending.
Comparative Vaginal Contraceptive Trials	Winston Liao	Cairo, Egypt (3) Dacca, Bangladesh (2) Cebu City, Philippines Alexandria, Egypt Sao Paulo, Brazil Bangkok, Thailand Taichung, Taiwan Belgrade, Yugoslavia London, England Montreal, Canada Gothenburg, Sweden Birmingham, England	IFRP	Prospective clinical trials with random allocation of patients to one of five vaginal contraceptives. Comparisons are: Collatex vs. Neo Sampoo, Collatex vs. spermicidal foam, Collagex vs. diaphragm with spermicide, Neo Sampoo vs. spermicidal foam, Neo Sampoo vs. diaphragm with spermicide, and Neo Sampoo vs "EVT" (a US made foaming vaginal tablet). Data on acceptability and use-effectiveness will be obtained. Ongoing studies include 2550 patients. A total enrollment of 6100 cases is planned.	6/79		Studies in progress. Preliminary data from four ongoing comparative trials of Collatex vs. Neo Sampoo show that the Collatex has a slightly lower pregnancy rate, but a higher discontinuation rate than the foaming tablet. After pregnancy, the primary reason for discontinuation was a personal reason other than discomfort.

V. BARRIER CONTRACEPTION

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Development of Sperm Enzyme Inhibitors as Vaginal Contraceptives	Lourens J.D. Zaneveld	University of Illinois at the Medical Center Chicago, Illinois USA	PARFR	To evaluate <u>in vitro</u> and <u>in vivo</u> a number of sperm enzyme inhibitors for their vaginal contraceptive activity.	10/79	6/81	<p>Significant progress has been made in the development and testing of acrosin and hyaluronidase inhibitors. Three of these were shown to possess high vaginal contraceptive activity, much more so than Delfen cream.</p> <p>The synthesis of guanidinobenzoic acid derivatives of FDA approved phenols has been worked out successfully and one compound has already been synthesized in gram quantities. Another guanidinobenzoic acid derivative of an FDA approved phenol was shown to have very low toxicity and to prevent the <u>in vitro</u> fertilization of mouse gametes. Vaginal contraceptive studies are planned with both of these agents.</p>

V. BARRIER CONTRACEPTION

28.

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Clinical Trials of Neo Sampooon Loop Tablets	Winston Liao	Dacca, Bangladesh Bogota, Colombia (2) Provinces, Colombia (4) Mexico City, Mexico Alexandria, Egypt	IFRP	Neo Sampooon is a foaming tablet manufactured in Japan and contains 60mg of a surface spermicidal agent p-methanylphenyl Polyoxyethylene (8.8) ether. The purpose of these trials is to obtain data on the effectiveness and acceptability of the method.	3/78	6/80	Phase II studies are complete. The 12-month pregnancy rate was 10.0 per 100 women and the total discontinuation rate was 31.9 per 100 women after 14,912 woman-months of use. After pregnancy, the most frequently reported reasons for discontinuation were burning sensation and partner objection to use of method. Low acceptability in Colombia.
Effect of Spermicidal Detergent Nonoxynol-9 on Liver Function	Milos Chvapil	The University of Arizona Tucson, Arizona	PARFR	To determine, in female volunteers, the effects on liver function of daily intravaginal administration of standard doses of nonoxynol-9.	7/79	6/80	No effect on liver function tests in humans.
Gossypol as Spermicide	Harold Nash	Population Council and Helsinki, Finland	ICCR	Development and testing of gossypol as a spermicide for vaginal contraceptives.	6/80		In vitro results encouraging. In vivo results pending.

VI. PREGNANCY TESTS

29.

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Evaluation of Capillary Tube Pregnancy Test	Sandor Balogh	Taipei, Taiwan Madison, Wisconsin Chicago, Illinois	IFRP	Multicenter clinical trial with 1200 patients to evaluate the accuracy of the capillary tube pregnancy test and the Pregnosticon Dri-Dot test, especially for the detection of early pregnancy.	2/79	12/80	Study complete, 614 admissions. No appreciable differences between the two tests. Overall accuracy ranged from 71% at <42 days LMP to 94% at 50-56 days LMP for capillary tube test and 79% to 99% for dri-dot. False positives were <11% for both tests at early pregnancy, <2% at LMP >42 days.

PROJECT TITLE	CONTACT PERSON	CLINIC LOCATIONS	FUNDING MECHANISM	PROJECT DESCRIPTION AND PURPOSE	PROJECT STATUS		RESULTS
					START DATE	FINISH DATE	
Reproductive Risks and Mortality Survey	Judith Fortney	Bali, Indonesia	IFRP	The purpose of the study is to estimate the risk of death associated with different contraceptive methods, including no method, and the risks of death associated with pregnancy and its outcomes. The causes of death of all women of reproductive age in Bali over a 7-year period will be evaluated.	9/80		Not yet available.
Reproductive Risks and Mortality Survey	Kay Omran	Cairo, Egypt	IFRP	Similar in design to Bali study (see above).	2/1/81		Not yet available.