

BIBLIOGRAPHIC DATA SHEET1. CONTROL NUMBER
PN-AAJ-3772. SUBJECT CLASSIFICATION (695)
PC00-0000-0000

3. TITLE AND SUBTITLE (240)

Progress report, Aug. 1980 - Jan. 1981

4. PERSONAL AUTHORS (100)

5. CORPORATE AUTHORS (101)

Int. Fertility Research Program

6. DOCUMENT DATE (110)

1981

7. NUMBER OF PAGES (120)

49p.

8. ARC NUMBER (170)

613.943.I61d-80/81

9. REFERENCE ORGANIZATION (190)

IFRP

10. SUPPLEMENTARY NOTES (500)

11. ABSTRACT (950)

12. DESCRIPTORS (920)

Sterilization
Fert
Intrauterine devices
Information disseminationContraceptives
Pregnancy
Research

13. PROJECT NUMBER (150)

932053700

14. CONTRACT NO.(140)

AID/pha-C-1172

15. CONTRACT
TYPE (140)

16. TYPE OF DOCUMENT (160)

613.943

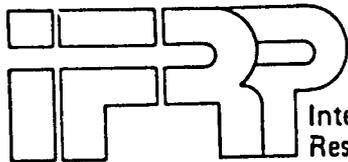
IGIF

1980/81

PN-AAJ-377

SEMIANNUAL REPORT
AID/pha-C-1172

August 1, 1980—January 31, 1981



International Fertility Research Program
Research Triangle Park, NC 27709 USA

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I. INTRODUCTION

This report on contract AID/pha-C-1172 covers the six months from August 1, 1980 through January 31, 1981. During this period the IFRP made important progress in developing a nonsurgical method of female sterilization and continued its program of clinical trials to evaluate and adapt newer methods in contraception with particular emphasis on the needs of lesser developed countries. Studies have centered on the postpartum IUDs (Delta Loops and Ts), that are about to be tested in a nationwide scale by two governments, the laprocator, Neo Sampooon and Collatex contraceptive sponge. It has proved difficult to recruit volunteers for crossover studies on different oral contraceptives. Studies to evaluate the long-term effects of Depo-Provera and vasectomy progressed according to schedule and are discussed in a later section of this report. The Reproductive Age and Mortality Study (RAMOS) in Bali, Indonesia, developed during the previous contract year, was initiated. In addition, the IFRP took a new initiative in providing technical assistance to developing countries' research programs through the provision of microcomputers.

II. RESEARCH AREAS

In the first six months of the contract year, the IFRP continued studies in its major research areas (female and male sterilization, intrauterine devices, systemics and barrier contraception). One of its major initiatives, the clinical trial of the Delta Loops and Delta Ts, provided sufficient data to demonstrate the improved

retention of these intrauterine devices over their non-modified counterparts when inserted in the immediate postpartum. Additional barrier contraception studies were also initiated.

Voluntary sterilization continues to be the single most important method of family planning worldwide. The IFRP is working to improve and adapt current surgical methods of voluntary sterilization and to explore fundamentally new nonsurgical techniques of tubal occlusion.

A. Surgical Female Sterilization

Immediate improvements in current methods of surgical sterilization have included collecting data on laproscator studies that include four studies of open laparoscopy with room air insufflation, four of suprapubic endoscopy, (modified minilap with Hasson trocar and blunt cannula), one of open laparoscopy with topical tubal anesthesia and one of suprapubic endoscopy with topical tubal anesthesia. Preliminary analysis of these laproscator studies, based on 1264 procedures (1038 laparoscopies and 226 suprapubic endoscopies), indicates that there were 17 technical failures, nine in the open laparoscopy series and eight in the suprapubic endoscopy series. The most common surgical difficulties encountered involved entering the peritoneum and visualizing, grasping and occluding the tubes. The rate of surgical difficulties was 3.3% with open laparoscopy and 44.5% with suprapubic endoscopy, but difficulty in visualizing the tubes, in fact, accounted for more than half the difficulties with suprapubic endoscopy. There were ten surgical injuries in

the laparoscopy series and 19 in the suprapubic endoscopy series, the most common being tubal injury (0.6% and 4.6%, respectively) and uterine perforation (0.3% and 3.7%, respectively).

Analysis of early data from the topical anesthesia studies in this series shows that a significantly ($\alpha = .05$) higher proportion of patients who did not receive topical anesthesia experienced pain.

The IFRP is currently recruiting centers to evaluate the Bleier clip (now called Secuclip manufactured by Colmed Ltd.) and expects to initiate these studies soon. Several investigators will evaluate a new piece of equipment, the Mini-Laparoscope from Gamma Industries, using a modified suprapubic endoscopy approach with the Pomeroy technique of tubal ligation. These evaluations will begin as soon as the equipment is available to the IFRP.

The IFRP continues to collect long-term follow-up data on women sterilized by different occlusive techniques and using different approaches to the fallopian tubes. Because of increasing evidence of ectopic pregnancies following sterilization, the IFRP will ask all past and present investigators to supply information regarding ectopic pregnancy among women sterilized in their practice. Early responses to this request are anticipated before the end of the contract year.

Plans for future clinical trials include evaluation of potentially reversible methods of sterilization such as the Teflon Sleeve and the Fimbrial Hood.

B. Nonsurgical Female Sterilization

A transcervical nonsurgical method of voluntary sterilization demands the use of a substance or procedure that will occlude the fallopian tubes without long-term damage to the endometrium and without danger of serious side effects if contact is made with the peritoneal cavity. The intrauterine insertion of quinacrine appears to fulfill these criteria.

The follow-up of women in clinical trials of the transcervical insertion of quinacrine pellets continues. Pellets were inserted in 373 women at three clinics. For those women receiving three administrations of quinacrine, the pellet method seems to be an improvement as indicated in the following table.

Gross Lifetable Pregnancy Rates for
Women Who Completed Three Administrations of
Quinacrine Hydrochloride

	6-Month Rate	Woman Months	12-Month Rate	Woman Months
Quinacrine solution (N=124)	5.7 ± 2.1	729	9.1 ± 2.6	1375
Quinacrine pellets with sodium thiopental (N=124)	0.8 ± 0.8	741	2.5 ± 1.4	1422
Quinacrine pellets without sodium thiopental (N=249)	1.5 ± 0.9	1217	1.5 ± 0.9	2035

The IFRP is making an effort to further simplify nonsurgical sterilization so that occlusion of the tubes can be achieved

with a single procedure. Work is being conducted on different anatomical presentations of the quinacrine, using quinacrine-loaded IUDs (TCu-220Cs over which a mixture of 80% quinacrine and 20% polyethylene oxide is molded) to carry the drug to the tubal ostia. The quinacrine mixture goes into solution within four hours and the IUDs were inserted in menstruating women awaiting hysterectomy for uterine prolapse. Extirpated uteri were examined to determine the presence of sclerosing lesions in the intramural portion of the tubes.

Several vectors have been used. When the drug is placed on the arms of a T-shaped device and the arms are kept in an upward flexed fashion, there is a closure rate of about 60%. With one simple modification of flexing the arms downward and reversing the molded quinacrine over it, tubal damage has been observed in 29 of the 32 specimens (90%). Work continues on studying the deployment of spring-activated IUDs in hysterectomy specimens, an Ypsilon configuration and the No Gravid device, which is made of nylon and has greater rigidity.

Sufficient progress has been made with chemical sterilization to necessitate the gathering of extensive toxicology data (relevant to FDA approval) and a move toward the investigation of possible rare adverse effects.

Under subcontracts from the IFRP, investigators at The Johns Hopkins University are conducting research on the toxicologic and teratologic effects to date. Data will be submitted to

obtain a Claimed Investigational Exemption for New Drug (IND) for the use of quinacrine hydrochloride as a sclerosing agent. The IFRP then expects to conduct additional limited clinical trials of quinacrine using pellets and several different IUD configurations as carriers for the quinacrine.

All material is prepared under a subcontract to the University of North Carolina School of Pharmacy to standards necessary for the preparation of the IND.

On January 15-16, 1981, the IFRP held a Meeting of Experts on chemical sterilization in an effort to develop a strategy for IFRP's future work with quinacrine hydrochloride. Future investigations will focus on the process and mechanism of action of quinacrine, dose and time-release rates, timing and number of insertions required, improved delivery system, expanded clinical trials and long-term follow-up of women who have received the transcervical administration of quinacrine. Some of these studies will start before the end of the contract year.

C. Male Sterilization

Vasectomy has been proven to be safe, effective and inexpensive. At present, the IFRP is not conducting trials of any new method of male sterilization. However, there is increasing concern over the interpretation of animal experiments that relate the evolution of atherosclerosis with previous vasectomy. The issue is one of great potential importance in developed and developing countries.

The IFRP has underway a subcontract with the Kaiser Research Foundation for a retrospective case-control study examining prior vasectomy and subsequent admission to the hospital. The relative risks of individual diseases, categorized by organ systems and by underlying pathophysiologic mechanisms, in relation to vasectomy, duration of vasectomy and age at vasectomy, will be explored. This project is proceeding on schedule and will be completed by December 31, 1981.

A feasibility study is also underway to determine the optimum locations to conduct case-control type studies of vasectomized men in one or more developing countries, and to explore any other methodologies to answer important questions that have been raised.

The IFRP also will continue to follow the developments made on percutaneous methods of male sterilization currently funded by PARFR, with a view toward conducting Phase II clinical trials in the future. A workshop on these methods will take place June 1981 to prepare IFRP research strategies for the study of these methods.

D. Pregnancy Testing, Pregnancy Termination and Menstrual Regulation

An evaluation of two pregnancy tests, the capillary tube and Dri-Dot, is complete. A final report, based on data of 614 women in three separate clinics, is being prepared for AID. The women were classified by the number of days from onset of last

menstrual period (LMP) to day of the pregnancy test. Measurements of sensitivity, specificity, false positive and negative rates and overall accuracy were used to compare the tests. Preliminary analyses show that both pregnancy tests were less accurate in the <42 days LMP group than in the later groups. In the <42 and 50-56 days LMP groups the Dri-Dot test yielded slightly more favorable results in terms of individual rates and overall accuracy, but it was somewhat less accurate than the capillary test in the 43-49 day period.

The University of North Carolina School of Pharmacy is conducting an evaluation, at the University of North Carolina-Chapel Hill Student Health Services, of five over-the-counter pregnancy tests available in the US. The tests were purchased by the IFRP. This collaborative project is now underway and the IFRP will be provided with a report assessing the accuracy, readability and sensitivity of each of the tests.

In response to requests by physicians working in countries where abortion is available, research has been initiated in an attempt to further reduce the dangers of abortion when done with limited medical facilities. The use of an intraamniotic injection of 10% saline is being evaluated in Yugoslavia. Another study is being conducted in which the insertion of laminaria is followed by the intraamniotic injection of 80 gm of urea and 5 mg of PGF_{2α}. A multicenter trial of a modification of the gynecologic syringe using a double valve that accepts 12-mm cannulae has been initiated at three centers.

A newly devised cervical osmotic dilator is being evaluated in a small multicenter trial. This synthetic dilator, composed of a polyvinyl alcohol sponge saturated with magnesium sulfate and compacted, promises to be not only easier but cheaper to manufacture than natural laminaria. Data on 18 cases have been received; blood samples from these patients have been analyzed for levels of magnesium, and results indicate they are within normal range.

No new studies of pregnancy termination are envisioned.

E. Intrauterine Devices

The IFRP is evaluating several types of IUD modifications that should result in improved IUD performance and acceptability: postpartum IUDs that reduce the risk of expulsion and tailless IUDs that may reduce the risk of infection.

At the end of the reporting period the IFRP reached a milestone in the clinical trial of the postpartum insertion of modified IUDs. The modification consists of adding biodegradable extensions of #2 chromic gut sutures to Lippes Loop D and TCu-220C IUDs. Thirty centers have been recruited in 20 countries for the 9000-case clinical trial of the Delta IUDs. Data show the following results from comparative studies:

Comparative Studies	Three-Month Life Table Expulsion Rates (Per 100 Women)
Lippes Loop D vs Delta Loop	19.6 16.1
TCu 220C vs Delta T	12.3 6.8
Delta Loop vs Delta T	4.9 6.4

It is concluded that biodegradable extensions reduce the risk of expulsion following postpartum insertion. Forceful steps will now be taken to test Delta IUDs in widespread use, to develop appropriate monitoring instruments and to find the most appropriate method of local manufacture.

The IFRP has recruited four centers in the United States to conduct studies of the Delta IUDs under the approved IND and IDE. A ten-center, 3500-case trial of the Delta IUDs has been initiated in Tunisia. A similar trial of 6000 cases will be conducted at ten centers in Turkey.

The significant reduction in the amount of IUD-related dysfunctional bleeding achieved with the introduction of the Cu-7 and TCu IUDs is generally attributed to their smaller size relative to the Loop and other IUDs. The IFRP is approaching this problem in two ways. In response to a request from Dr. Zipper to further reduce the size of the IUD carrying the copper, the IFRP developed the ICu IUD. It employs the same

principle of anchoring that has been successful with the postpartum suture IUDs. In this case, the "X" configuration of projections 0.5 cm long anchor into the opposing, anterior-posterior endometrial surfaces. These projections are made of elastomeric ethylene vinyl acetate so that removal of the device should be atraumatic. Results should be available before the end of the contract year.

Secondly, the IFRP is continuing trials of medicated IUDs. Although blood loss and not expulsion is the focus of these studies, preliminary data on 91 insertions from a comparative study of a Lippes Loop D containing Trasylol versus a standard Lippes Loop D show higher expulsion rates at six months for the medicated devices, 34.4 compared with 4.5 per 100 women for the nonmedicated IUDs. Reasons for this unexpected finding are being investigated.

Several approaches to the same problem of excessive blood loss are being tried. Quantitative blood loss studies are being conducted to evaluate the Lippes Loop D containing aminocaproic acid (AMCA) or Trasylol. No data are yet available at the IFRP for analysis.

The IFRP, in collaboration with The Population Council, is funding studies of levonorgestrel-releasing IUDs. A three-center comparative clinical trial of the levonorgestrel-releasing IUD and the Nova T will provide efficacy data and a general clinical evaluation of the benefits of the slow release

of levonorgestrel from an IUD. A subcontract with the Population Council for these trials has been approved and will be initiated shortly. Two subcontracts with the Steroid Research Laboratories in Helsinki, Finland, have also been initiated to evaluate the long-term effects on the endometrium of the continuous release of small amounts of levonorgestrel and to measure the accumulation of levonorgestrel in specific tissues (endometrium, fallopian tubes, ovaries and subcutaneous fat) 4-8 weeks following the insertion of a levonorgestrel-releasing IUD.

Two studies comparing the Nylon T (a T-shaped IUD wound with nylon rather than copper) and the TCu-200B are being conducted to determine whether the effectiveness of the copper IUD is due to the increase in surface area or the addition of the copper itself. Data on 214 insertions show a pregnancy rate of 2.1 for the Nylon T and 0.0 for the TCu 200B at one month.

A clinical trial to evaluate the Population Council's TCu-380 Ag has been initiated. The TCu-380 Ag has a tightly wound copper wire with a silver core on the vertical stem. The silver core prevents the wire from fragmenting as the copper dissolves, increasing the effective lifetime of the device. Seven centers have been supplied with devices, and studies in two other centers are pending approval. The TCu-380 Ag is being compared to the Multiload Cu-375 and the Cu-7. Data on 253 insertions from two centers show a one-month continuation rate of 100.0 for the TCu 380 Ag and 98.8 per 100 women for the Multiload Cu-375. Additional data are being collected.

This is the last year of a three-year subcontract to the Institute for Population Studies at the University of Exeter, England, for IUD research.

In the area of IUD safety, the IFRP is conducting a clinical trial of the TCu-200B with and without strings. The purpose of these studies is to evaluate the incidence of pelvic inflammatory disease (PID) associated with the use of IUDs, in an effort to determine the role of the monofilament IUD strings in the development of upper genital tract infections. Three centers have been recruited. Data on 144 insertions have been collected from one study, which was initiated in September 1980. Recruitment for additional centers with the facilities to conduct the necessary tests continues. Preliminary results should be available before the end of the contract year.

Under a subcontract from the IFRP, Southern Research Institute will develop a fibrous delivery system for povidone-iodine (an antimicrobial agent) to be used in conjunction with an IUD. An IUD tail that slowly releases an antimicrobial agent may prevent bacterial migration through the cervix and significantly reduce the incidence of IUD-associated PID. This subcontract was initiated in January 1981.

F. Systemic Contraception

Oral Contraceptives

Work relating to the possible risks and benefits of oral contraceptives is reviewed later.

Ongoing comparative and crossover clinical trials of various combined oral contraceptives are progressing slowly due to difficulties with slow recruitment and follow-up of patients. The following tables present preliminary data on pregnancy and discontinuation rates for three comparative trials with sufficient cases for analysis.

Brevicon vs Loestrin: Cumulative 6-Month
Life-Table Rates Per 100 Women

Reasons for Discontinuation	Brevicon, N=55			Loestrin, N=58		
	No.	Rate	± S.E.	No.	Rate	± S.E.
Pregnancy	1	8.0	± 7.7	2	6.5	± 4.6
Menstrual irregularity	0	0.0	± 0.0	1	2.0	± 2.0
Other medical reasons	1	4.0	± 3.9	0	0.0	± 0.0
Not needed	1	8.0	± 7.7	1	3.1	± 3.0
Other personal reasons	0	0.0	± 0.0	1	3.1	± 3.0
Total terminations	3	18.8	± 10.2	5	13.9	± 3.0
Woman-months of use	532.0			511.0		

Brevicon vs Lo-Ovral: Cumulative 6-Month
Life-Table Rates Per 100 Women

Reasons for Discontinuation	Brevicon, N=152		Lo-Ovral, N=142	
	No.	Rate \pm S.E.	No.	Rate \pm S.E.
Pregnancy	0	0.0 \pm 0.0	0	0.0 \pm 0.0
Menstrual irregularity	10	8.6 \pm 2.7	1	0.8 \pm 0.8
Other medical reasons	1	1.0 \pm 1.0	1	1.2 \pm 1.2
Other personal reasons	1	0.8 \pm 0.8	0	0.0 \pm 0.0
Total terminations	12	10.3 \pm 2.9	2	2.0 \pm 1.4
Woman-months of use	1423.0		1420.5	

Comparative: Norinyl vs Nordette
Cumulative 6-Month Life-Table Rates Per 100 Women

Reasons for Discontinuation	Norinyl, N=124		Nordette, N=124	
	No.	Rate \pm S.E.	No.	Rate \pm S.E.
Pregnancy	0	0.0 \pm 0.0	0	0.0 \pm 0.0
Planning pregnancy	0	0.0 \pm 0.0	0	0.0 \pm 0.0
Menstrual irregularity	1	1.2 \pm 1.2	0	0.0 \pm 0.0
Nausea/vomiting	1	1.2 \pm 1.2	0	0.0 \pm 0.0
Other medical reasons	7 ¹	22.2 \pm 9.8	7 ²	19.9 \pm 7.0
Not needed	0	0.0 \pm 0.0	2	5.0 \pm 3.8
Other personal reasons	2	6.2 \pm 5.0	3	3.7 \pm 2.1
Total terminations	11	28.8 \pm 9.8	12	26.7 \pm 7.2
Woman-months of use	477.5		446.5	

¹Gastrointestinal (1), pelvic abnormalities (1), weight gain (2), medical and psychological: two or more reasons (3).

²High blood pressure (1), pruritis (1), medical and psychological: two or more reasons (5).

Preliminary data from one ongoing crossover study of Norinyl to Norinyl, Brevicon or 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. The majority of those discontinuing use reported non-medical reasons, such as contraceptive not needed or other personal reasons. One third of the women who discontinued gave a medical reason for discontinuing use. There are insufficient data from the follow-up phase after switching to another pill for meaningful analysis.

Injectables

The subcontract with the Emory/Grady Family Planning Program in Atlanta to study the Association between Contraceptive Methods and Negative Health Outcomes is progressing well. After the identification of patients with selected morbid conditions who had made at least one visit to the Grady Family Planning Program activities will be directed at the planning of a large-scale case/cohort study. This second phase will review morbidity patterns among women using various methods of contraception and determine if women who have ever used Depo-Provera are at an increased risk of severe adverse effects.

The use of injectable contraceptives has proved popular in developing countries and controversy has surrounded the US-FDA decision not to license the use of Depo-Provera as a contraceptive.

Under a subcontract from the IFRP, a study is being conducted at the Hasan Sadikin Hospital, Bandung, Indonesia, to evaluate the long-term effects of Depo-Provera provided some years ago under

a non-AID program. Previous and current users of Depo-Provera are being contacted, and their health status evaluated. The study is progressing smoothly, and preliminary results should be available by the end of the contract year. Duplicate histopathology slides prepared from endometrial biopsies have been sent to an IFRP consultant, Dr. Scully, Department of Pathology, Harvard University, for independent evaluation. So far, no adverse effects associated with Depo-Provera use have been detected.

The largest long-term, well-monitored use of Depo-Provera has been in Thailand. In cooperation with the Ministry of Public Health, a study is planned to survey the health of Depo-Provera users and a group of controls in Northern Thailand. Depo-Provera has been used for more than 14 years in this area in an International Planned Parenthood Federation (IPPF) program, and it is expected that valuable data will be obtained on the long-term use of this method. This study has been delayed due to certain local problems. However, the Ministry of Public Health is anxious to initiate the study as soon as circumstances permit.

On January 23, 1981, 14 researchers and physicians met with the staff at the IFRP to discuss the current status of once-a-month injectable contraceptives and the direction of future studies. There is a demand for once-a-month injectables in several developing countries, and this method is used by 300,000 women in Mexico alone, although the product is poorly investigated and

monthly injections of a steroidal contraceptive has shown a lower rate of amenorrhea and better menstrual regularity than that associated with the three-month and six-month injections. Currently, two new systems are being tested to administer steroids intramuscularly. Dr. Harry Rudel, Centro de Investigación Sobre Fertilidad y Esterilidad in Mexico, has developed a compound that consists of a dry powder of micronized crystals of NET and mestranol. Dr. Lee Beck, University of Alabama in Birmingham and researchers at the Southern Research Institute, Alabama, have developed a system consisting of microcapsules made of a biodegradable polymer in which the steroid is homogeneously dispersed. The WHO is supporting studies of Cyclo-Provera and the "Task-Force Cocktail," which consists of a combination of NET and estradiol valerate. The group unanimously concluded that there was a need and a demand for a once-a-month injectable contraceptive, and that the IFRP could contribute significantly to its development.

G. Barrier Contraception

There is a renaissance of interest in spermicides and barrier methods of contraception, and the IFRP is testing their applicability and acceptability in developing countries.

Data from Phase II studies of the Collatex sponge and Neo Sampoo foaming tablet have been analyzed. Selected data on effectiveness and discontinuation are presented in the following tables.

Collatex: Cumulative Life-Table Rates Per 100 Women

	1-Month Rate \pm SE	3-Month Rate \pm SE	6-Month Rate \pm SE
Pregnancy	1.4 \pm 0.5	4.6 \pm 1.3	6.0 \pm 1.6
Planning pregnancy	0.8 \pm 0.5	2.0 \pm 0.8	3.0 \pm 1.2
Discomfort	2.7 \pm 0.8	6.7 \pm 1.5	12.9 \pm 2.9
Other personal reasons	6.7 \pm 1.3	13.1 \pm 2.0	18.7 \pm 2.8
Medical reasons	1.9 \pm 0.7	4.9 \pm 1.3	5.6 \pm 1.5
Total terminations	12.9 \pm 1.7	28.0 \pm 2.5	39.0 \pm 3.4
Woman-months of use	338.0	1491.0	3075.5

Neo Sampoo: Cumulative Life-Table Rates Per 100 Women

	1-Month Rate \pm SE	3-Month Rate \pm SE	12-Month Rate \pm SE
Pregnancy	0.2 \pm 0.2	6.3 \pm 1.4	10.0 \pm 2.0
Planning pregnancy	0.0 \pm 0.0	0.6 \pm 0.4	6.3 \pm 2.0
Discomfort	1.7 \pm 0.6	5.1 \pm 1.3	6.8 \pm 1.6
Other personal reasons	1.0 \pm 0.4	5.2 \pm 1.3	12.8 \pm 2.5
Medical reasons	0.0 \pm 0.0	0.5 \pm 0.4	0.5 \pm 0.4
Total terminations	2.8 \pm 0.7	16.7 \pm 2.1	31.9 \pm 3.1
Woman-months of use	533.5	5765.5	14,912.0

Currently, there are seven ongoing comparative trials of vaginal contraceptives. Fourteen other clinical trials are either in the planning phases or to be initiated, including four comparing Neo Sampoo with a newly developed foaming tablet containing 100 mg nonoxynol-9 manufactured by Schering. Preliminary data to date from four active comparative trials of Collatex versus Neo Sampoo show slightly higher six-month pregnancy and

discontinuation rates among users of the Collatex sponge, as shown in the following table.

Collatex vs Neo Sampooon: Cumulative 6-Month
Life-Table Rates Per 100 Women

Reasons for Discontinuation	Collatex Rate \pm SE	Neo Sampooon Rate \pm SE
Pregnancy	4.8 \pm 1.8	3.3 \pm 1.8
Planning pregnancy	1.4 \pm 1.4	0.0 \pm 0.0
Discomfort	2.2 \pm 1.6	2.7 \pm 1.4
Other personal reasons	4.2 \pm 1.6	1.2 \pm 0.9
Medical reasons	1.5 \pm 1.2	0.0 \pm 0.0
Total terminations	13.4 \pm 3.0	7.0 \pm 2.3
Woman-months of use	2366.0	2266.5

A comparative trial involving a small, single-sized diaphragm to be used with and without adjunctive spermicide will be initiated in several centers in the developing world.

The IFRP continues to explore research strategies for investigating vaginal chemoprophylaxis and sexually transmitted diseases.

H. Fertility Awareness Methods

The IFRP has responded to the International Security and Development Cooperation Act of 1980, Title III, SEC 302.(a) Section 104(b) and established contact with organizations teaching the Ovulation (Billings) method of contraception. A study of the efficacy and acceptance of the ovulation method in a Phase II

clinical trial has been developed. Three studies are proposed, one of which will take place in the U.S. and the others in Latin America and Africa. These studies will be initiated after completion of an in-house research document to supplement the strategy.

I. Breast-feeding

No clear guidelines exist about when lactating women should adopt additional contraceptive protection. A subcontract has been awarded to the Universidad de Juarez, Durango, Mexico, for a longitudinal breast-feeding study. The objective of this research is to study the relationship between return of ovulation after childbirth and the pattern of infant feeding, with special emphasis on the introduction of supplementary feeds. The study will also evaluate the effect of other factors, such as resumption of menses and sexual practices of the women on the return of fertility after childbirth. This project is scheduled to be initiated in February 1981.

Breast-feeding is of great importance in developing countries both for the welfare of the infant and as a natural mechanism for spacing pregnancies. At any one time, up to half the married women in a traditional society may be breast-feeding, yet no effort has been made to tailor contraceptives to their needs.

Four clinical trials of progestogen-only oral contraceptives in lactating women have been initiated. Preliminary analysis of data from the 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 into the study. Problems associated with slow recruitment and follow-up continue to impede the progress of these studies.

III. CONTRACEPTIVE SAFETY STUDIES

An adverse side-effect reporting system has been instituted to provide information on significant clinical events that occur to contraceptive users. The IFRP's network of investigators is being encouraged to report all unexpected adverse effects regardless of whether they are thought to be related to the method of contraception used.

The Reproductive Age Mortality Survey (RAMOS) in Bali, Indonesia, received approval at the beginning of this reporting period. The purpose of this study is to determine the pattern of mortality in a traditional society with limited access to modern medicine. It will compare the total pattern of mortality from all causes among contraceptive users and nonusers and make a systematic search for any deaths that might be related to contraceptive use.

A ten-day training period of the interviewers took place in September 1980, and interviewing for the study began immediately afterwards. Deaths to married women of reproductive age are being recorded and investigated from September 1, 1980.

Kim Streatfield, consultant to the IFRP from the Australian National University and temporary Bali resident, is checking the completeness

of death coverage by traveling to banjar (village) meetings and comparing the list of deaths reported at the banjar meeting with the list of deaths prepared by the family planning fieldworker. Problems arising from the complicated system of naming individuals in Bali are to be thoroughly investigated by the project monitor and Mr. Streatfield in February and March.

Questionnaires received by the IFRP show a surprisingly high percentage of the deaths attributed to delivery complications, specifically postpartum hemorrhage. The second most common cause of death is cancer of various sites. For the majority of the cases investigated so far, determining the cause of death was not particularly difficult. Of the several problems anticipated in this research, the registration of the deaths is by far the most important, and may well involve considerable time and effort to resolve. In November Dr. Roger RoCHAT of the Center for Disease Control and Dr. Oscar Harkavy of the Ford Foundation visited Bali and reviewed the project.

A second Reproductive Age Mortality Survey (RAMOS) is planned in Egypt. A three-year subcontract with the Social Research Center of the American University in Cairo, Cairo, Egypt, was finalized, submitted to AID and is awaiting approval. The study proposes to evaluate the causes of death to all married women of reproductive age (15-49 yrs) in Menufia Governorate located in the Nile Delta. These data, combined with the ongoing Integrated Development Project for Health, Social Services and Family Planning and the Community-Based Distribution of contraceptives, will provide good estimates of

risk of death associated with the use of different contraceptive methods including the use of no methods. A feasibility study was completed in October 1980 and a survey questionnaire was pretested on site. The study is scheduled to cover deaths reported as of January 1, 1981.

IV. OTHER RESEARCH PROJECTS

Channels of contraceptive distribution can be as important as pharmacological and mechanical differences between methods in responding to cultural needs and in relating to the health consequences of contraceptive distribution.

During the reporting period, the IFRP sponsored a project to assess Egyptian pharmacists' knowledge of and attitudes toward contraception and family planning practices. The survey was completed in October 1980 using a sample of 450 randomly selected Egyptian pharmacists from a comprehensive list. Data have been keypunched, and plans for analysis are underway. It is hoped that the results of the survey will help devise ways to enhance the role of pharmacists in family planning. Product-oriented bulletins are being prepared for distribution and will ensure the regular provision and dissemination of relevant technical information. A second study will assess the effectiveness of the bulletins.

Although female circumcision is widely practiced in the Sudan, scarcely any research has been conducted on the subject. Data on female circumcision in the Sudan are being received at the IFRP.

Analysis plans are currently underway and will begin when sufficient data are available.

As maternity services improve in many parts of the world, death and disease relating to congenital anomalies become relatively more important. The topic is of increasing significance in maternity care in developed and developing countries and also relates to contraceptive use as expressed in patterns of childbearing (age, parity and birth interval) and possibly to the use of certain specific methods such as systemic contraceptives.

The IFRP has begun investigating the feasibility of conducting an epidemiologic study of congenital malformations. The Philippines has been selected as a possible site and travel plans to follow-up on such a project have been finalized.

Extensive analysis of the determinants of contraceptive use, reproductive goals and birth spacing in relation to infant and child mortality, breast-feeding and previous contraceptive use was completed in the reporting period. This study, using recent data collected from over 20,000 women delivering at selected maternity hospitals in Africa and the Middle East, has shown that breast-feeding has a significant impact on the length of the pregnancy interval, but only if it continues for a prolonged period. The desire for additional children is found to be affected by the survival status of the last two pregnancies; plans for postpartum contraceptive use were a direct function of (only) the most recent pregnancy outcome. The impact of improved child survivorship on the use of contraception

and breast-feeding was assessed with respect to the length of the pregnancy interval.

Poverty can exclude many women from needed family planning services. A project to follow-up the women who did not obtain sterilizations as reported in the study on access to sterilization in Campinas, Brazil, was initiated. Under a subcontract from the IFRP, interviewers are attempting to locate all women who requested a post-partum sterilization but did not receive one, and obtain information on whether they were later sterilized. Results of this follow-up phase will be available during the next reporting period.

A second accessibility/acceptability sterilization study, similar to the one in Campinas, Brazil, is being conducted in Honduras. The fieldwork is currently underway, and although some preliminary analysis on admission forms has been conducted, results are not available yet.

V. RESEARCH ACTIVITIES

As a result of new initiatives in Africa and of the large multicenter clinical trial of Delta IUDs, the number of research centers collaborating with the IFRP has increased. Studies of the Delta devices in the United States needed to satisfy the requirements of a Claimed Investigational Exemption for a New Drug (IND) and an Investigational Device Exemption (IDE), have also added

centers to the IFRP's network. The number of centers, by geographic region, presently participating in IFRP research are given below:

<u>Regions</u>	<u>Number of Centers</u>
Latin America	35
Middle East and Africa	24
Far East	27
Europe and North America	<u>21</u>
Total	107

Data from individual studies are analyzed and a Consultant Report (CR) is prepared as a service to the participating investigator. Appendix A lists the 20 CRs completed during this reporting period. Appendix B lists the type and number of forms received at the IFRP and loaded into the computer. Appendix C lists the major computer programs and study documents completed during the reporting period.

The IFRP staff share their technical skills with personnel from collaborating research centers. During the first half of the contract year, Dr. Anek Hirunraks of CBFPS, Bangkok, Thailand, came to the IFRP to improve his skill in computer technology. Ms. Rebecca Ramos, an anthropologist working with family planning clinics in Ciudad Juarez, Mexico, visited the IFRP to acquire training in basic programming skills and data analysis.

A large number of researchers and clinicians come to the IFRP for discussions of ongoing or planned research projects. Noteworthy during this period were the many representatives from African countries who visited the Research Triangle Park office. Among them were individuals from Kenya, Zaire, Zambia, Liberia, Zimbabwe and Togo.

At times, the IFRP receives special requests for assistance from governments. Requests were received from the governments of Tunisia and Turkey for technical assistance in establishing nationwide post-partum IUD programs using Delta IUDs. The Tunisia program is underway, while the Turkey program is in the late planning stages. The Government of Mali requested IFRP's assistance in evaluating its family planning program. This project will be undertaken in collaboration with the Center for Disease Control in Atlanta.

One of the most innovative ideas for providing technical assistance is the Microcomputer-Based Data Collection and Analysis System. During the period covered by this report, concept approval was obtained for the system that, as its name indicates, uses the new generation of computers now available to aid in the collection and analysis of clinical trial and maternity care monitoring data in the concerned field sites. The system will reduce possible errors in data collection, allow the rapid feedback of clinical and management information and be more cost effective than the systems it will replace.

Specifications for the hardware required were developed and bids let to determine the most economical and best-serviced hardware available on the market today. In January approval from AID was obtained to buy Texas Instruments microcomputers through an OEM (original equipment manufacturer) agreement. This will result in low costs for the systems proposed for field use. The IFRP has ordered a multiple user system (TI 990 Model 4) that is completely compatible with the field systems to be used in the development of the software

to be distributed with the microcomputer systems. Delivery of the development systems is expected in early March 1981. The first production system to be installed in the field is planned for early 1982.

The IFRP continues to strengthen its ties with other research organizations by collaborating in projects, meetings and the exchange of information.

VI. INFORMATION DISSEMINATION

The list of papers published during the first six months of this contract year is found in Appendix D.

In several areas the IFRP now has the most extensive data bank of information available at any site in the world. The staff and collaborators have intensified their efforts to utilize this data bank as fully as possible. Important contributions have been made to the study of rare events related to voluntary female sterilization.

From August 1980 to January 1981, the IFRP continued to edit, produce and publish the International Journal of Gynaecology & Obstetrics while completing final contract negotiations with Elsevier/North Holland Biomedical Press in Amsterdam for a transfer of publishing responsibilities. To facilitate this transfer, the IFRP accelerated its Journal production schedule and published the six issues of Volume 18 in six rather than the usual twelve months, enabling Elsevier to begin publishing Volume 19 in January 1981. In October 1980, contracts between IFRP and Elsevier were approved and

signed, transferring publication and distribution responsibility for the Journal to Elsevier.

The IFRP will continue to co-sponsor the Journal with the International Federation of Gynecology and Obstetrics, and will edit all reviewed and accepted manuscripts written by physicians and researchers working in the developing world. The IFRP has purchased 2323 reduced-rate, Volume 19 subscriptions from Elsevier for distribution to AID Missions and to selected health care professionals in the developing world.

The IFRP's quarterly newsletter, Network, is now in its second volume year of publication. The initial positive response has been maintained and reader interest and general recognition has increased. The number of readers continues to grow, with the most recent issue (January 1981) being mailed to 5500 individuals.

The January 1981 issue was also the first eight-page edition of Network, an expanded format necessitated by increased coverage of research topics. Reader response to Network's content has been encouraging. Potential investigators have written to request information on how to participate in clinical trials of the postpartum IUD and quinacrine sterilization. Further, several other family planning agencies have written to request permission to use Network material in their publications, some of which are published in foreign languages. Mailing lists have been obtained from related agencies that will enable the IFRP to plan a selective increase in the circulation of Network.

The IFRP monograph RAMOS was published during the reporting period. This first in a series of occasional monographs on key topics in fertility regulation presented an analysis of the needs and possibilities for conducting studies on the risks and benefits of family planning in developing countries involving the Reproductive Age Mortality Survey. The second monograph, Surgical Family Planning Methods: The Role of the Private Physician, is in press and scheduled for publication in March 1981.

Under its AID contract, the IFRP continued to sponsor conferences on fertility control and family planning. In September 1980, an international group of experts met in Juarez, Mexico, to participate in a workshop on taking family planning to the urban poor. This workshop will result in a monograph, now in preparation, addressing this important issue.

In collaboration with the Program for Applied Research in Fertility Regulation (PARFR), the IFRP sponsored a conference, Recent Advances in Fertility Regulation, in Surabaya, Indonesia, December 1980. Proceedings from this conference have been printed.

In addition, two expert meetings were held at the IFRP in January 1981. The results of these meetings, the first on chemical female sterilization and the second on once-a-month injectable contraceptives, were presented earlier in this report. Additional meetings are planned for 1981. One, to take place in June, will focus on percutaneous male sterilization. The IFRP has profited greatly from these expert meetings, since they afford appropriate staff the

opportunity to exchange ideas with experts in the field and set optimum directions for IFRP research.

In the second half of the contract year, the IFRP will sponsor two large conferences, one in Tunisia and a second one in Brazil. The first, an International Symposium on Regulation of Fertility, will include participants from many African nations and will focus on current issues in fertility research. The second conference will concentrate on IUDs. It is hoped that this conference will disseminate information that will help increase the acceptability of intra-uterine devices as a method of contraception.

VII. MANAGEMENT

As of January 31, 1981, the staff at the IFRP numbered 104. IFRP personnel transactions are shown in the table below:

IFRP PERSONNEL TRANSACTIONS:
August 1, 1980 - January 31, 1981

Position Grade	Hired	Number of Employees	
		Departed	On Staff*
10	1	0	7
9	0	0	6
8	1	0	7
7	0	0	9
6	0	1	11
5	3	1	16
4	0	1	11
3	3	1	23
2	1	1	9
1	2	1	5
	<u>11</u>	<u>6</u>	<u>104*</u>

*As of January 31, 1981

Recruitment is ongoing for several upper level positions for the International Projects and Research Departments. In November 1980, Mr. John Ganley was hired for the position of Deputy Director. Mr. Ganley comes to the IFRP with experience in both government and private business. His management expertise is of invaluable use to the IFRP.

The IFRP Administrative Committee, composed of the Executive Director, Deputy Director and Associate Directors, continues to deal with the management of the organization. During the reporting period, a Scientific Review Committee was formed. This committee, which includes the Executive Director, Deputy Director, Medical Director, Senior Program Officer and Associate Directors for International Projects and Research, sets scientific priorities for the IFRP and reviews and approves recommendations made by the Task Forces.

The IFRP Board of Directors held their annual meeting September 14-15, 1980, and re-elected the seven Directors and two ex-officio (non-voting) Directors. The Board replaced IFRP's Corporate Counsel with the appointment of John R. Jordan, Jr., member of a Raleigh, N.C. law firm. A three-member Audit Committee was appointed by the Board to oversee IFRP's corporate fiscal management. The Audit Committee held their first meeting September 15, 1980. The Executive Committee of the Board met twice: September 15 and December 11, 1980. Following the recommendation of the Audit Committee, the independent accounting firm of Ernest and Whinney was appointed by the Executive Committee to replace the auditing services heretofore

provided by Price Waterhouse. During 1981 two new Directors will be appointed to the Board bringing the total to nine, as permitted by the By-laws.

The Protection of Human Subjects Committee met twice, on November 21 and December 12, 1980. At the December meeting, which included the annual review of all IFRP research, a new Chairman was selected, Mr. William Campbell. Mr. Campbell replaced Ms. Linda Staurovsky and will serve a two-year term.

Scientific Directions 1980, a broad document including ongoing, planned and possible scientific initiatives for the IFRP, will be updated in early 1981. The review and revision process began late in the reporting period.

The IFRP expended a total of \$1,620,902 during the first half of the contract year. Expenditures are summarized in the following table.

IFRP Expenditures, Contract 1172:
August 1, 1980 - January 31, 1981

Salaries	\$ 375,737
Fringe benefits	96,093
Consultants	25,691
Travel	
Domestic	27,926
Foreign	95,658
Equipment	1,965
Material and supplies	33,790
Subcontracts	124,841
Service Center	
Computer usage	161,975
Data Entry	13,580
Duplicating	4,276
Graphics	16,782
Text Processing	78,842
Home department	75,936
Forms payments	58,769
Conference expense	16,181
Foreign office expense	4,772
IJGO	48,742
Printing and publications	34,003
Other	<u>26,818</u>
Total direct costs	\$1,322,377
General and administrative	269,959
Fixed fee	<u>28,566</u>
TOTAL COSTS	<u>\$1,620,902</u>

VIII. FUTURE DIRECTIONS

The IFRP will continue its successful program of clinical trials, evaluating new contraceptive developments whenever they become available for evaluation. Nonsurgical sterilization will continue to receive top priority. Subcontracts with The Johns Hopkins University to evaluate the toxicology and teratology of quinacrine hydrochloride as a means of female sterilization are nearing completion, and will provide the necessary data to support the IND application to the Food and Drug Administration now in preparation.

The IFRP will give special attention to the continued evaluation of IUDs for immediate postpartum insertion that will include a ten hospital study of the Delta Loop in Turkey. Studies to critically evaluate barrier contraceptive methods will also be given priority. Limited efforts will be expended on the evaluation of methods of fertility awareness.

Three additional longitudinal breast-feeding studies are under development. Possible sites are Nigeria, Tunisia and Thailand. The fourth, in Durango, Mexico, is to be initiated February 1, 1981.

In an endeavor to transfer research skills and provide technical assistance to developing countries, the IFRP will initiate work on computer programs that will be transferred to regional research centers scheduled to receive microcomputers. Professional staff will travel to selected centers to provide aid in research program development and training in research methodology and data analysis.

Continued emphasis will be placed on: clinical Phase III and IV (postmarketing) trials to evaluate contraceptive safety and efficacy. Among the scientific projects to be implemented during the remainder of the contract year is a second Reproductive Age and Mortality Study (RAMOS), modeled after the Bali RAMOS, to be conducted in Egypt in collaboration with the Social Research Center of the American University in Cairo.

In addition to continuing ongoing studies on injectable contraceptives and other topics, the IFRP will investigate issues and controversies related to contraceptive safety. Failure to resolve these issues adequately would present a major obstacle to expanded provision of contraceptive services to those most in need of them. Among the planned investigations by the IFRP are epidemiologic investigations of congenital malformations among women who become pregnant while contracepting, the long-term effects of male and female sterilization and issues related to carcinogenesis and oral contraceptive use.

bbx35

APPENDIX A

Completed Consultant Reports (CRs)

August 1, 1980 - January 31, 1981

<u>Title</u>	<u>Prepared For</u>	<u>Center #</u>	<u>Study #</u>
Evaluation of the Multiload Copper 250 and Postpartum T in Jose Fabella Hospital Manila, Philippines	Dr. R. Apelo	600	541,555
Evaluation of Postpartum T - PRIF Colombia	PRIF	804,819 876,880	555
Comparison of Lippes Loop D and Ypsilon, Siriraj Hospital	Dr. Suporn Koetsawang	075	467
Comparison of Ypsilon Y and Lippes Loop D IUDs	Dr. Rugamas Castaneda	821	467
Comparison of LLD and Ypsilon at Hospital Sotero del Rio, Chile	Dr. Mario Medel	087	467
Evaluation of Postpartum T, Silastic Loop and Sutured Loop at Hospital Sotero del Rio, Chile	Dr. Mario Medel	087	508,555
Female Sterilization via Laparoscopy using Tubal Ring Technique of Occlusion, Lady Wellington Hospital, Lahore, Pakistan	Prof. N. A. Seyal	065	623
Female Sterilization via Laparoscopy using Tubal Ring Technique of Occlusion, Chelsea Hospital for Women	Dr. I. Craft	292	623
Evaluation of the Copper T 200 at the Hospital Barros Luco in Santiago, Chile	Dr. P. Lavin	852	526
Evaluation of the Tapered Photoreduced Lippes Loop D with Inserter, Sir Salimullah Medical College Hospital, Dacca, Bangladesh	Dr. Suraiya Jabeen	705	559
Interval Minilaparotomy with the Pomeroy Technique of Tubal Occlusion, Maternity Hospital, Kuala Lumpur, Malaysia	Dr. B. Mehra	795	630
Analysis of Collatex Sponge in Dacca, Bangladesh	Dr. Halida Akhtar	721	781

APPENDIX A (Cont'd)

<u>Title</u>	<u>Prepared For</u>	<u>Center #</u>	<u>Study #</u>
Electrocoagulation via Laparoscopy Employing Three Different Anesthesia Schedules	Dr. Suporn Koetsawang	075	614
A Comparison of the Lippes Loop D and the Lippes Loop D with Copper, Rijeka, Yugoslavia	Dr. L. Randic	022	506
Female Sterilization by Laparotomy	Dr. Ariawan Soejoenoes	794	621
A Comparison of the Multiload Plain and the Multiload Copper 250	Dr. Ibtisam Said	314	540
Long-term Follow-up Data on 299 Women Sterilized by Laparoscopic Electro- coagulation or Application of the Tubal Ring	Dr. Cecilio Aranda	831	652
Evaluation of the Lippes Loop C and Lippes Loop D in Interval and Post- abortion Women	Dr. L. Randic	022	433
Evaluation of the Multiload Copper 250 and the Multiload Plain, Essen University Clinics, Essen, West Germany	Dr. Peter Tauber	250	488,541 543,592
Evaluation of the Delta Loop and the Delta T, Jose Fabella Memorial Hospital, Manila, Philippines	Dr. R. A. Apelo	600	556

APPENDIX B

Forms Received and Loaded into the Computer

August 1, 1980 - January 31, 1981

Intrauterine Devices	Admission	1995
	Follow-up	3312
	Method List	1150
	Other	<u>862</u>
	Total	7319
Intrauterine Devices Patient Summary	Admission	366
	Follow-up	301
	Other	<u>2</u>
	Total	669
Systemic Contraception	Admission	753
	Follow-up	598
	Physical	<u>220</u>
	Total	1571
Female Barrier Short Forms	Admission	70
	Follow-up	<u>386</u>
	Total	456
Female Barrier Long Forms	Admission	534
	Follow-up	<u>785</u>
	Total	1319
Lactation	Admission	143
	Follow-up	<u>132</u>
	Total	275
Male Sterilization	Admission	75
Female Sterilization	Admission	817
	Follow-up	591
	Additional Information	2
	Method List	312
	Pregnancy Confirmation	<u>2</u>
	Total	1724

APPENDIX B (Cont'd)

Chemical Female Sterilization	Admission	26
	Follow-up	295
	Instillation	<u>88</u>
	Total	409
Pregnancy Termination	Admission	15
Menstrual Regulation	Admission	148
Total Forms Processed		13,980

APPENDIX C

Major Computer Programs Completed

August 1, 1980 - January 31, 1981

1. Program for performing the MANTEL-HAENZEL procedure on a set of 2 X 2 contingency tables
2. PEARSON CHISQUARE program
3. Sample size determination for clinical trials program
4. Frequency distribution program
5. Interactive preprocessor for the Searching for Structure program
6. Implementation of the PARCAT program
7. Brazil contraceptive prevalence study load and contingency program
8. Major revisions to the MR and PT load and standard tables programs
9. Interactive coding program for lactation data
10. Lactation update program
11. IUD patient summary to IUD5 conversion program
12. Major rewrite of file manipulation program SHERLOCK
13. Development and implementation of programmers' tool: I/O package QUIN
14. First stage development of the users' interface to the generalized load program

Completed Documents

SYSTEMIC CONTRACEPTION

Longitudinal Breast-feeding Study Forms

BARRIER CONTRACEPTION

Strategy

Nonspermicide Fit-Free Diaphragm Study

APPENDIX C (Cont'd)

Forms

Female Barrier Contraceptive Study - Physical Examination Record
Female Barrier Contraceptive Study - Daily Coital Log
Female Barrier Contraceptive Study - Two-Week Visit Form

FERTILITY AWARENESS METHODS

Strategy

Natural Family Planning Methods Study

APPENDIX D

International Fertility Research Program

Publications

August 1, 1980 - January 31, 1981

PREGNANCY TERMINATION

Goldsmith A, Edelman DA: Aborto o anticoncepcion. *Reproduccion* 4:55, 1980. (PT-8?)

Potts M, Lewis JH: Social factors in abortion. In Proceedings of the IXth World Congress of Gynecology and Obstetrics, Tokyo, Japan, October 25-31, 1979, p 63. Excerpta Medica, Amsterdam. (PT-119)

MENSTRUAL REGULATION

Edelman DA, Berger GS: Menstrual regulation. In Abortion and Sterilization: Medical and Social Aspects (ed JE Hodgson). Academic Press Inc, Ltd, London (in press). (MR-27)

Potts M, James S: Instrumentation in fertility control: menstrual regulation. In Proceedings of International Seminar: Recent Advances in Fertility Regulation, Surabaya, Indonesia, December 18-19, 1980, p 178. (MR-49)

FEMALE STERILIZATION

Zipper J, Cole LP, Goldsmith A, Wheeler RG, Rivera M: Quinacrine hydrochloride pellets: preliminary data on a nonsurgical method of female sterilization. *Int J Gynaecol Obstet* 18(4):275, 1980. (FS-103)

Kwak HM, Chi I-c, Gardner SD, Laufe LE: Menstrual pattern changes in laparoscopic sterilization patients whose last pregnancy was terminated by therapeutic abortion--a two-year follow-up study. *J Reprod Med* 25(2):67, 1980. (FS-106)

Mumford SD, Bhiwandiwalla P: Tubal ring sterilization: experience with 10,086 cases. *Obstet Gynecol* 57(2):150, 1981. (FS-120)

Chi I-c, Mumford SD, Gardner SD: Pregnancy risk following laparoscopic sterilization in nongravid and gravid women. *J of Reprod Med* (in press). (FS-122)

Arqueta G, Henriquez E, Amador MN, Gardner SD: Comparison of laparoscopic sterilization via spring-loaded clip and tubal ring. *Int J Gynaecol Obstet* 18(2):115, 1980. (FS-124)

Diaz MO, Atwood R, Laufe LE: Laparoscopic sterilization with room-air insufflation: preliminary report. *Int J Gynaecol Obstet* 18(2):119, 1980. (FS-125)

Mumford SD, Bhiwandiwalla P, Chi I-c: Laparoscopic and minilaparotomy female sterilization compared in 15,167 cases. Lancet 2:1066, 1980. (FS-126)

Chi I-c, Mumford SD, Laufe LE: Technical failures in tubal ring sterilization: incidence, perceived reasons, outcome and risk factors. Am J Obstet Gynecol 138(3):307, 1980. (FS-129)

Janowitz B, Nunez J: Access to sterilization in Honduras. Bull Pan Am Health Organ (in press). (FS-131)

Chi I-c, Laufe LE, Atwood RA: Ectopic pregnancies following female sterilization. Adv Plann Parenth (in press). (FS-137)

Laufe LE, Atwood R: Air for pneumoperitoneum. In Proceedings of JHPIEGO Conference on Surgical Equipment and Training in Reproductive Health, Key Biscayne, Florida, September 16-18, 1979, p 22. (FS-138)

Laufe LE: Female surgical contraception: state-of-the art. In Proceedings of International Seminar: Recent Advances in Fertility Regulation, Surabaya, Indonesia, December 18-19, 1980, p 168. (FS-146)

INTRAUTERINE DEVICES

Goldsmith A, Young AB, Colven CE: The IUD: its role in the population programs of the developing world. In IUDs and Family Planning (eds ESE Hafez, WAA van Os), p 65, GK Hall Medical Publishers, Boston, 1980. (IUD-61)

Batar I, Taylor R Jr, Lampe L: Can inert IUDs be further improved? Proceedings of the Medicated IUDs and Polymeric Delivery Systems International Symposium, Amsterdam, Holland, June 27-30, 1979 (eds ESE Hafez, WAA van Os). Martinus Nijhoff BV, The Hague, Holland (in press). (IUD-63)

Wheeler RG: IUD decision guide: determinants of IUD continuation. In Medicated Intrauterine Devices Physiological and Clinical Aspects (eds ESE Hafez, WAA van Os), p 195, Martinus Nijhoff Publishers BV, The Hague, Holland, 1980. (IUD-64)

Laufe LE, Friel PG: Improving IUD performance with biodegradable materials. In Biodegradables and Delivery Systems for Contraception (eds ESE Hafez, WAA van Os), p 97, GK Hall Medical Publishers, Boston, 1980. (IUD-68)

Berger GS, Keith LG, Edelman DA: IUDs and ectopic pregnancies. In IUD Pathology and Management (eds ESE Hafez, WAA van Os), p 169, GK Hall Medical Publishers, Boston, 1980. (IUD-69)

Batar I: Fertility after IUD removal. In Medicated Intrauterine Devices Physiological and Clinical Aspects (eds ESE Hafez, WAA van Os), p 159, Martinus Nijhoff Publishers BV, The Hague, Holland, 1980. (IUD-71)

SYSTEMIC CONTRACEPTIVES

Potts M: Is the Pill natural? *Populi* 7(1):12, 1980. (SYS-24)

EVALUATION

Edelman DA: Contraceptive practice and ectopic pregnancy. *IPPF Med Bull* 14(3), 1980. (EVAL-55)

Potts M, Whitehorne E: Contraception and the lactating woman. *In Proceedings of the International Workshop on Research Frontiers in Fertility Regulation*, Mexico City, Mexico, February 10-14, 1980. Harper & Row, Hagerstown, MD, p 117. (EVAL-56)

Shelton JD, Taylor R: The Pearl pregnancy rate reexamined: still useful for clinical trials of contraceptives. *Am J Obstet Gynecol* (in press). (EVAL-60)

Edelman DA, Berger GS: Contraceptive practice and tuboovarian abscess. *Am J Gynecol Obstet* 138(5):541, 1980. (EVAL-64)

Nakamura MS, Morris L, Janowitz B, Anderson JE, Fonseca JB: Contraceptive use and fertility levels in Sao Paulo State, Brazil. *Stud Fam Plann* 11(7/8):236, 1980. (EVAL-68)

Edelman DA, Goldsmith A, Shelton JD: Postpartum contraception. *In Proceedings of International Seminar: Recent Advances in Fertility Regulation*, Surabaya, Indonesia, December 18-19, 1980, p 145. (EVAL-69)

Potts M: Male contraception today. *IPPF Med Bull* 14(5), October 1980. (EVAL-71)

METHODOLOGY

Wheeler RG, Friel PG: Release of drugs from IUDs using an ethylene vinyl acetate matrix. *In Proceedings of the Seventh International Symposium on Controlled Release of Bioactive Materials*, Ft. Lauderdale, Florida, July 1980. Plenum Publishing Corp, New York (in press). (METH-52)

BARRIER CONTRACEPTION

Liao WC, McCann MF, Taylor RF, Begum SF: A clinical trial of neo sampooon vaginal contraceptive tablets. *Cont* (in press). (BAR-3)

Edelman DE: Nonprescription vaginal contraception. *Int J Gynaecol Obstet* 18(5):340, 1980. (BAR-8)

MATERNITY RECORD

Bernard RP, Kessel E, Kendall EM: International maternity care monitoring. *In Proceedings of the First Pakistan Congress of Obstetrics and Gynaecology*, Lahore, Pakistan, November 20-26, 1978, p 45. (MAT-21)

Bernard RP, Kendall EM, Potts M: Promotion of postpartum contraception using MCM as a tool of management. A 1978 status report from Asia based on 17 studies involving 59,386 women. In Voluntary Sterilizations: A Decade of Achievement, p 197. Association for Voluntary Sterilization, New York, 1980. (MAT-28)

Fortney J, Janowitz B, Goldsmith A: Adolescent mothers and birth weight in Latin America. In Proceedings IXth World Congress of Gynecology and Obstetrics, Tokyo, Japan, October 25-31, 1979, p 54. Excerpta Medica, Amsterdam. (MAT-31)

Bernard RP, Omran AR, Kendall EM: Monitoring of risk groups for improved maternity care. In Proceedings of the IXth World Congress of Gynecology and Obstetrics, Tokyo, Japan, October 25-31, 1979, p 853. Excerpta Medica, Amsterdam. (MAT-36)

Estellita Lins F, Fortney J: Cesarean section in four Rio de Janeiro hospitals. Int J Gynaecol Obstet (in press). (MAT-37)

Bhatt RV, Pachauri S, Bernard RP, Jamshedji A: Maternity care monitoring (MCM) at the Baroda Medical College Hospital, Baroda, India. In Proceedings of the IXth World Congress of Gynecology and Obstetrics, Tokyo, Japan, October 25-31, 1979. Excerpta Medica, Amsterdam (in press). (MAT-38)

Bernard RP, Sastrawinata S, Agoestina T, Kendall EM: Maternity care monitoring (MCM) in Indonesia: early findings and implications for the 1980's. In Proceedings of the BKS PENFIN Contributors Conference, Bandung, Indonesia, November 30-December 1, 1979 (in press). (MAT-40)