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30 September 1985 — 30 September 1986

Cooperative Agreement

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Annual Report

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I. INTRODUCTION

As Family Health International (FHI) completes the second year of its Cooperative Agreement AID/DPE-0537-A-00-4047-00, we continue to be proud of our responsiveness to AID's requirements. We consider ourselves exceptionally well placed to bring additional skills and resources to bear on some of the key problems facing contraceptive and other family planning research throughout the world. During the past year considerable emphasis was placed on long-term planning for contraceptive systems development and the consolidation of our position as a leader in the conduct of research on family planning services, evaluation of programs and the conduct of Clinical Trials in over 50 countries. With the approval of AID's Technical Monitor, the FHI staff was further strengthened by the addition of new staff capabilities in the process of carrying drugs and devices through the FDA system, up to and including application for new drug approval (NDA). The excellent technical relations FHI enjoys with both AID and FDA staff in the development of new and improved methods of contraception have promoted both growth and maturity in FHI's capability to manage and implement all aspects of contraceptive research and development.

In 1986, FHI further demonstrated its capability to manage the long, slow processes of basic research and Phase I and II clinical trials by making highly focused contributions to the development of spermicides and immunocontraceptives. The management of FHI is aware that population growth is particularly unforgiving of delays in the introduction and adoption of needed new methods of contraception and

feels an obligation to use its fifteen years of worldwide experience to question every step in the development of new contraceptive methods and devices with an eye to acceleration of the process.

FHI, agreeing with AID's population program managers, continues to regard the timely approval by the Food and Drug Administration (FDA) of one or more sustained-release steroidal contraceptives as its number one priority and is working toward that end by formatting all documentation to FDA requirements at the earliest stages of development. Also, during 1986 FHI moved closer to FDA approval for use of the Filshie Clip for voluntary female sterilization.

The Cooperative Agreement anticipates self-help and growth; FHI has worked hard in the past year to secure support from philanthropic foundations and to contribute towards its own growth by accepting some commercial work.

Money from non-AID sources is used to underwrite long-term strategies and to support such activities as highly experimental, initial investigations of possible new methods of contraception and feasibility of new ideas. These strategies include work in countries where AID may not find it easy to support family planning activities or where the use of non-AID resources would be more convenient or necessary in order to meet schedules or exploit opportunities imaginatively.

In the reporting period, FHI's Clinical Trials priorities centered around sustained-release steroids and we continued development of the

NET injectable programs and expanded the NORPLANT® trials into a number of new countries.

We are also eager to find ways to move forward with the subdermal pellets inasmuch as they promise to be simpler to use and cheaper to manufacture than some other methods of delivering long-acting steroids.

In 1986 we continued to strengthen the Family Health Research Centers, and we are particularly proud of the important roles which those autonomous institutions are playing in the overall development of family planning in countries such as Bangladesh and Egypt. In Reproductive Epidemiology, we continued to give considerable emphasis to the study of the interrelationship between contraception and the control of sexually transmitted diseases and foresee this area of activity as providing potential solutions to increasingly important public health problems. In the reporting period FHI provided assistance in the initiation of studies under the Cooperative Agreement that AID has established with Georgetown University to continue and expand the program of research in Natural Family Planning which FHI pioneered.

In 1986 FHI increased its efforts in disseminating the findings from its studies through many scientific journals and other media. The lists of publications, studies, status and consultant reports for the year are attached as Appendices to the report.

As we move into the next year of our AID program we have a knowledgeable organization with a worldwide network of contacts, a great deal of accumulated insight and experience in all aspects of family planning, a cost-effective operation and responsive management. We look forward to implementing the remainder of our Cooperative Agreement as effectively as possible. We also plan to make our skills and experience increasingly more useful to a broader range of family health programs, by building on our past successes.

II. CONTRACEPTIVE DEVELOPMENT

FHI manages the clinical evaluation of new contraceptive products throughout many parts of the world. However, the timing and management of initiatives undertaken prior to FHI's involvement substantially determine when new methods of contraception become available for widespread human use. FHI is, therefore, closely concerned with these early stages, including scientific initiatives in the laboratory, the early recognition of a product's potential, and the plans and interactions between scientists of various disciplines, all of which are necessary to move the product forward to the market place. FHI has probably given more attention to the staff and management necessary to conclude a successful development in the shortest possible interval than any comparable agency.

FHI sponsored a workshop in Houston, Texas, during February 1986, for an international group of researchers who specialize in immunological research with the zona pellucida. The use of unified terminology was agreed on by the attendees, each of whom also described the state of the art in his respective laboratory. More communication between these specialists was requested and will be followed-up by FHI. In another area of immunocontraceptive research, fifty-two antisperm antibodies were collected from 33 collaborating laboratories by Drs. Deborah Anderson and Nancy Alexander at Harvard Medical School and the Oregon Primate Center, respectively. These monoclonal antibodies were coded and subjected to screening and characterization tests and the best candidates were revealed for more testing and development as antifertility agents. This FHI sponsored research was presented at a

Monoclonal Antibodies to Human Sperm Workshop at Toronto, Canada on 30 June 1986. The workshop was co-sponsored by World Health Organization (WHO). In March 1986, FHI entered into an agreement with the Department of OB/GYN, University of North Carolina, to provide the annual salary of a post-doctoral student.

Dr. Robert Shabanowitz was hired to fill this post-doctorate position utilizing extra zonae pellucidae from the in vitro fertilization laboratory for research, and keeping FHI alert to new leads in immunocontraception.

In December 1985, FHI convened a meeting of experts on spermicides. Much interest was generated with regard to the need for new safe and effective spermicides, and also for new delivery systems.

Using AID and Andrew W. Mellon Foundation support, FHI sponsored preclinical and Phase I clinical studies of D-propranolol as a potential vaginal contraceptive. This led to the preparation of a detailed development and evaluation plan for the product which was submitted to National Institutes of Child Health and Human Development (NICHD) for funding consideration. In response, NICHD awarded to FHI a contract for the formal full-scale development of this potential new advance in vaginal contraception. Work continues in several areas specified in the original work plan, although the sequence in which certain sub-projects will be implemented has been modified pursuant to discussions with AID and NICHD.

The stereospecific synthesis of D-propranolol, undertaken by Sython Laboratories, has proved extremely difficult, primarily due to

problems associated with scaling up the synthesis. A 50 gm sample was delivered in March 1985, followed by an additional 120 gm sample in May 1985. Attempts to identify alternate suppliers are continuing. While small scale synthesis is difficult, there is no reason to assume that such synthesis would be a bottleneck in large scale use, if the method proves effective.

Dr. James Swarbrick, University of North Carolina at Chapel Hill, has completed the development of prototype formulations of D-propranolol. Extensive studies of in vitro release profiles of these prototypes have yielded two acceptable formulations, one cream and one gel. Both were found to have acceptable retention characteristics in the vagina of the stumptailed macaque, in which postcoital efficacy studies are to be done.

The cream and gel formulations of D-propranolol (in concentrations of 1-5%) have undergone in vitro testing by Dr. Patricia Saling at Duke University, who has studied the acute spermicidal efficacy (Sander-Cramer test), the effects on sperm penetration of cervical mucus (Penetrak Test) and the effect on fertilization (the Zona-free hamster egg, or ZHFE, test). In both cream and gel formulation, concentrations of 4-5% D-propranolol showed good results in the Sander-Cramer and Penetrak tests. Pure D-propranolol did not appear effective in the ZHFE test.

Preliminary tests of the acute postcoital spermicidal activity of the formulations in the stumptailed macaque have been completed by

Dr. Lourens Zaneveld, Rush-Presbyterian/St. Luke's Medical Center, Chicago. At 5% D-propranolol, both cream and gel are effective, but results obtained with the gel are more reproducible. The topical irritation potential of the most promising formulations are being investigated by means of the rabbit vaginal irritation test, conducted by Dr. Donald Waller, University of Illinois at Chicago. Preliminary studies are in progress.

In the next 12 months, emphasis will be placed on the completion of ongoing preclinical studies of D-propranolol and the initiation of several additional preclinical and two Phase I clinical investigations. Upon the request of the AID and NICHD, preclinical teratology and toxicology testing will be delayed until after completion of the first Phase I human trial. This initial study will assess the acute safety of administering D-propranolol vaginally. Upon successful completion of this trial, an additional Phase I study of the spermicidal efficacy of intravaginal D-propranolol in protected females will be initiated at two clinics.

FHI is conducting animal studies, required by the FDA, on the Filshie Clip as part of a submission for marketing approval in the USA. A two year carcinogenicity study in female rats and mice is being sponsored by FHI jointly with FemCare, Ltd and Cabot Medical Corporation at The University of Nottingham, Nottingham, England. The study, underway since February 1986, will assess the potential tumorigenic effect of the titanium silicone rubber Filshie Clip and Falope Ring, both used to occlude the Fallopian tubes in female sterilization.

FHI has continued to support clinical studies of non-surgical female sterilization methods. A coordinated plan of work has been funded from both the Mellon Foundation and AID. In addition, a preclinical program is underway to identify new tubal sclerosing agents that might provide better efficacy and improved safety than the products currently in human trials. During 1985-86, preclinical efficacy studies were conducted in rats using quinacrine hydrochloride and lysine. In experiments conducted at the University of Aberdeen in Scotland, both agents, when injected into the uterine horns, produced either fibrosis or leucocytosis which resulted in occlusion of the uterine lumen. Although the extent of occlusion varied considerably from animal to animal, the degree of occlusion generally appeared much the same at 10 and 45 days after drug administration. Experiments conducted at Wright State University in Ohio focussed on the reproductive capacity of treated rats. Both agents significantly lowered the number of embryonic implantation sites in the uteri in both short-term (approximately 10 days) and long-term (approximately 2 months) trials which correlates with the results from the study in Scotland.

III. CLINICAL TRIALS

In response to the continued demand for family planning products and services around the world, FHI has maintained an emphasis on the evaluation and introduction of approved, established products in new settings in addition to developing and evaluating new steroid formulations and devices for the ultimate purpose of obtaining FDA marketing approval; only products approved by the FDA can be purchased as commodity supplies by AID. As of September 1986, the Clinical Trials Division of FHI was conducting 60 studies of contraceptive products in over 20,000 volunteers through the collaboration of about 200 investigators in 48 countries.

The development of a variety of long-acting contraceptive steroid delivery systems remains FHI's priority for the development of new modalities of contraceptive. In collaboration with Program for Applied Research in Fertility Regulation (PARFR), Stolle Research and Development and Ortho Pharmaceuticals, FHI has assisted in the Phase I evaluation of a 30-day norethindrone microencapsulated injectable formulation. Having accepted the transfer of the IND for a 90-day norethindrone microencapsulated injectable formulation from Northwestern University (PARFR), FHI has taken a leading role in two multi-center Phase II studies of this new product. A preliminary review of study progress indicates that the 90-day injectable should be a safe and effective contraceptive. Menstrual bleeding patterns, ovulation and norethindrone serum concentrations appear to be dose-dependent. Interim analyses of these studies is expected by December 1986 leading to Phase III studies in early 1987.

FHI is working to get a satisfactory supply of NET biodegradable subdermal implants. Pre-introductory clinical trials of the NORPLANT® implant system are underway in 8 countries at 22 sites and the rates of enrollment and apparent acceptability of the method have surpassed the original expectations at virtually each study site. FHI's efforts include a full strategy to build within each country the infrastructure which will be required to provide the product on a national level. The safety profile and the contraceptive efficacy of the product are fully consistent with the earlier clinical studies conducted by the Population Council and Leiras Pharmaceuticals. The primary problem for the user of the method continues to be disruption of regular bleeding patterns with up to 80% of women reporting changes. Amenorrhea, which occurs very commonly, seems to be an acceptable phenomenon in most users. Current research activities are designed to assist investigators to become fully comfortable with the method and to obtain local data which will be useful in establishing the method in the countries concerned. FHI's policy will be to try to continue to supply current sites with NORPLANT® and to maintain local skills and interest until such time as FDA approval of the method is forthcoming.

The Filshie Clip is another new product which is being evaluated for the ultimate purpose of regulatory approval in many countries including the United States. The clip may be applied to fallopian tubes via laparoscopy or minilaparotomy and is being compared with other devices and approaches such as the Wolf clip, the tubal ring and electrocautery in a total of 29 studies in 16 countries by 25

investigators. Clinically, it is believed that the fallopian tubes are easier to repair after clip application than after alternative forms of tubal occlusion. Studies being conducted in Canada and Europe are pivotal for submission to the FDA whereas the other studies will be supportive in this application. Marketing approval from the FDA will be sought in late 1988. In parallel with these clinical studies, FHI, Cabot Medical, and Femcare, Ltd. are supporting carcinogenicity studies of the Filshie Clip and the tubal ring in rats and mice. The results of this study will be submitted together with the clinical data in application for marketing approval.

The simplification of female sterilization methods remains a high priority for FHI; the non-surgical approach continues to be evaluated. During the past year, a comparative study of the direct placement of quinacrine or tetracycline into the fallopian tubes was completed in Mexico, and a Phase I study of the intrauterine placement of slow-releasing quinacrine neared completion in Los Angeles. Phase I studies of tetracycline and quinacrine were also initiated at two other centers in the U.S. but volunteer recruitment has been slow, resulting in the initiation of 2 additional centers late in the fiscal year. All Phase I studies are expected to be completed in 1987 and should lead to Phase II efficacy trials early in 1988.

Although the majority of the intrauterine devices (IUDs) previously available to American women have been withdrawn from the market by pharmaceutical manufacturers for purely economic reasons, the demand

for these products continues to be strong throughout other parts of the world. In view of the convincing evidence of the excellent efficacy and relative safety of the 380A IUD and the FDA marketing approval of the product, FHI is assisting investigators in 19 countries to compare this product with other IUDs available in their respective countries for the purpose of determining which product is most acceptable for local populations. It is expected that the outcome of these studies will encourage the adoption of the 380A IUD into family planning programs throughout the world, particularly where inferior products are now being used.

Since oral contraceptives (OCs) continue to serve as a primary method of contraception in many countries, FHI has for over 3 years been providing assistance to clinicians to become familiar with low-estrogen-dose products. These studies are not only permitting a comparison between the low-dose pills and standard-dose products, but also are providing an opportunity for the comparison of a variety of formulations of the low-estrogen-dose OCs. These studies will provide an insight into the clinical safety and efficacy of these products when used by third world women, not only in individual countries, but will provide an unprecedented, broad international objective evaluation. The majority of these studies are nearing completion and will result in publications over the next 12 months.

Since the triphasic oral contraceptives are becoming available throughout the world, FHI is sponsoring the comparative evaluation of these and monophasic products. These studies are important since triphasic products may present special problems of patient compliance

with recommended regimens. The latter studies are proceeding slowly since the pharmaceutical manufacturers have been reluctant to make these new products available for international evaluation. Other studies of oral contraceptives are evaluating the impact of routinely administering iron supplements for one week following 3 weeks of steroid therapy with an emphasis being placed on product safety and hematology.

Although vaginal contraceptive products have not enjoyed the widespread international popularity of oral contraceptives, IUDs and female sterilization methods, these products do have the potential for a high level of acceptability in certain countries. Studies, recently completed or now drawing to a close, which compared foaming vaginal tablet formulations as well as contraceptive foams indicate that these products may be highly acceptable in countries such as Ghana, Yugoslavia and Egypt. In contrast, couples in Bangladesh were generally not satisfied with these products. A comparative study of vaginal tablets just begun in Thailand indicates that these products may have some appeal to this culture at this time even though earlier studies in the same region were not successful. Other countries now expressing an interest in these methods include Pakistan and Chile. Like condoms, spermicides have a deterrent action against sexually transmitted diseases (STDs) and therefore may become the focus of increasing interest.

Recognizing that the ideal vaginal contraceptive products have as yet not been identified, FHI has continued a program to identify new spermicides and also new contraceptive devices. A program for the

development and evaluation of D-propranolol as a spermicide has begun by FHI with joint funding of NICHD and AID. Initial formulations have been prepared and in vitro and in vivo screening studies indicate that the product may have substantial spermicidal efficacy. Phase I human trials are expected in mid-1987. Plans have also been developed to evaluate in women the safety and efficacy of a new non-spermicide-containing disposable vaginal barrier which could be worn by a woman for over 24 hours following insertion.

The comprehensive research program conducted by the Clinical Trials Division is, thus, dedicated and designed to make available to couples throughout the world the best contraceptive products which are currently in Western markets, to test the acceptability of such products by users and the logistics of making them available in different countries, as well as developing new and improved products which may be more acceptable than those agents and devices currently being offered.

A. Systemic Contraception

1. Long-acting Steroids

a) 90-Day NET Biodegradable Injectable

FDA marketing approval for an injectable contraceptive remains FHI's first priority. The 90-day injectable biodegradable formulation of norethindrone (NET) that permits the continuous low-dose administration of the progestin is midway in Phase II testing. In a

joint project with PARFR, a comparison of 100 mg and 65 mg of NET was initiated at eight centers in Spring 1986. A single-site Phase I study comparing 50 mg and 30 mg was completed in September 1986. FHI is providing regular monitoring of the studies, processing and analyzing the data, and working closely with AID, Stolle R&D Corporation, and Ortho Pharmaceutical on planning the Phase III clinical trial program that will lead to FDA marketing approval for the product. Studies are expected to begin in the spring of 1987. FHI continues to support work at Stolle R&D to scale up the production of the formulation in preparation of the Phase III trials.

In September 1986, a meeting of the NET injectable coordinating committee was held at AID to review a report prepared by FHI on the progress of the ongoing 90-day NET trials. The report covered the clinical experience available to FHI as of August 25. Over 100 women have been enrolled in the Phase II research program. No disturbing side effects have been observed and no pregnancies have been reported. Following the injection of either the 65 mg or the 100 mg dose, ovulation is apparently inhibited in virtually all women for the subsequent 90-day interval. The 30 and 50 mg doses apparently result in considerably more bleeding irregularities than the two higher doses, thus potentially limiting product acceptability. Following injection, NET blood levels are well-controlled after each dose and the serum concentrations of NET are apparently proportional to dose. A decision was made to use the 65 mg dose for Phase III clinical trials.

FHI, Stolle R&D, Ortho, NICHD and AID representatives participated in a meeting at the FDA to review FDA requirements for carcinogenicity studies of long-acting NET formulations. A study protocol will be developed for a two-year carcinogenicity study in rats. This study is expected to be applicable to the NET pellet formulation as well (See Future Plans).

The 30-day NET injectable entered Phase I study in May 1986. Twenty-one women have been enrolled in this 15 mg and 30 mg once a month injectable study.

b) NORPLANT[®] Implants

FHI has undertaken a number of pre-introductory, Phase III clinical trials of the NORPLANT[®] contraceptive subdermal implant system. The objective of these studies is to introduce the NORPLANT[®] system into countries that have no previous experience with the method, to provide proper training to physicians in the insertion and removal techniques and in patient counseling, and to determine overall acceptability of the implants in different populations. Pregnancy rates, rates of removal for menstrual problems, side effects or other medical reasons, and continuation rates will be used to evaluate safety, efficacy and acceptability.

FHI has set up an in-house team representing various disciplines to attempt to identify some of the sociodemographic characteristics and culture-specific factors that may affect widespread acceptability of NORPLANT[®] implants. The clinical trials provide the opportunity to

administer interview questionnaires to potential acceptors in selected centers. The purpose of these questionnaires is to assess how much appeal the method may have among potential users, to explore reasons why potential users would be willing or unwilling to use the method, and to compare characteristics of acceptors with those of women opting not to use the method.

In addition to the Acceptability Surveys administered to all potential acceptors, actual acceptors and providers participating in the clinical trials are asked their subjective opinions about the method at the six-month follow-up visits.

All investigators participating in the clinical trials receive standardized training in the proper insertion and removal techniques at a regional training site. To date, 11 investigators from Asia have been trained at Raden Saleh Clinic in Jakarta, Indonesia, and 13 investigators from West Africa, Haiti and Venezuela have been trained in Santo Domingo, Dominican Republic. Additional investigators from El Salvador, Pakistan, Peru and Senegal are expected to be trained during FY 1987.

The total number of centers currently participating in NORPLANT[®] pre-introductory clinical trials is 19 sites in 7 countries. A summary of admissions is presented in Table 1.

Insertions have been performed in 2178 women to date. There have been a total of 90 removals, 8 due to accidental pregnancy, 34 for menstrual problems, 27 for medical reasons, 5 for a planned pregnancy

and 16 for personal reasons. Of the eight pregnancies, only one is a possible method failure; in the others, the women were likely pregnant at admission. Additional data are being sought to more accurately estimate dates of conception in relation to dates of NORPLANT[®] insertion. All eight pregnancies were intrauterine. Two of these have resulted in live births with no fetal abnormalities and one was terminated by induced abortion.

Of the 34 removals for menstrual-related problems, 28 (82.4%) were due to menorrhagia/prolonged bleeding. The remaining menstrual-related removals occurred in women who discontinued because of amenorrhea (3 cases) and spotting/intermenstrual bleeding (3 cases). Infection at the implant site led to discontinuation in 7 (26.0%) of the 27 removals due to other medical reasons. Depression and combined side effects (e.g. headaches, blurred vision, nausea, vomiting) were the second most frequent other medical reason given, each accounting for 3 cases. The remaining removals in this category were due to changes in weight, tuberculosis and jaundice (2 cases each), a decrease in libido, unhealed implant site, respiratory problems, hypertension, elective surgery, excessive salivation, hepatitis and fainting (one case each).

A summary of cumulative life-table event rates across all study sites is presented in Table 2. The pooled continuation rates are 100.0, 99.1 and 96.7, respectively, after 1, 3 and 6 months of use. The corresponding follow-up rates are 96.4, 86.8 and 58.8.

Table 1
Status of Ongoing NORPLANT® Clinical Trials

	Initiation Date	Planned Caseload	Insertions Performed
Bangladesh			
Center 704	Feb. 1985	200	200
Center 718	Feb. 1985	200	200
Center 721	Feb. 1985	200	200
Ghana			
Center 041	Oct. 1985	100	0
Haiti			
Center 8017	Nov. 1985	100	98
Center 8331	Nov. 1985	100	100
Center 8332	Nov. 1985	50	50
Nepal			
Center 729	Feb. 1985	300	307
Center 731	May 1985	100	100
Nigeria			
Center 040	Oct. 1985	70	68
Center 042	Oct. 1985	50	51
Center 435	Jan. 1986	50	49
Center 437	Oct. 1985	50	54
Center 453	Nov. 1985	50	36
Philippines			
Center 600	Feb. 1986	100	61
Center 602	Jun. 1986	100	5
Sri Lanka			
Center 703	May 1985	200	200
Center 749	May 1985	200	200
Center 758	May 1985	200	200
Total		2420	2178

TABLE 2
 NORPLANT® Clinical Trials
 Cumulative Life-table Event Rates

Event	Rate per 100 users
Accidental pregnancy	
1 month	0.0
3 months	0.1
6 months	0.5
Removal for menstrual problems	
1 month	0.0
3 months	0.2
6 months	0.7
Removal for medical problems	
1 month	0.0
3 months	0.5
6 months	1.3
Continuation	
1 month	100.0
3 months	99.1
6 months	96.7
Follow-up*	
1 month	96.4
3 months	86.8
6 months	58.8

*Represents women who have returned for scheduled follow-up visits to date. The decreasing rates over time largely reflect the overall progress of all FHI studies to date.

Future Plans

Interim analysis of the Phase II 90-day NET injectable study will be performed by December 1986 and a meeting with the FDA will be held to finalize plans for the early initiation of Phase III studies.

FHI will continue to support the development of the 30-day NET injectable with study monitoring, data collection and analysis and will design and implement Phase II and III clinical trials.

NET biodegradable implants are being formulated, with Endocon providing funding and raw materials for the process. Preclinical studies will be conducted to assure product quality. FHI has assumed responsibility for the IND and for communications with the FDA. FHI is eager to move forward with this potentially low cost, easy to use method of long-term contraception and plans to conduct a Phase I evaluation of the NET pellets to ensure bioequivalence to previously studied pellets, and then initiate and conduct Phase III trials in preparation for the submission of an NDA.

If the subdermal pellets continue to perform satisfactorily they could make a major contribution to worldwide family planning programs in the 1990s and as development proceeds, some important policy decisions will have to be made about how to introduce the method to selected LDCs.

During 1987, pre-introductory clinical trials of NORPLANT® subdermal implants are expected to begin in El Salvador, Pakistan, Peru,

Senegal and Venezuela. Training of investigators from Venezuela is complete, whereas physicians from the other countries will be trained in either Jakarta or Santo Domingo in late 1986 or early 1987. Other countries being explored as possible study sites include Panama and Zimbabwe.

Due to the seemingly universal demand for sustained release steroids, several proposals have been prepared for expanded clinical trials of NORPLANT® in countries having prior introductory experience with the NORPLANT® system. The objective of these proposals is to increase the caseloads at existing centers, while at the same time establishing the framework for training new investigators in the insertion and removal techniques and gaining wider experience with the method. Another major component of the expanded trials phase is the development of user-oriented materials tailored to the cultural and educational characteristics of the client populations in each of the countries. A prototype standardized training curriculum has been developed in collaboration with the Association for Voluntary Surgical Contraception (AVSC), the Population Council (PC), and the Program for the Introduction and Adaptation of Contraceptive Technology (PIACT). PIACT has also prepared prototype versions of various counseling materials, brochures and handouts, and will provide technical assistance in their adaption for local use. Many of the expanded clinical trials projects (e.g. Bangladesh, Haiti, Nigeria) and new pre-introductory trials efforts (El Salvador, Pakistan, Senegal) will be supported directly by the local USAID Missions.

In the long-term, building skills and experience using NORPLANT® is not only expected to lay a secure foundation for the wider use of this method when it receives FDA approval and if it can be made available in larger quantities, but should assist in the acceptance and use of all the new generation of sustained release steroids likely to enter use in the 1990s.

2. Oral Contraceptives

FHI has continued to compare the efficacy, safety and acceptability of oral contraceptive formulations. In past years, the evaluation of the safety and efficacy of low-estrogen-dose pills and their acceptability in the developing world has been the major focus; new trials are evaluating progestogen-only pills in breastfeeding women, oral contraceptive regimes with and without iron, triphasic pills, and the clinical impact of changing from standard- to low-dose products.

a) Norinyl 1/35

Norinyl 1/35 is being evaluated in a 15-center clinical trial in comparison with Brevicon or Lo-Ovral, two other low-dose pills, and Norinyl 1/50, a standard-dose pill. Acceptability is being measured by continuation rates at one year. Analysis of these studies is presented in the three tables found at the end of this section.

Table 3 shows data from the four centers in the Norinyl 1/35 versus Brevicon trial. Brevicon users have significantly higher

discontinuation rates for menstrual problems and side effects, resulting in a significantly lower 12-month continuation rate, 36.3, compared with 50.1 for Norinyl 1/35 users. The most frequently reported side effect causing discontinuation for Brevicon users is headaches, whereas breakthrough bleeding is the most commonly reported menstrual problem causing pill discontinuation in the Brevicon group.

A Norinyl 1/35 versus Lo-Ovral comparison is being conducted at six centers. Norinyl 1/35 has a significantly higher 12-month termination rate for menstrual problems (Table 4). Breakthrough bleeding is the most frequently reported menstrual problem for Norinyl 1/35 users. However, the two products are similar in all other measures. Cumulative life-table continuation rates at 12 months are 78.1 in the Norinyl 1/35 group and 80.9 in the Lo-Ovral group.

Five centers are participating in the Norinyl 1/35 versus Norinyl 1/50 trial. There have been no differences between the two pill groups with respect to event or continuation rates (Table 5). Continuation rates at 12 months are 75.0 for Norinyl 1/35 and 77.1 for Norinyl 1/50.

TABLE 3
 Cumulative Life-Table Rates for Comparative Studies
 of Norinyl 1/35 versus Brevicon

	Norinyl 1/35 (N=496)	Brevicon (N=497)
Accidental Pregnancy		
1 month	0.2	0.2
4 months	0.5	0.5
8 months	0.8	0.5
12 months	0.8	0.5
Menstrual Problems		
1 month	2.0	4.4
4 months**	8.6	16.8
8 months**	14.2	28.3
12 months**	20.3	36.3
Side Effects		
1 month*	1.3	4.2
4 months**	2.4	8.1
8 months**	6.0	11.2
12 months**	6.7	12.2
Other Medical Reasons .		
1 month	0.9	2.4
4 months	4.3	4.5
8 months	5.9	8.1
12 months	5.9	8.1
Planned Pregnancy		
1 month	0.7	0.7
4 months	2.5	2.8
8 months	5.5	8.2
12 months	7.4	8.7
Other Personal Reasons		
1 month	2.8	2.2
4 months	8.0	9.1
8 months	12.5	12.9
12 months	15.2	17.0
Continuation		
1 month*	90.0	84.8
4 months**	72.8	60.7
8 months**	58.8	43.6
12 months**	50.1	36.3
Follow-Ups		
1 month	96.0	95.2
4 months	92.1	91.3
8 months	88.8	85.5
12 months	81.0	75.9

*p<0.05
 **p<0.01

TABLE 4
Cumulative Life-Table Rates for Comparative Studies
of Norinyl 1/35 versus Lo-Ovral

	Norinyl 1/35 (N=656)	Lo-Ovral (N=653)
Accidental Pregnancy		
1 month	0.0	0.0
4 months	0.6	0.0
8 months	0.6	0.0
12 months	0.9	0.9
Menstrual Problems		
1 month	1.1	0.5
4 months	2.8	1.2
8 months*	3.7	1.2
12 months*	4.2	1.2
Side Effects		
1 month	0.5	0.6
4 months	2.0	1.6
8 months	2.9	2.6
12 months	3.7	3.1
Other Medical Reasons		
1 month	0.3	0.3
4 months	0.5	1.4
8 months	1.4	1.6
12 months	1.4	2.5
Planned Pregnancy		
1 month	0.0	0.6
4 months*	0.0	1.8
8 months	1.1	2.4
12 months	2.1	2.8
Other Personal Reasons		
1 month*	1.6	1.0
4 months	3.7	3.7
8 months	6.7	5.0
12 months	8.0	5.2
Continuation		
1 month	96.0	96.5
4 months	88.4	87.8
8 months	81.7	83.9
12 months	78.1	80.9
Follow-Ups		
1 month	91.6	95.1
4 months	84.2	87.8
8 months	76.6	79.6
12 months	68.5	69.1

*p<0.05

**p<0.01

TABLE 5
 Cumulative Life-Table Rates for Comparative Studies
 of Norinyl 1/35 versus Norinyl 1/50

	Norinyl 1/35 (N=769)	Norinyl 1/50 (N=763)
Accidental Pregnancy		
1 month	0.0	0.0
4 months	0.2	0.0
8 months	0.3	0.2
12 months	0.3	0.2
Menstrual Problems		
1 month	1.1	0.8
4 months	2.6	3.4
8 months	4.2	4.7
12 months	4.9	5.5
Side effects		
1 month	0.8	1.3
4 months	2.2	2.8
8 months	3.0	3.7
12 months	3.5	4.3
Other Medical Reasons		
1 month	0.0	0.4
4 months	0.5	1.1
8 months	1.2	2.0
12 months	1.8	2.2
Planned Pregnancy		
1 month	0.3	0.1
4 months	0.9	0.5
8 months	2.5	1.0
12 months	3.8	2.0
Other Personal Reasons		
1 month	0.8	0.6
4 months	3.6	3.0
8 months	6.0	4.4
12 months	7.6	5.7
Continuation		
1 month	96.5	95.7
4 months	88.2	87.5
8 months	80.2	81.6
12 months	75.0	77.1
Follow-ups		
1 month	94.0	93.7
4 months	87.9	87.8
8 months	83.7	84.1
12 months	79.8	80.9

b) Loestrin versus Lo-Femenal

FHI is conducting a comparative evaluation of two other low-dose oral contraceptives, Loestrin (Parke-Davis) and Lo-Femenal (Wyeth). Low-estrogen-dose oral contraceptives are being introduced in government programs throughout the world in an attempt to reduce long- and short-term side effects. A 1,500-case comparison will be conducted at five centers, located in Mexico, Indonesia, Malaysia and Colombia. Three of the studies have been initiated recently.

c) Crossover Pill Studies

FHI is evaluating the acceptability of switching from a standard- to a low-dose estrogen pill. Concern has been expressed that a switch from one oral contraceptive formulation to another may result in an increase or change in side effects that will lead to discontinuation. Of particular concern is the change from a standard- to low-estrogen-dose. The objective of the study is to determine the acceptability of switching from Norinyl 1/50 (Syntex) to Lo-Femenal (Wyeth) in comparison with switching from Lo-Femenal to Norinyl 1/50. The 1,200-case trial will be conducted at four centers located in Yugoslavia, the Philippines, Mexico and Brazil. Three of the centers are active and 429 women have been admitted. Continuation rates at 4 months are 86.4 for the Norinyl 1/50 to Lo-Femenal group and 84.3 for Lo-Femenal to Norinyl 1/50 group.

d) Progestogen-only Oral Contraceptives

FHI continues to introduce progestogen-only pills around the world, with particular emphasis on the contraceptive needs of breastfeeding women. A 4,000 case, 20 center noncomparative clinical trial of the progestogen-only oral contraceptive, Ovrette, is ongoing. The trial has been designed to evaluate the acceptability, safety and effectiveness of this minipill among breastfeeding women.

Preliminary data on 3,262 women from 20 centers in Latin America and Africa show a 6-month continuation rate of 75.0. Most discontinuations were for "other personal reasons", such as the women desired a change, forgetfulness, or the pill was no longer needed. Sixty-three percent of the women have returned for the 6-month visit.

In order to establish the acceptability of the progestogen-only pill in a large population of breastfeeding women, a 10,000-case expanded strategy has been developed to distribute and evaluate Ovrette in several countries, often through a community-based or health post system. Six centers have begun the study in Mali, Ghana and Brazil. Preliminary data on 753 women show a 2-month continuation rate of 88.7. The majority of discontinuations were for the same "other personal reasons" as described above; 71.0 percent of the women have returned for the 2-month visit. In Thailand, a 750-case multicenter introduction of progestogen-only pills has been initiated by the Thailand Fertility Research Association (TFRA). The study is evaluating overall acceptability and efficacy of progestogen-only oral contraceptives, examining the contraceptive practices of breastfeeding women, and assessing the attitudes of health personnel

to the introduction of the progestogen-only pill. Admissions are complete and follow-up is continuing.

An 800-case comparative study of progestogen-only oral contraceptives versus non-hormonal methods in lactating women is being conducted at three centers located in Egypt and Argentina. In addition to evaluating acceptance and side effects of this pill among breast-feeding women, the differences over time in the weight of breastfed infants for both groups will be compared. To date, 310 women have been admitted to the study, and 150 women have completed 3 months of use. No discontinuations have been reported.

e) Oral Contraceptives With and Without Iron

A double-blind placebo controlled trial is being initiated to study the effects of iron supplement tablets on the reported side effects, the acceptability of oral contraceptives and their effect on iron levels in the blood. FHI has obtained the standard-estrogen-dose oral contraceptive, containing 1.0 mg Norethindrone and 50 mcg Mestranol, for this study from Kimia Farma of Indonesia. A 1,920-case comparison will be conducted at six centers, located in the Philippines, Ecuador, Thailand, Indonesia and Mexico. Three centers have been initiated.

f) Triquilar versus Lo-Femenal

Triphasic formulations vary the ratio of progestogen and estrogen to simulate natural hormonal changes in the menstrual cycle. A 1,500

case comparison of the effectiveness, side effects and acceptability of the triphasic oral contraceptive, Triquilar (Schering), and the low-dose contraceptive, Lo-Femenal (Wyeth), will be conducted at five centers. Center selection has been completed with locations in Brazil, the Dominican Republic, Chile, Sri Lanka and the Sudan. Four centers are active and 251 women have been admitted, 141 of whom have completed their one-month follow-up visit.

Future Plans

FHI plans to develop three additional studies of oral contraceptives: 1) an evaluation of the influence of in-depth counseling on the acceptability of switching from a standard to a low-dose estrogen pill, 2) an assessment of the effect of progestogen-only oral contraceptives on milk yield during lactation, and 3) a comparison of a progestogen-only pill with a low-dose pill in non-breastfeeding, not recently pregnant women.

B. Vaginal Contraceptives

FHI has proceeded with the evaluation of several vaginal contraceptives during the past year including: the diaphragm (Ortho All-Flex™) without spermicide; the diaphragm with spermicide (Gynol-II® jelly); Neo Sampoo foaming vaginal tablets containing the spermicide, menfegol; Ortho (OVT) vaginal tablets containing the spermicide, nonoxynol-9; Ortho vaginal tablets containing menfegol (Neo Sampoo repackaged); and Emko® and Delfen® spermicidal foam, both containing nonoxynol-9. Three multi-center comparative trials

evaluating foaming tablets and a single-center comparative trial evaluating the diaphragm with and without spermicide versus foam were ongoing during 1985-1986. Eight study centers were active during the year, including five that were actively recruiting volunteers.

Tables 6 and 7 summarize the results of these trials. One active site compared Neo Sampooon with foam (Study 785); one compared the fitted diaphragm with and without spermicide, and spermicide alone (Study 7788); and six compared Ortho vaginal tablets containing menlogol with Ortho tablets containing nonoxynol-9 (Studies 7798 and 7799).

In Study 785 conducted in Yugoslavia, no significant differences in effectiveness or acceptability were observed between Neo Sampooon and Emko[®] foam users, with the exception that significantly more foam users reported male discomfort/irritation than Neo Sampooon users. The twelve-month life-table accidental pregnancy rates (11.7 for Neo Sampooon; 19.3 for foam) were higher and the twelve-month continuation rates (Neo Sampooon 48.4, foam 39.5) were lower than those of a similar trial previously completed in Egypt. Product-related complaints reported most often included itching, product troublesomeness and male discomfort/irritation; vaginal discharge was greater than before adopting the method in approximately 20% of product acceptors. The results for Study 785 should be considered the final report for this trial.

In a continuing trial, 19 women have accepted the diaphragm with spermicide, 16 have accepted the diaphragm alone, and 18 have

accepted foam alone in Study 7788 (England). No significant differences in acceptability have been observed between diaphragm with and without spermicide and spermicide alone users. Of 5 pregnancies reported to date, none have been reported in the Delfen® foam group, and 3 have been attributed to failure to use the diaphragm with or without spermicide correctly.

Two comparative studies of OVT with nonoxynol-9 versus OVT with menfegol have completed the admission phase and are proceeding satisfactorily in Ghana and one study has begun in Thailand (Study 7798). At one site in Ghana, significantly more OVT-nonoxynol users than OVT-menfegol users reported product messiness and failure of the tablet to dissolve, yet only one user discontinued because of these complaints. Few discontinuations or product-related complaints have been noted at the other site in Ghana. The study in Thailand was initiated in late July, and 50 cases have been admitted during the first two months of recruitment.

Three comparative studies of the two Ortho tablets have also been underway in the United States (Study 7799), although recruitment has continued to be extremely difficult at these sites. Lost-to-follow-up rates are high and most women have reported some type of method-related complaint; common complaints have included burning, product messiness, difficulty with proper placement, and retention of foam. Reports of occasional and frequent nonuse of the tablets are relatively common compared to reports of irregular use at the international study sites. The primary reasons given for irregular

use in these U.S. tablet studies include user neglect and the women's belief that one cannot get pregnant during menses.

FHI has also begun a double-blind study in Costa Rica to evaluate whether or not the use of tioconazole 2% vaginal cream compared to a placebo reduces the risk of contracting gonorrhea and chlamydia in women at high risk for contracting these infections (Study 7800). Twenty-one potential study volunteers have been screened and six have been enrolled. The remaining fifteen are being treated for chlamydia or gonorrhea and will be enrolled following a test of cure. To date, one volunteer has discontinued from the study because of intense vulvo-vaginal burning and family problems.

TABLE 6
 Twelve-month Gross Cumulative Life-table Rates
 per 100 Women for Selected FHI Comparative Vaginal Contraceptive Studies

	Study 785		Study 7798		Study 7799*	
	Neo Sampoo (N=135)	Foam (N=131)	OVT-n** (N=97)	OVT-m** (N=93)	OVT-n** (N=29)	OVT-m** (N=29)
Accidental pregnancy	11.7	19.3	10.3	15.5	12.1	13.9
Planned pregnancy	5.6	6.8	1.4	1.3	11.8	0.0
Allergic reaction	0.0	0.0	0.0	0.0	0.0	0.0
Other medical	0.0	0.0	0.0	9.6	0.0	0.0
Discomfort	24.6	32.1	4.8	1.3	16.7	15.1
Product-related	1.4	2.1	1.1	0.0	8.0	6.5
Other personal	21.7	20.9	7.2	6.6	22.4	4.1
Continuation rate	48.4	39.5	77.4	69.4	46.1	65.5
Follow-up rate	86.8	91.1	54.4	52.1	25.0	57.1
Women months of use	1040	921	742	682	92	136

*Only six-month life-table rates available for this study

** OVT-n = OVT with nonoxynol-9 OVT-m = OVT with menfegol

Table 7

Reasons for Discontinuation
for FHI Comparative Vaginal Contraceptive Studies
of OVT-Nonoxynol-9 vs OVT-Menfegol

	Study 7798		Study 7799	
	OVT-n* (N=97)	OVT-m* (N=93)	OVT-n* (N=29)	OVT-m* (N=29)
Accidental pregnancy	9	8	2	5
Planned pregnancy	1	1	1	0
Medical	0	5	1	0
Discomfort				
Penile irritation	0	0	1	2
Burning	3	1	0	0
Vaginal soreness	0	0	0	1
Unspecified female discomfort	1	0	0	0
Product-related				
Messy				
Messy, inconvenient	0	0	1	1
Failure to dissolve	1	0	0	0
Other personal				
Lessens spontaneity	0	0	1	1
Partner objects	2	1	0	0
Irregular intercourse	2	4	1	0
Women completing 12-month study	43	38	2	4

* OVT-n = OVT with nonoxynol-9

OVT-m = OVT with menfegol

Future Plans

FHI will continue to study the effectiveness and acceptability of several vaginal contraceptives in the coming year. Comparative trials of foaming tablets will continue, primarily at international sites. FHI plans to initiate several programmatic studies of spermicides, possibly in Pakistan, Haiti, Chile and in one or more African countries. The diaphragm study in England (Study 7788) and the tioconazole study in Costa Rica (Study 7800) will continue. Tioconazole is expected to have spermicidal activity and will be studied as a potential vaginal contraceptive pending successful results of the study of its prophylactic effect against STDs.

FHI is also sponsoring the submission of an Investigational Device Exemption (IDE) for an entirely new vaginal contraceptive device. Two Phase I clinical trials are planned to assess the efficacy (in postcoital tests) and the safety (in a short-term tolerance study) of Lea's Kap, a non-spermicide fitted vaginal barrier device. Studies involving a disposable diaphragm, vaginal rings and potential new spermicides, such as chlorhexidine, will also be kept under close review.

C. Voluntary Surgical Sterilization

1. Female Sterilization

The primary emphasis in female sterilization strategies has been on the evaluation of the Filshie Clip. Because this is a relatively new

device it is being compared with the tubal ring, the Wolf Clip, the Secuclip, bipolar electrocautery and the Pomeroy method of tubal occlusion. Comparisons will examine the ease of use, and the complications and pregnancy rates as reported by 24 centers in which trials are being conducted. Non-comparative trials in England and Canada will provide the basis for requesting FDA approval for marketing.

FHI is also continuing the long-term follow-up of a variety of surgical sterilization techniques:

a) Filshie Clip versus Wolf Clip

The Filshie Clip is being compared with the Wolf Clip in minilaparotomy procedures in interval women in Panama, the Dominican Republic and in Malaysia. To date 487 procedures have been performed. There have been no technical failures. The following table (Table 8) details the surgical difficulties.

Two women (0.8%) in the Wolf Clip group were reported as having a major complication from sterilization to discharge. Early follow-up (<30 days post-sterilization) visits have occurred for more than 75% of the cases. Twenty-seven Wolf Clip cases (12.2%) and 32 Filshie Clip cases (14.5%) reported one or more complications at early follow-up. One luteal phase pregnancy was reported in the Filshie group. Long-term (>30 days post-sterilization) follow-up visits are underway. Half of the women in each group have returned for long-term follow-up visits. One woman in the Filshie Clip group was

readmitted to the hospital as were two women in the Wolf Clip group. In all, eleven Filshie Clip cases and eight Wolf Clip cases reported one or more complications. One more center is being sought for this comparison.

The two clips are also being compared in laparoscopic procedures. Four sites are now active, one in Haiti and three in Latin America. Interval sterilizations have been performed on 680 patients; one technical failure has been reported in a case (Wolf) where only one tube was found. Surgical difficulties, injuries and complications are detailed in the following Table 9. Over 85% of the women in both groups have returned for early follow-up visits (<30 days post-sterilization). Twenty-five Filshie Clip cases (8.4%) and ten Wolf Clip cases (3.3%) reported one or more complications at early follow-up. Long-term follow-up visits (>30 days post-sterilization) are in progress.

TABLE 8
 Filshie Clip versus Wolf Clip
 via Minilaparotomy

	Filshie Clip (N=240)		Wolf Clip (N=234)	
	No.	%	No.	%
A. Events at Surgery				
<u>Surgical difficulties</u>				
With equipment	0	-	1	0.7
Entering the peritoneum	1	0.4	4	1.7
Visualizing/grasping tubes	3	1.3	5	3.5
Occluding tubes	0	-	1	0.4
<u>Surgical Injuries</u>				
Tubal injury without bleeding	0	-	1	0.4
Tubal bleeding	0	-	2	0.8
Cornual lesion	1	0.4	0	-
Uterine tear	1	0.4	1	0.4
Apnea	0	-	1	0.4
Uterine perforation	0	-	2	0.8
Total women with 1+ surgical injuries/ complications	1	0.4	7	2.9
B. Events Reported at Early Follow-up*				
Women returning	220	91.7	221	94.4
Readmissions	1	0.5	1	0.5
Pregnancy	1**	0.5	1	0.5
<u>Complications</u>				
Serous discharge	10	4.5	12	5.4
Hematoma	5	2.3	2	0.9
Inflammation at incision	7	3.2	6	2.7
Abscess	6	2.7	2	0.9
Perineo-plastic surgery	0	-	1	0.5
Women with 1+ complications	32	14.5	27	12.2

TABLE 8 (Continued)

	Filshie Clip (N=240)		Wolf Clip (N=234)	
	No.	%	No.	%
C. Events Reported at 6-month follow-up*				
Women returning for 6-month follow-up	122	50.8	118	50.4
Readmission†	1	0.8	2	1.7
Total women with 1+ complications	11	9.0	8	6.8

*Eleven non-interval cases are excluded from analysis.

**Luteal phase

TABLE 9
 Filshie Clip versus Wolf Clip
 via Laparoscopy

	Filshie Clip (N=337)		Wolf Clip (N=343)	
	No.	%	No.	%
A. Events at Surgery				
<u>Surgical difficulties</u>				
With equipment	0	-	2	0.6
Entering peritoneum	4	1.2	9	2.6
Visualizing/grasping tubes	6	1.8	19	2.9
Occluding the tubes	6	1.8	11	3.2
<u>Surgical injuries</u>				
Cervical laceration	0	-	2	0.6
Tubal bleeding	2	0.6	0	-
Clip left in pelvis	0	-	1	0.3
Soft tissue emphysema	1	0.3	4	1.2
Apnea	1	0.3	0	-
Total women with 1+ surgical injuries or complications	4	1.2	7	2.0
B. Events Reported at Early Follow-up*				
Women returning	302	89.6	297	86.6
Readmissions	1	0.3	0	-
<u>Complications</u>				
Serous discharge/Abscess	3	1.0	3	1.0
Hematoma	0	-	2	0.7
Inflammation at incision	2	0.7	5	1.7
Bleeding at incision	0	-	4	1.3
Ecchymona	0	-	2	0.7
Vaginal bleeding	4	1.3	7	2.4
Other	1	0.3	0	-
Total women with 1+ complications follow-up	10	3.3	25	8.4

*technical failure cases and non-interval cases are excluded from follow-up analysis.

b) Filshie Clip versus Tubal Ring

A comparison of the Filshie Clip and the Tubal Ring via laparoscopy is underway in Panama, Indonesia and Mexico. Volunteer admissions should begin at a center in the Dominican Republic this fall. To date 388 procedures have been performed. There have been seven technical failures. Surgical injuries and complications were reported in 15 (7.7%) of the ring patients and 12 (6.3%) of the clip patients (Table 10).

The only major complications or complaints reported during recovery were two cases of vaginal bleeding in Tubal Ring patients. One luteal phase pregnancy was reported. About 70% of the women in each group have returned for early (<30 days post-sterilization) and 6-month follow-up visits. Over one-third (34.5% of the ring patients and 42.3% of the clip patients) have returned for 12-month-follow-up visits. The center in Panama is beginning 24-month visits.

TABLE 10
 Filshie Clip versus Tubal Ring
 Via Laparoscopy

	Filshie Clip (N=191)		Tubal Ring (N=196)	
	No.	%	No.	%
A. Events at Surgery				
<u>Technical Failures</u>				
Change in approach	2	1.0	0	-
Change in technique	0	-	2	1.0
Two techniques used	0	-	3	1.5
Total	2	1.0	5	2.6
<u>Surgical Difficulties</u>				
Entering the peritoneum	5	2.6	1	0.5
Visualizing/grasping the tubes	3	1.6	9	4.6
Occluding tubes	2	1.0	3	1.5
With equipment	2	1.0	0	-
<u>Surgical injuries/complications</u>				
Cervical laceration	5	2.6	3	1.5
Uterine perforation	1	0.5	1	0.5
Tubal bleeding	1	0.5	9	4.6
Bladder injury	1	0.5	0	-
Lesions	0	-	1	0.5
Soft tissue emphysema	5	2.6	2	1.0
Blood loss > 100 ml	0	-	1	0.5
Total women with 1+ injuries/complications	12	6.3	15	7.7
B. Events Reported at Early Follow-up*				
Women reporting	139	72.3	156	77.0
Readmissions	1	0.7	1	0.7
<u>Complications</u>				
Serous discharge	8	5.8	5	3.3
Hematoma	0	-	2	1.3
Incomplete dehiscence	2	1.4	3	2.0
Inflammation/infection	2	1.4	2	1.3
Eczema	1	0.7	0	-

TABLE 10 (continued)
 Filshie Clip versus Tubal Ring
 Via Laparoscopy

	Filshie Clip (N=191)		Tubal Ring (N=196)	
	No.	%	No.	%
Total women with 1+ complications at early follow-up	15	10.9	12	7.9
C. Events Reported at Long-Term Follow-up				
Women reporting for 6-month follow-up*	145	76.7	140	72.2
Women reporting for 12-month follow-up*	80	42.3	66	34.5
Pregnancies	1	0.7	0	-
Total women with 1+ complications at long-term follow-up**	13	9.0	7	5.1
Readmissions**	2	1.4	3	2.1

* excludes technical failures and non-interval women.

** includes 6-, 12- and 24-month data.

Three centers in Latin America have been equipped to undertake the comparative study of the Filshie Clip and Tubal Ring via minilaparotomy. One center in Kenya began admissions in May. Of the 505 interval procedures performed thus far, (Table 11) eight have resulted in technical failures. These failures were evenly divided between the two techniques. Surgical injuries and complications were reported for 26 (10.1%) of the ring procedures and for 20 (18.1%) of the clip procedures. Nearly 65% of the women have returned for their early follow-up visit (<30 days post-sterilization). The percentage of women reporting one or more complications at the early follow-up visit was 14.9% in the ring group and 19.6% in the clip group. Two pregnancies, one in each group, were reported at early follow-up. Six-month follow-up exams have been completed for over half of the patients; the rate of complications reported at this follow-up visit was 4.8% in the clip group and 9.0% in the ring group. One center has begun 12-month follow-up visits.

TABLE 11
 Filshie Clip versus Tubal Ring Via Minilaparotomy

	Filshie Clip (N=247)		Tubal Ring (N=258)	
	No.	%	No.	%
A. Events at Surgery				
<u>Technical Failures</u>				
Change in approach	2	0.8	2	0.7
Two techniques used	2	0.8	2	0.7
Total	4	1.6	4	1.4
<u>Surgical Difficulties</u>				
With equipment	0	-	2	0.8
Visualizing and/or grasping tubes	16	6.5	24	9.3
Occluding tubes	1	0.4	6	2.3
Entering peritoneum	0	-	2	0.8
Closing incision	0	-	1	0.4
Ovarian cyst	1	0.4	0	-
<u>Surgical Injuries/Complications</u>				
Tubal injury without bleeding	7	2.8	8	3.1
Tubal injury with bleeding	4	1.6	10	3.9
Uterine perforation	4	1.6	1	0.4
Cervical laceration	0	-	3	1.2
Spasm of larynx	0	-	2	0.8
Blood loss > 100 ml	1	0.4	0	-
Vasovagal reaction	1	0.4	0	-
Lesions	2	0.8	0	-
Laceration of ligament	0	-	2	0.8
Laceration of ovary	1	0.4	0	-
Adhesions	0	-	1	0.4
Cardiorespiratory arrest	1	0.4	0	-
Bowel injury	1	0.4	0	-
Total women with surgical injuries/complications	20	8.1	26	10.1
Total women reporting major complications during recovery	14	5.8	13	5.1

TABLE 11 (continued)
 Filshie Clip versus Tubal Ring Via Minilaparotomy

	Filshie Clip (N=247)		Tubal Ring (N=258)	
	No.	%	No.	%
B. Events Reported at Early Follow-up*				
Women returning for early follow-up	218	89.7	238	93.7
Readmissions	1	0.5	2	0.8
Pregnancy (luteal phase)	1	0.5	1	0.4
<u>Complications/Complaints</u>				
Serous discharge/abscess	6	2.8	4	1.7
Inflammation	14	6.4	7	2.9
Hematoma	9	4.1	4	1.7
Incomplete dehiscence	6	2.8	10	4.2
Complete dehiscence	2	0.9	0	-
Infections	3	1.4	2	0.8
Vaginal bleeding	2	0.9	3	1.3
Other complications	5	2.3	6	2.5
Total women reporting 1+ complication at early follow-up visit	48	22.0	36	15.1
C. Events Reported at Long Term Follow-up				
Women returning for 6-month follow-up*	200	82.3	215	84.6
Readmissions	0	-	3	1.8
Women returning for 12-month follow-up*	105	43.2	133	52.4
Total women reporting 1+ complication at long term follow-up**	24	12.0	37	16.9

* excludes technical failures and non-interval women.

**includes 6- and 12-month follow-up visits

c) Filshie Clip versus Pomeroy

A comparison of the Filshie Clip with the modified Pomeroy method via minilaparotomy in postpartum women is underway in four centers in Thailand, the Philippines, Taiwan and Panama. A total of 1022 procedures have been performed to date. Six procedures have resulted in technical failures: four among the Pomeroy cases and two among the Filshie clip cases. Table 12 details the technical failures, surgical difficulties and surgical injuries and complications that have occurred. One case of bleeding, one case of complete dehiscence and a case of postpartum anemia occurred during the recovery period in Filshie Clip patients (data not shown). A Pomeroy patient had a urinary tract infection during recovery. Early follow-up (<30 days post-sterilization) is now complete for more than 80% of the women. During the early follow-up period, complications were reported for a total of 51 (11.2%) Filshie Clip patients and 54 (12.4%) Pomeroy patients.

Approximately 60% of the women in each group have also returned for their six-month follow-up visit. Only two of the complications required hospitalization for overnight observation. During long-term follow-up, 11 women, eight in the Pomeroy group and three in the Filshie Clip group, were readmitted to the hospital. Only one of these readmissions, a hernia operation at the incision site (Pomeroy group), was considered by the investigator to be a complication related to the sterilization.

Almost half of the women in both groups have returned for their one-year follow-up visit. Although almost 20% of them have reported complications at this visit, most of these are reports of keloids at one center. Four pregnancies have been reported, three in Filshie Clip cases and one in a Pomeroy patient. Three centers are conducting two year-follow-up visits.

TABLE 12

Filshie Clip and Modified Pomeroy

	Filshie Clip (N=508)		Modified Pomeroy (N=514)	
	No.	%	No.	%
A. Events at Surgery				
<u>Technical Failures</u>				
Change in approach due to adhesions	0	-	1	0.2
Two techniques used due to:				
Obesity	0	-	1	0.2
Tumors	1	0.2	0	-
Difficulty in application	1	0.2	0	-
Only one tube	0	-	1	0.2
Total	2	0.4	3	0.6
<u>Surgical Difficulties</u>				
Entering peritoneum	3	0.6	0	-
Visualizing tube	7	1.4	15	2.9
Grasping tubes	10	2.0	13	2.5
Occluding tubes	2	0.4	0	-
Uterine involution	0	-	2	0.4
Obesity	1	0.2	0	-
Mesosalpinx varicose	0	-	1	0.2
PID complicated by incision	1	0.2	0	-
<u>Surgical injuries/complications</u>				
Tubal/mesosalpinx injury without bleeding	1	0.2	1	0.2
Tubal/mesosalpinx injury with bleeding	5	1.0	6	1.1
Soft tissue emphysema	0	-	1	0.2
Total women with 1+ injuries/complications	6	1.2	8	1.6

TABLE 12 (continued)
 Filshie Clip and Modified Pomeroy

	Filshie Clip (N=508)		Modified Pomeroy (N=514)	
	No.	%	No.	%
B. Events Reported at Early Follow-up*				
Women returning for follow-up*	454	89.4	435	84.6
Readmissions	1	0.2	1	0.2
<u>Incision Complications</u>				
Serous discharge	26	5.7	22	5.1
Inflammation	14	3.1	16	3.7
Abscess	5	1.7	6	1.4
Bleeding	1	0.2	1	0.2
Incomplete dehiscence	3	0.7	8	1.8
Other	1	0.2	0	-
Total women with 1+ complications*	51	11.2	54	12.4
C. Events Reported at Long Term Follow-up**				
Women returning for 6-month follow-up visit*	292	57.5	307	59.7
Women returning for 12-month follow-up visit*	251	49.4	268	52.1
Total women with 1+ complications	60	17.8	66	18.8
Readmission to the hospital	3	0.9	8	1.6
Pregnancy	3	0.9	1	0.3

* excludes technical failures

** includes 6-, 12- and 24-month follow-up visits

d) Filshie Clip versus Secuclip

A comparative evaluation of the Filshie Clip and the Secuclip via minilaparotomy in interval women is in the follow-up phase at two active centers in Latin America. A total of 158 procedures were performed prior to 1985. Surgical difficulty rates were 5.6% and 3.5% for the Filshie Clip and Secuclip, respectively. Rates of surgical injuries/complications were 1.4% for the Filshie Clip groups and 1.2% for the Secuclip group. Few major complications occurred during the recovery period; five (6.9%) Filshie Clip patients and five (5.8%) Secuclip patients developed problems at that time. Most of these complications were related to the surgical incision.

Early follow-up visits were completed for 91% of the women in the studies. Complications were noted for 16 (20.8%) of the Filshie Clip patients and 13 (19.4%) of the Secuclip patients at the early follow-up visit. The majority of these complications were incision related. There was one readmission of a patient in the Filshie clip group for hematoma drainage.

Six-month follow-up data were collected for 70 (95.2%) of the Filshie Clip group and 84 (94.4%) of the Secuclip group. Two pregnancies were reported among Secuclip patients and one luteal phase pregnancy was reported in the Filshie Clip group. At long-term follow-up visits, 12 Secuclip patients (17.1%) and 13 Filshie Clip patients (15.5%) reported complications. Most of these were tender or enlarged adnexa. More than half (87%) of the Filshie Clip patients

and 89.3% of the Secuclip patients have returned for one-year follow-up visits.

e) Filshie Clip versus Bipolar Electrocoagulation

Because bipolar electrocoagulation is the most commonly used method of sterilization in industrialized and in more advanced developing nations, a comparison of the Filshie Clip versus bipolar electrocoagulation is planned in five sites. Studies in Austria and Taiwan have been initiated; other studies in Finland, Holland and Korea will be initiated this year.

f) Non-Comparative Filshie Clip Studies

One investigator in Brazil is undertaking a comparison of the minilaparotomy and laparoscopic techniques using the Filshie Clip. Minilaparotomies were performed on 96 interval patients and 94 interval patients had laparoscopic sterilizations. There was one technical failure in the minilaparotomy group in which a salpingectomy was performed on one tube. There were no surgical difficulties reported with the laparoscopic approach. Three cases of difficulty entering the peritoneum and one case of difficulty occluding the tubes were reported with the minilaparotomy technique. There were two cases of surgical injuries in the minilap group, one case of tubal injury without bleeding and one case of a severed anomalous vein. The rate of injuries/complications was 2.1% for the minilap group, 0% for the laparoscopic group. There was one case (1.1%) of vaginal bleeding prior to discharge in the minilap group.

All minilap patients and 98.9% of the laparoscopic patients have returned for early follow-up visits. Uterine infections were reported for two minilap patients (2.2%).

Six-month follow-up visits have been completed for all patients. No pregnancies, hospitalizations or subsequent surgeries have been reported. However, a surprisingly high rate of uterine infections, 53.2% in the minilap group and 30.9% in the laparoscopic group, were reported. A monitoring visit was carried out to verify the accuracy of this diagnosis. A misunderstanding of the infection question on the form led to the high rate of uterine infections.

A non-comparative trial of the Filshie clip applied via laparoscopy is underway in two Canadian centers and four centers in England. One additional center in Canada and two centers in England are expected to start in the fall. One Canadian center has withdrawn from the study because of difficulty in obtaining approved consent forms from study participants. The consent forms used are those approved by the FHI Protection of Human Subjects Committee. Sterilization procedures have been completed on 175 interval patients. Surgical difficulties have included: five cases of difficulty with the equipment, five cases of difficulty entering the peritoneum, three cases of difficulty visualizing/grasping the tubes, and eight cases of difficulty occluding the tubes. The rate of surgical injuries/

complications is 3.4%; there were two cases of tubal or mesosalpingeal bleeding, one case of a ruptured ovarian cyst and one case of vasovagal reaction. There were no reports of major complications from sterilization to discharge. At the early follow-up visit, 15.4% of the 136 women returning reported one or more complications. There were four cases of bleeding at the incision, four cases of inflammation, three cases of serous discharge, one case of incomplete dehiscence and three cases of vaginal bleeding. Endometrial aspiration was performed for one of these cases.

TABLE 13
Non-comparative Filshie Clip
Trials

	Filshie Clip (N=175)	
	No.	%
A. Events at Surgery		
<u>Surgical Difficulties</u>		
With equipment	5	2.9
Entering peritoneum	5	2.9
Visualizing/grasping tubes	3	1.7
Occluding tubes	8	4.6
<u>Surgical Injuries</u>		
Cervical laceration	1	0.6
Uterine perforation	1	0.6
Tubal/mesosalpingeal bleeding	2	1.1
Ruptured ovarian cyst	1	0.6
Total women with 1+ surgical injuries/complications	6	3.4
B. Events Reported at Early Follow-up		
Women returning for early follow-up	136	77.1
Readmissions	1	0.7
<u>Complications</u>		
Serous discharge	3	2.2
Inflammation	4	2.9
Bleeding	4	2.9
Incomplete dehiscence	1	0.7
Other	2	1.5
Women reporting 1+ complications at early follow-up	21	15.4

g) Long-Term Follow-up of Sterilization Techniques

FHI has also been assessing the long-term effect of surgical female sterilization at two sites, one in Thailand and one in Bangladesh. In Thailand, 499 women have returned for a long-term follow-up visit four to twelve years post-sterilization. These women were sterilized as part of three previous clinical trials: one non-comparative study of the Hulka Clip, one comparative trial of the Hulka clip versus electrocoagulation, and another comparative study of the tubal ring and electrocoagulation. A total of 27 (5.4%) post-sterilization pelvic surgeries have been reported. Fifteen of these surgeries were performed on women sterilized with the Hulka Clip, including nine hysterectomies, one diagnostic laparoscopy, one bilateral salpingectomy, and one colpoperineorrhaphy and one salpingectomy-oophorectomy. Eight surgeries were reported for women sterilized by electrocoagulation. These surgeries included four hysterectomies, two cases of dilatation and curettage, one salpingectomy-oophorectomy for ovarian cysts, and one reanastomosis. Four ring patients also had hysterectomies. Two ectopic pregnancies and one intrauterine pregnancy were reported in the electrocoagulation group; one ectopic pregnancy was reported in a clip patient. Most women (99.6%) have indicated satisfaction with their decision concerning sterilization. A final report has been prepared.

Long-term follow-up data is also being collected at an additional site in Bangladesh where a comparative evaluation of the Tubal Ring and the Pomeroy method was done in 1978. To date 60 women have

returned for a long-term follow-up visit. No pregnancies, surgeries or complications have been reported. This study will close in October 1986.

h) Other Sterilization Studies

The first phase of data collection for a Thailand study of voluntary sterilization performed by nurse-midwives has been completed. Between June and December 1985 data on more than 5000 sterilization procedures by nurse-midwives and a control group of physicians was collected. A sample of 900 cases has been selected for follow-up with the attitudinal questionnaire developed by FHI's Program Evaluation Division. The first 4000 sterilization cases are being followed up at 1- to 3- months and 12-months post-sterilization. Early follow-up continued for the approximately 5,500 subjects who have been admitted to this study and a sampling scheme (3 out of 5 admissions) was devised in order to reduce the number of cases to be followed up at one year. Data analysis will be done in Thailand by the Thailand Fertility Research Association (TFRA). Admission data has been keypunched by the TFRA and follow-up data is being added as received. The Chulalongkorn University Institute for Population Studies is working with the TFRA to administer and analyze the attitudinal research component. The TFRA's Research Analyst, Ms. Pattaka Piyapinyo, is scheduled to visit FHI to work on further analysis of these TFRA data in 1987.

A pilot study of the Femtest device for determining tubal patency is underway in Chile. To date, results using the Femtest device have

been compared with results from a hysterosalpingography in 101 women undergoing testing before sterilization and in 78 (78.2%) of them after sterilization. There was agreement in 96% of the cases before sterilization and in 100% of the cases after sterilization.

This study will be expanded to two additional sites in Indonesia. At each center 25 women will be tested before sterilization and another 25 women will be tested after sterilization. Each woman will have both the Femtest procedure and an HSG procedure. Those studies began in September 1986.

A retrospective evaluation of the Filshie Clip has begun in Malaysia. Admission, early and one-year follow-up data on 800 women sterilized with the Filshie Clip from 1980-1985 is being transferred from clinic records to FHI forms. Attempts will be made to contact these women and ask them to return for a long-term follow-up visit. Analysis will focus on complications, pregnancies and subsequent surgeries.

2. Male Sterilization

Improvements in vasectomy techniques have been rare. However, the possibility of occluding the vas without a surgical incision in the scrotum is a potentially significant step forward.

Admissions are complete at one center in England for a comparative study of percutaneous occlusion of the vas by diathermy and the standard incision with diathermy. A total of 51 percutaneous

procedures and 50 standard incision procedures were performed. The percutaneous cases also had an incision to verify occlusion. One surgical difficulty was reported in which there was a problem with verification of the occlusion site in the first percutaneous procedure. A case of excessive bleeding was reported in the incision group. Early follow-up evaluations (within 15 days) have been completed for 96% of the patients. The most common complaint at the early follow-up contact was serous discharge reported for 6.3% of the incision group and 8.2% of the percutaneous group. Hematomas were reported for 18.4% of the percutaneous patients and 10.4% of the incision patients. Six percutaneous patients (12.2%) complained that the wound was not healing. Incision infection was reported in three (6.3%) incision patients and four (8.2%) of the percutaneous patients. Almost all (98%) of the percutaneous group completed three or more long-term (>15 days post-sterilization) follow-up contacts; 100% of the incision group completed two or more follow-up contacts. Complaints at long-term follow-up included three cases of pain or tenderness in the incision group and two cases in the percutaneous group, one case of granuloma, one case of discharge and one case of adhesions in the percutaneous group and one case of infection and one case of swelling in the incision group. One case in each group was declared a sterilization failure. A final report has been written. Because cases in the percutaneous group also had an incision, comparisons on pain and complications cannot be clearly differentiated. Once the needle for percutaneous procedures is refined, a randomized comparative trial can be conducted.

Future Plans

In order to determine the effect of occlusive devices on tubal tissue and the effects of tissue on occlusive devices, a study is planned which will examine devices and tissue removed from 500 patients having hysterectomy.

Other plans include:

- A comparison of open versus closed laparoscopy.
- Comparative trials of vasectomy by incision and ligation versus puncture and ligation techniques.
- Comparative trials of chemical male sterilization via a puncture versus an incision and ligation technique.

D. Nonsurgical Female Sterilization

FII continues to work on the development of a rapid, effective and safe nonsurgical method of sterilization that can be performed by paramedical personnel.

1. Quinacrine Hydrochloride

Long-term follow-up of women who have been sterilized by three transcervical administrations of quinacrine hydrochloride pellets, 250 mg, has been completed in Chile. The 60-month, cumulative life-table pregnancy rates for three studies shown in Table 14 range from 5.0 to 8.9 per 100 women.

TABLE 14

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

	6-mo. rate	12-mo. rate	24-mo. rate	36-mo. rate	48-mo. rate	60-mo. rate
Quinacrine Solution Santiago, Chile N=124	6.5 (95.2)*	9.9 (88.9)	11.7 (49.6)	- -	- -	- -
Quinacrine Pellets with Sodium Thiopental Santiago, Chile N=148	2.1 (96.6)	6.4 (93.6)	6.4 (83.5)	8.9 (78.1)	8.9 (59.6)	8.9 (37.5)
Quinacrine Pellets with- out Sodium Thiopental Santiago, Chile N=123	1.7 (97.5)	3.3 (96.6)	6.7 (96.5)	6.7 (88.7)	6.7 (62.6)	8.4 (31.6)
Quinacrine Pellets with- out Sodium Thiopental Valdivia, Chile N=149	0.7 (100.0)	0.7 (99.3)	3.4 (99.3)	4.2 (94.4)	5.0 (87.9)	5.0 (66.7)
Quinacrine Pellets with- out Sodium Thiopental Baroda, India N=81	0.0 (100.0)	0.0 (100.0)	1.2 (100.0)	3.7 (100.0)	3.7 (74.4)	- -

* Follow-up rate

Two Phase I studies conducted under an IND to determine the effect of intrauterine insertion of 250 mg of 10-minute releasing quinacrine hydrochloride pellets in 10 women one month before hysterectomy have been initiated at the University of Texas Health Sciences Center in San Antonio and at the State University of New York in Buffalo. These studies include histological evaluation of uterine and fallopian tube tissue in addition to a determination of quinacrine pharmacokinetics.

An independent study conducted by Dr. J. Zipper has provided preliminary evidence that 100-minute releasing quinacrine pellets, 250 mg, may be as effective as the 10-minute releasing product when given with only one or two insertions rather than with three. Two insertions in 107 women have resulted in a 12-month pregnancy rate of 2.0 per 100 women. Eighty-four percent of the women have completed 12-month follow-up. A Phase I 30-day pre-hysterectomy study of this slower releasing formulation is being conducted at the University of Southern California.

2. Tetracycline Hydrochloride

The Phase I Study of the transcervical insertion of 1 gram of tetracycline hydrochloride pellets 24 hours before hysterectomy that was initiated at the University of North Carolina at Chapel Hill has been cancelled because of inability to enroll patients. A replacement study has been initiated at the University Hospital of Jacksonville, Florida. The study will evaluate tetracycline pharmacokinetics and include histological examinations of uterine and fallopian tube tissues.

A Phase I study comparing the sclerosing activity of quinacrine and tetracycline when pellets are placed directly into the Fallopian tubes one month before hysterectomy was conducted in Mexico with the aim of providing an objective comparison of the effect of the two chemicals. All of the 12 planned cases have been completed. Data from two patients have not yet reached FHI. The Hospital General de Seguridad Social y Asistencia, where the hysterectomies were performed, was completely destroyed in the earthquake in September 1985. Records for four patients were lost.

Future plans

The use of quinacrine hydrochloride as a technique of female sterilization has been approved as a service method by the Ministry of Health in Brazil. However, FHI feels additional data on effectiveness, long-term follow-up and possible toxicity is required before recommending widespread use. FHI intends to continue its

dual track approach to the problem of nonsurgical sterilization: while obtaining additional information on quinacrine FHI will also pursue alternative options including tetracycline and iodine containing compounds.

During the next year, a study will be designed to determine the capability of adjunctive therapies to prevent fallopian tube spasm upon intrauterine quinacrine insertion in the interest of improving the sclerosing activity of quinacrine.

A study will be conducted in Santiago, Chile to assess whether one insertion of quinacrine can be as effective as two in terms of demonstrated tubal closure by the Femtest[®] tubal patency testing device. Treated women will be divided into those who may rely on the method and those (with evidence of tubal patency) who will need referral for an alternative family planning method. In addition, upon successful completion of the 30-day pre hysterectomy studies of quinacrine hydrochloride, FHI will meet with the FDA to discuss initiation of a small-scale Phase II study to evaluate the safety and efficacy of the method.

Evaluations of the safety and sclerosing effect of tetracycline pellets (1000 mg) on uterine and fallopian tube tissue when administered 30 days before a scheduled hysterectomy will be initiated after the 24-hour pre hysterectomy study is well underway.

FHI is preparing material for FDA submission of an IND for the use of iodine containing tubal sclerosing mixtures. As previously in the

field of chemical sterilization, a coordinated program of work is planned using both AID and non-AID funding.

E. Intrauterine Devices

FHI is conducting studies to evaluate the acceptability of newly approved IUDs in various geographical locations and to explore possible ways of decreasing side effects associated with IUD use.

1. Long-Term Evaluation of the TCu 380 Ag

The TCu 380 Ag with copper sleeves and a silver core in the copper wire has a projected effective life span of 10 to 15 years. Because of this projected long-term effectiveness, investigators who participated in previous FHI clinical trials of the device were asked to conduct long-term follow-up of study patients. Investigators in Yugoslavia, Panama and the Philippines have been collecting long-term data (> 24 months). All data have now been received, and analysis will begin shortly. The follow-up rate for this evaluation was high; a total of 681 (85.1%) patients returned for a long-term follow-up visit.

2. Copper T IUD With and Without Strings

A clinical trial comparing TCu 200 IUDs with and without marker strings to determine the possible role of strings in the etiology of pelvic inflammatory disease (PID) has progressed well during the past year. Preliminary analyses of 1210 women from five centers, with an

overall 12-month follow-up rate of approximately 60%, reveal no difference between the two groups with respect to the incidence of infection and inflammation. There is, however, a significant difference between the two groups in the removal rates for bleeding and pain. The 12-month removal rate is 6.0 for the string group and 1.4 for the without string group ($p < 0.01$). Because the number of women in each group reporting bleeding/pain complaints are comparable, this difference may be due to the relative ease of removing an IUD with attached strings compared to removing an IUD without strings. Expected completion date for all the studies under this strategy is December 1988.

3. Evaluation of the TCU 380A

A multi-center trial of the TCU 380A IUD has been designed to assess acceptability of the FDA-approved device by comparing it to locally used IUDs throughout the world.

The largest comparison under this strategy is between the TCU 380A and the TCU 200 or TCU 220. Data on 1376 cases have been received from Brazil, Cameroon, Chile, Egypt, El Salvador, Honduras, Mexico, Pakistan and Sudan. Additional studies comparing these devices will be initiated during the next six months in Costa Rica and the Philippines. The Egyptian Fertility Care Society (EFCS) is also coordinating a multi-center trial in Egypt of 1000 cases and will analyze the data.

Two studies designed to compare the TCu 380A with the LLD have begun in Peru and Nigeria, and admissions are near completion in Venezuela, where the TCu 380A is being compared to the Nova T. However, sufficient data have not yet been received to note any significant differences between devices in terms of life-table event rates.

Studies comparing the TCu 380A with the Multiload Cu 250 are underway in Malaysia, Sri Lanka and Thailand. A total of 1594 women have been admitted to date, with approximately 67% followed-up at three months. No significant differences between these devices are apparent at three months.

A-3000 case multi-center study comparing the TCu 380A with the ML Cu 375 and the LLD is being conducted by the BKS PENFIN in Indonesia. As with the EFCS study, the data will be analyzed in-country with the BKS PENFIN computer facilities. For both the BKS PENFIN and EFCS studies, data on printouts and disks will be made available to FHI periodically.

All admissions to this strategy should be complete by November 1987 and it is expected that all follow-up visits will be complete by November 1988.

4. Adapted T versus TCu 200

The technique of trimming the horizontal arms of the TCu 200 to fit the width of a woman's uterus is being evaluated in a study comparing the trimmed (adapted) T to an untrimmed (standard) TCu 200.

Measurements of the fundal width are determined by the use of the Cavimeter II, an instrument designed for this purpose. A small pilot study of 200 cases was initiated in Thailand in May 1985. A total of 120 women have been admitted to date. With a three-month follow-up rate of 79.2%, no differences between the devices are apparent at this time.

5. Post-Cesarean Section IUD Insertion

IUDs placed in the uterus through the incision immediately following cesarean section continue to be a topic of interest to many FHI investigators. A study to evaluate the safety of post-C-section IUD insertions and IUD expulsion rates was recently initiated in Mexico. No data are yet available.

Future Plans

Under the supervision of the Clinical Trials Division, a site in Nigeria will be added to the Reproductive Epidemiology Division trial comparing groups of women who have IUDs inserted with or without the administration of a single dose of the broad spectrum antibiotic, doxycycline. The original trial was conducted at one site in Kenya. Results from the initial study indicated that the infection rate was lower than expected when the sample size was first calculated; the site in Nigeria will be included in order to provide an adequate sample size to detect a difference between the two groups should one exist.

The IUD String Retriever (formerly named the Brush Retriever), a device developed at FHI to retrieve IUD strings that have retracted into the uterine cavity, will be evaluated initially at one or two sites in the US or Europe in a small pilot study, pending FDA approval of an application for an Investigational Device Exemption (IDE).

A proposal is also being developed for a retrospective study to determine whether there is a relationship between side effects experienced by women wearing IUDs and subsequent fertility. Three groups of women will be studied, including those who have their IUDs removed for (1) pain and bleeding, (2) other medical reasons and (3) planned pregnancy. Contraception rates calculated by the life-table method will be compared for these three groups, controlling for possible relevant factors such as age, parity, type of IUD, duration of use and number of sexual partners. Sites in Taiwan, Korea and Yugoslavia are being considered for this study.

FHI's interest in conducting clinical trials of the levonorgestrel-releasing IUDs in developing countries continues.

F. Investigator Network Needs (INN)

FHI's worldwide network of investigators is one of its prime strengths. An active program of recruiting new investigators is always taking place. The INN helps gain experience with various methods of contraception in many different parts of the world and it permits FHI staff to help train and evaluate new investigators and

familiarize themselves with the type of case load and degree of follow-up a new investigator can achieve.

There have been eleven studies conducted under FHI's Investigator Network Needs Strategy during this fiscal year; six are now complete. These studies encompass a variety of contraceptive methods and, according to the objectives of the strategy, all address special research interests of the investigators. In many instances they have also served to introduce the investigators to the clinical research process. They are reported here by study area.

1. IUD Studies

Two non-randomized studies were conducted, one in Egypt and one in Nigeria, to compare the TCu 200 and the LLD IUDs. Both studies are now complete. In Egypt, the TCu 200 performed better than the LLD in terms of expulsion rates and rates of removal for bleeding and pain ($p < 0.05$). In Nigeria, no significant differences between the devices were found.

A randomized study comparing the ML Cu 250 and the TCu 200 inserted immediately postpartum (via forceps) is nearing completion in Thailand. All of the proposed 300 women have been admitted and the follow-up rate at six months is about 80%. The expulsion rate for both devices is high: 24.6 for ML Cu 250 cases and 30.6 for TCu 200 cases; high expulsion rates are not unusual for postpartum IUD insertion. The Multiload Cu 250 is the copper IUD provided by

Thailand's national family planning program. This study will provide the government with important information concerning its use during the immediate postpartum period.

Another study conducted this fiscal year in Nigeria was a surveillance study of interval women using Lippes Loop IUDs. The follow-up rate of the 150 women at six months was about 60%. These data will be analyzed and a consultant report prepared within the next six months.

2. Sterilization Studies

In Kenya, 500 women were enrolled in a female sterilization surveillance study. The procedures used primarily in this study were the Pomeroy technique via puerperal laparotomy (N=197) and via minilaparotomy (N=247), and tubal ring via laparoscopy (N=54). One technical failure occurred in the study; a change in approach was made because of obesity. One surgical injury was reported in the laparoscopy group (1.8%). Incision infections and complications were the most common problem in each of the groups at the early follow-up visit; at the three-month follow-up visit PID was diagnosed for one woman in the minilaparotomy group. This study is now complete and a consultant report will be written soon.

An additional surveillance study of 200 sterilization procedures has begun in Nigeria. To date 35 women have been enrolled in the study.

3. Systemics Studies

During this fiscal year, data continued to be collected from two retrospective studies designed to evaluate the safety and acceptability of Depo-Provera (DMPA) supplied by agencies other than AID. Both studies are now complete. One study in Brazil compared two groups of women, both of whom used DMPA for at least a year before study entry, but at two different dosages and intervals: 25 mg once a month versus 150 mg once every three months. The data indicated that more women receiving 150 mg of DMPA every three months experienced amenorrhea (56.3%) than women receiving 25 mg of DMPA monthly (20.5%). The six-month continuation rate was significantly higher ($p < .05$) at 89.4% for the 150 mg group than for the 25 mg group at 68.4%. Twelve-month follow-up rates were 91.4 for the 150 mg group and 65.4 for the 25 mg group.

In the other Depo-Provera study, the Gambia Family Planning Association conducted a retrospective study comparing women who used DMPA with women who used oral contraceptives. Retrospective admission forms were completed for four hundred women who began using each method prior to June 1981. Follow-up visits were completed for 80% of the women; no differences in continuation or termination rates were demonstrated. Consultant reports are planned for each of these studies.

Another systemic study is in progress in Mali, at the Maternal and Child Health Center associated with the Ministry of Health. This study compares Noriday and Lo-Femenal, two locally available oral

contraceptives. Two hundred women have been admitted into this study. With about 65% follow-up at four months for these women, there appear to be no differences between the pills in terms of reasons for discontinuation or side effects.

A study designed to compare two types of progestogen-only oral contraceptives, Micronovum and Ovrette, is ongoing in Zimbabwe. Three hundred seventeen women have been admitted to this study. There are not sufficient follow-up data to report at this time.

An additional systemic study was initiated in Malaysia in January 1986. This study was designed to compare the triphasic Triquilar with the low-dose combination pill, Marvelon. One hundred thirteen women have been enrolled in the study. It is too early in the follow-up period to note any results.

Future Plans

FHI's policy continues to be to attempt, whenever possible, to meet local needs, as brought out by AID Missions and/or local investigators. In addition to answering locally defined questions, investigator needs studies also assist FHI in continuing to recruit proven investigators for new studies.

Initiation of two systemic studies to be conducted by Clinical Trials Workshop participants in the Philippines is planned for the first half of next fiscal year. The investigators will compare two oral

contraceptive preparations: Nordette (Wyeth), a low-dose combination pill currently available in the Philippines, and Trinordial (Wyeth), a triphasic pill that the manufacturer will begin marketing in the Philippines this year.

An additional surveillance systemics study will be initiated soon in Niger. Data will be collected on the use of locally available standard- and low-dose oral contraceptives.

It is also expected that six participants of the Clinical Trials Workshop held in Panama will conduct studies under the INN strategy. These study proposals will be developed and finalized during the first half of next fiscal year.

G. Other Studies

1. World Pill Survey

A 1985 American College of Obstetrics and Gynecology (ACOG)-sponsored Gallup poll showed that 75% of American women thought there were substantial health risks associated with using oral contraceptives. To see if there are similar concerns about the safety of pill use in the developing world, FHI has conducted a survey of 100 urban, middle-class women in each of eight countries.

The most striking finding in the survey is the similarities in perceptions of the Pill's health effects between samples despite the small numbers in each sample and the differences in socioeconomic

levels between the countries' middle-class communities. The major findings are:

- a. Taking the Pill is considered to have substantial health risks by 50-75% and is considered to be more hazardous than childbearing by over 40% of respondents except those in the African samples.
- b. Women who had never taken the Pill were equally unaware of the serious cardiovascular adverse effects as the never-users (e.g. about 10-35% of ever-users and never-users thought the risk of heart disease and stroke was increased).
- c. The protective effects of the Pill are virtually unknown.
- d. The greatest inconsistency between scientific evidence and public perception by 30-60% of respondents (except Egypt) is of an increased risk of sterility and birth defects attributed to the Pill.

FHI intends to use this data to help refine information material for both users and providers of OCs and to plan ways of countering the serious misinformation which exists about OCs.

2. Egypt: Introduction of Long-Acting Steroids in Egypt

A major, interdepartmental project involving the introduction of long-acting steroids in Egypt has been implemented with the support of an in-country FHI field office and staff member. The project is designed to evaluate the performance of NORPLANT®-2 subdermal implants in a broad population and is being conducted jointly with the National Population Council of Egypt. The initial objectives of

the project are: 1) to identify and follow-up the acceptors who participated in the original NORPLANT® field trials in Egypt, 2) to establish at least two in-country training centers (Assiut and Alexandria), and 3) to initiate a multicenter university-based 1200-case clinical trial of NORPLANT®-2 rods. Responsibility for implementation of the project has been assigned to the Egyptian Fertility Care Society (EFCS), which hopes to initiate these activities by early 1987.

IV. REPRODUCTIVE EPIDEMIOLOGY

The work of the Reproductive Epidemiology Division focuses on factors that affect reproductive health, with an emphasis on contraception. The division researches the long-term indications and consequences of contraceptive use, including sexually transmitted diseases and cardiovascular disease. A major emphasis over the past year has been integrating the benefits and risks of contraception in order to allow policy decisions that compare the use of contraceptives against its alternative, pregnancy.

A. Completed Projects

1. Breast and Cervical Cancer and Hormonal Contraception in Costa Rica

It is well established that the combined pill reduces the risk of ovarian and uterine cancer. However, it is generally agreed more research is needed on possible association between OC use and breast cancer and between progestational agents used by themselves and all reproductive cancers. Animal studies suggest that DMPA might increase the risk of breast cancer. No human study has shown this, but fear of cancer was the primary reason the US Food and Drug Administration (FDA) failed to approve DMPA for contraceptive use in the United States. Animal studies also suggest increased risk for cervical cancer, and data from a WHO collaborative study show a slight increase in risk for women who used DMPA for more than four years. FHI, in collaboration with the Centers for Disease Control (CDC), the Costa Rican Demographic Association and the Social Security Administration

of Costa Rica, has completed a case-control study of cervical and breast cancers and their relationship with contraceptive history. The study included 171 cases of breast cancer, 415 cases of carcinoma in situ of the cervix, and 149 cases of invasive cervical cancer. The 770 controls were drawn at random from the nation's population.

2. Breast Cancer

No relationship was found between oral contraception and breast cancer (RR = 1.1; 95% CI = 0.8, 1.8), and the lack of association persisted when latency, recency and age at first use were accounted for.

Although an increased risk (RR = 2.0; 95% CI = 1.0, 4.1) was found among women who had used oral contraception for 3-5 years, there was no trend with duration of use, and women who had used for more than 5 years had no increased risk.

A statistically significant association was found between DMPA use and breast cancer (RR = 2.6; 95% CI = 1.4, 4.7 between ever users and never users of DMPA). However, duration of use had no effect on the risk -- short-term users had a higher risk than long-term users. The time since first use did have an effect; women who first used DMPA more than 10 years ago had a four-fold increase in risk of developing breast cancer. Because of small numbers (only 19 cases and 49 controls had ever used DMPA) it was not possible to control for the effects of known risk factors for breast cancer such as family history of the disease, or a history of benign breast disease. It is possible that bias arising from different utilization of medical services by users and nonusers might explain some of the associations. A paper

reporting this analysis will be submitted to the International Journal of Epidemiology.

3. Cervical Cancer

No relationship was found between DMPA and invasive cervical cancer (RR = 0.9; 95% CI = 0.5, 1.4), and the lack of association persisted when duration of use, recency and latency of use and other factors were accounted for.

A relationship was found between oral contraceptive use and in situ cervical cancer (in situ: RR = 1.6; 95% CI = 1.2, 2.2). However, it can be explained by the fact that, in Costa Rica, women who use oral contraception are more likely to be screened for cervical cancer. For example, in the capital city of San Jose, 94% of the controls who had used OCs had had a Papanicolaou smear, compared with only 72% of controls who had never used OCs. In rural areas, where health care is less accessible, the difference was even more pronounced--81% and 38% for ever users and never users, respectively. If we look at the risk of contracting cervical cancer, we find that among women who had at least 10 Pap smears before 1982, ever users of OCs had 0.9 (95% CI = 0.4, 1.8) times the risk of never users; among women who had never had a Pap smear the relative risk was 2.2 (95% CI = 1.9, 2.6); and for the intermediate group the relative risk was 1.7 (95% CI = 1.1, 2.5). The fact that ever users of OCs have 0.8 (95% CI = 0.5, 1.3) times the risk of invasive (i.e. symptomatic) cervical cancer when compared to never users also contributes to the interpretation that the association between in situ (i.e. asymptomatic) cervical cancer and OC

use can be attributed to the increased probability of screening in OC users. A paper describing this analysis will be submitted for publication shortly.

4. Reproductive Age Mortality Survey (RAMOS)

The RAMOS studies conducted in Egypt and Indonesia were designed to provide information on the causes of death to women of reproductive age, in particular, to determine the proportion of deaths that are due to pregnancy, childbirth, abortion and contraception. It is clear from the response to the RAMOS report that this study fills an important gap in reproductive epidemiology. In a recent review of maternal mortality by the WHO, drawing in all available research data bases, the RAMOS studies provided the largest series available for study and helped to formulate international policymaking in the area of maternal mortality. Recent WHO work is based on the design of the RAMOS studies.

Maternal mortality was the leading cause of death to women of reproductive age in Bali, and the second cause in Menoufia (after deaths from diseases of the circulatory system). Among the maternal deaths, hemorrhage accounted for one third in Menoufia and almost one half in Bali. It is estimated that about two thirds of maternal deaths could be prevented if women over 30 and who had three or more children chose to have no more children. Data from the RAMOS studies make it clear that the risk of uncontrolled childbearing greatly outweighs any risk attributable to contraceptive use. These data were presented at the WHO in November 1985.

In Egypt and Indonesia, reproductive mortality was dominated by maternal mortality which accounted for one quarter of all deaths to women of reproductive age. At most, only 2% of all reproductive deaths could be ascribed to contraception. The rates were 1.9 per 1000 live births or 44.9 per 100,000 married women 15-49 in Menoufia, and 2.4 per 1000 live births or 67.2 per 100,000 married women 15-49 in Bali. They represent the first significant large scale efforts anywhere in the world to obtain data on causes of death to women in a traditional society, and their findings have policy implications for family planning and for public health in general. Seven papers using data from the RAMOS studies have been published or are ready for submission for publication.

5. Balancing the Risks and Benefits of Contraception

A great deal of information has accumulated from many sources on immediate and long-term benefits and risks of oral contraceptive use. FHI has developed a model which takes into account the risks and benefits reported in the literature for various diseases and estimates the net effect of oral contraceptives on life expectancy.

For women under 30 who use oral contraceptives, there is a very slight **increase** in life expectancy as compared with nonusers; for women over 30, there is a small decrease in life expectancy. In both cases the changes associated with oral contraceptive use are small (+12 days and -88 days respectively in developed countries) and trivial in comparison with such risk factors as smoking (4 years or more).

However, the demonstration that the protection offered against malignancy later in life more than outweighs the risks of cardiovascular disease among women under age 30 is most important, as most users in the United States are under 30 years old. A paper describing this analysis appeared in the May 1986 issue of Studies in Family Planning and the same analytic technique was recently used to put findings about a possible association between hepatocellular carcinoma and OC use in perspective. FHI intends to disseminate up-to-date perspectives on the pill to users and providers and looks forward to working with other AID funded agencies in this task.

Ongoing analysis focuses on the distribution of causes of death, and the number of deaths per 100,000 users compared with nonusers of oral contraception.

Fertility and its control is seeming increasingly safe in the United States. Between 1975 and 1982, the number of deaths attributable to pregnancy and childbirth, abortion, and contraception declined from 1083 to 732. The mortality rates for each of these components also decreased, by 38%, 89% and 35%, respectively, and the overall reproductive mortality rate dropped by 38%. A paper documenting these changes has been submitted to the American Journal of Public Health.

Although in the total population more women now die from fertility control (contraceptives and induced abortion) than from pregnancy and childbirth-related complications, the risk of death during a specific pregnancy and delivery is twenty-four times greater than that due to induced abortion and seven times more than contraceptive mortality.

The more numerous contraceptive deaths reflect the far greater number of women who use contraceptives than those who become pregnant: nearly thirty million women used contraceptives, while slightly fewer than four million women were pregnant to term.

The decrease in the contraceptive-related mortality rate between 1975 and 1982 probably reflects a combination of safer contraceptives, notably oral contraceptives, fewer women using contraceptive methods that may not be the safest for them, and an increasing number of sterilizations, which remove women from the group of those at highest risk of contraceptive-related mortality. Maternal mortality appears to be slowing its rate of decline, while abortion mortality is very low due to the absence of illegal procedures. A paper describing a similar analysis for Britain is now in preparation.

Work was also begun to assess the reproductive mortality rate around the world as a means of summarizing the mortality risk of fertility and its control. A first draft of this international perspective was presented as part of a Harvard School of Public Health Continuing Medical Education course on current perspectives in obstetrics.

6. Prostatic Cancer and Benign Prostatic Hyperplasia

In collaboration with Kaiser Permanente of California, FHI has examined the relationship between vasectomy and prostatic cancer and benign prostatic hyperplasia. Data collection began in July 1984 and was completed in March 1986. One animal study suggested that

vasectomy may increase the risk of renal carcinoma, while several large follow-up studies indicate no effect on this or other cancers. However, long-term follow-up on prostatic effects was previously lacking.

Ninety cases of prostatic hypertrophy and 17 cases of cancer were identified through a computer search. This study compared medical records of cases and controls and calculated incidence rates for men with and without vasectomy. Nonsignificant relative risks of 1.2 for prostatic cancer and 1.2 for benign prostatic hyperplasia were found. These data are currently being reviewed and organized for publication.

7. Contraindications to Contraceptive Methods

Few developing countries have reliable mortality and morbidity data or information on the prevalence of conditions that contraindicate use of specific contraceptive methods (especially oral contraceptives). Availability of this information is important for public health officials in making choices about contraceptive methods for country programs. In collaboration with the National Family Planning Coordinating Board of Indonesia (BKKBN), and Yayasan Kusuma Buana (YKB), FHI collected information on hospital discharge diagnoses for women of reproductive age. All teaching hospitals in Java participated. By providing data on morbidity for women in this age group, the study supplemented the RAMOS study in Indonesia (which collected data on mortality only).

Thirty-eight percent of all hospitalizations were for complications of pregnancy. The proportions of hospitalizations for cancer, respiratory and digestive diseases were also similar to the proportions dying of these disease groups in the RAMOS study; but the proportion hospitalized for infectious and parasitic diseases, and circulatory diseases was less, and the proportion hospitalized for genito-urinary conditions and "other & unknown" conditions was more. The low prevalence of circulatory disease in Java is reassuring in the light of nonmedical distribution of oral contraceptives in Indonesia. Only three oral contraceptive users were hospitalized for a circulatory disease, but the specific conditions are not known.

8. Surgical Contraception by Nonphysicians

To determine whether trained paramedical workers can perform vasectomies with safety and efficacy rates comparable to those of physicians, FHI evaluated almost 3000 procedures done by paramedical workers in a program in Indonesia. Five hundred sixty-nine vasectomies done in a hospital by paramedical workers were evaluated prospectively and compared with 2344 vasectomies done in remote areas by a mobile team of paramedics which were evaluated retrospectively. Men were visited in their homes and asked about complications experienced with the procedure. Although very similar in age, men vasectomized in a hospital were better educated and had fewer children than the men vasectomized in rural areas by the mobile team. Both groups were similarly satisfied both with the vasectomy and with the way in which it was done (more than 97% of both groups would have the procedure again under the same circumstances). However, far more of

the retrospective cases recommended the procedure to their friends (this is probably more due to the time since the operation than to the circumstances under which the procedure was performed). The reported complication rate was 0 among the men vasectomized in a hospital compared with 0.43% among the men vasectomized by the mobile team. Because of recall difficulties in the retrospective evaluation, minor complications may have been under-reported. The most common complication was infection (6 cases); single cases of dehiscence, hematoma, syncope and spermatocele occurred. These complication rates are substantially lower than rates reported from the USA, UK or Korea (Population Reports, 1975).

9. Contraceptive Use and the Prevalence of Sexually Transmitted Diseases (STDs)

A cross-sectional study of the relationship between contraceptive use and the prevalence of STDs was conducted at the Margaret Sanger Center, Planned Parenthood of New York City. The study indicates that users of barrier methods and spermicides have a risk of gonorrhoea 0.7 times and of chlamydia 0.4 times that of oral contraceptive users. These data are being prepared for publication.

B. Continuing Projects

1. Cervical Cancer and Hormonal Contraception in Jamaica

FHI is collaborating with the Jamaica Cancer Society and the University of the West Indies in a case control study of cervical cancer and hormonal contraception in Jamaica. Several factors make Jamaica an excellent site for examining this relationship:

(1) Jamaica has one of the world's highest incidence rates of cervical cancer; (2) it has a tumor registry that is relatively complete for the Kingston Corporate Area; and (3) more than half (55%) of women in union use contraception, and approximately 15% of women have used DMPA.

Study personnel were trained by staff from FHI and Survey Research Associates in October 1985. The first case was interviewed in November 1985. Interviewing is progressing slowly because of limitations on access to the Tumor Registry; to date, 81 women have been interviewed (43 cases and 38 controls). No physician has declined to participate, and the response from cases has been excellent. Five percent of the cases have died. At the last site visit, procedures were implemented which are intended to hasten recruitment into the study.

FHI is collaborating with the Viral Disease Division of the CDC to look for evidence of human papillomavirus (HPV) in the tumors of the women in the study. Where HPV is found, the CDC will identify the DNA

type. This study is being conducted with the Departments of Pathology and Microbiology of the University of the West Indies.

2. Human Papillomavirus (HPV) and Cervical Cancer

Only a few of the more than 30 HPV types appear to be etiologic agents of cervical cancer. To discover if OC use has an effect on the relationship between HPV and cervical dysplasia, a prospective study is about to begin in Panama. HPV DNA typing will be done in the US. Newly available data suggest that women with "high risk" cervical warts (Types 16 and 18) have a 10-fold increased risk of cervical dysplasia compared to women without cervical warts. A recent study implied a causal role for oral contraceptives in cervical cancer when it found long-term oral contraceptive use (>5 years) was associated with a 10-fold increased risk of having genital (not necessarily cervical) warts. The FHI study will be useful in Latin America where cervical cancer is the leading cause of death to women of reproductive age and where treatment for cervical warts is not always available.

3. Anovulation and Risk of Breast Cancer

Several investigators have examined the number of menstrual ovulatory cycles (MOCs) as a risk factor for breast cancer with conflicting results. Because of small sample sizes, these studies failed to separate clearly the effect of the number of MOCs from that of other risk factors. Yet, because of the significance of breast cancer in the overall pattern of female disease, it is essential to get a further insight into this important problem. FHI will use the CDC's

Cancer and Steroid Hormones (CASH) case-control study to examine the association between breast cancer and MOCs. Almost 5000 cases of breast cancer in the CASH data permit simultaneous control of other risk factors. In addition, the effect of oral contraceptive use on the association between anovulation and breast cancer will be studied. Cases are women aged 20-54 with a new diagnosis of primary breast cancer. Analysis began in January 1986. Preliminary results indicate a significant trend of increasing risk associated with greater number of ovulatory cycles after controlling for recognized risk factors for breast cancer.

4. Sickle Cell Disease

Many doctors consider oral contraception to be contraindicated in women with hemoglobinopathies such as sickle cell disease. However, for women in many countries in the world where sickle cell disease is prevalent, childbirth is more than usually hazardous and few contraceptive alternatives are available. One study of DMPA showed that this form of contraception benefits women who are homozygous for sickle cell anemia by decreasing the frequency of sickling crises. Building on this study, FHI is conducting a study with the Medical Research Council of the University of the West Indies in Jamaica. The study design is randomized double-blind crossover and thirty patients will be followed through six months on oral contraceptives and six months on placebo, with a 3 month "washout" period between the two phases. To date, 15 patients have been admitted to the study and 7 have completed the first phase. Patients with sickle cell disease typically have frequent episodes of illness; in this study there have

been 4 patients with attacks of gallbladder disease (3 have had cholecystectomies), 2 episodes of acute chest syndrome, one case of duodenal ulcer, and one leg ulcer requiring hospitalization. Although more of the complications have occurred in patients taking the oral contraceptive than in patients taking the placebo, the difference is not statistically significant. One patient in this study died of massive bilateral pulmonary infarct two weeks after a cholecystectomy; although this patient had been taking the active medication, she was 4 weeks into the washout period at the time of the procedure. The investigator believes that the medication did not contribute to her illness or death.

Some preliminary analysis of this study will begin shortly, and results from the completed study should be available by mid-1988. A similar study in Nigeria of patients with sickle cell disease who use the NORPLANT[®] contraceptive system will be initiated during 1987. This will not be a randomized study, but the hematologic parameters of patients will be evaluated for 6 months while using a nonhormonal method of contraception, and these parameters will be compared with the same parameters at various intervals after NORPLANT[®] insertion. As far as possible the same data collection instruments and the same tests will be used in Nigeria as are being used in Jamaica in order to make the two studies comparable.

5. Effects of in utero Steroid Exposure

Two studies are being conducted. In Thailand, approximately 1200 children have been identified who were exposed to DMPA and 200 who

were exposed to oral contraception while in utero, either because of unnoticed pregnancy at the time of the injection or because of contraceptive failure. These children are being examined to determine whether their developmental indices (including sexual maturation) differ from those of unexposed children. Interviewing began in June 1984 and is approximately three fourths complete. The study is being conducted in collaboration with the Johns Hopkins University.

A similar study, that looks at more subtle indices of development, is being conducted in Israel with children exposed to medroxyprogesterone acetate (MPA) used to treat threatened abortion. Handedness, degree of aggression, psychological factors and masculine-feminine orientation are being evaluated. The questionnaire was pretested in 1984, and data collection began in August 1985. Hebrew University in Jerusalem is the collaborating institution.

6. The Effect of Prophylactic Antibiotics on Post-IUD Insertion PID

The possibility of infertility following IUD use became increasingly apparent to lay and professional groups in 1985. FHI is conducting a randomized double-blind trial to study whether prophylactic antibiotics given at IUD insertion help prevent pelvic inflammatory disease (PID). The pilot study for this project was carried out in November 1984. Data from the 190 subjects in the pilot study were analyzed. The main study began in December 1984. FHI and CDC are collaborating with Kenyatta National Hospital to conduct this study. Eighteen hundred women were screened for gonorrhea and chlamydia before IUD insertion. They were then given a single dose of 200 mg

doxycycline or placebo and the IUD inserted. Women were followed for one month to determine whether there is a lower rate of PID among women given the antibiotic than among those given the placebo. If the gonorrhea or chlamydia cultures were positive, women were treated at follow-up visits. Prevalence of gonorrhea and chlamydia infection at the time of IUD insertions can be useful in judging the background rate in asymptomatic women. By 1 September 1986, 1800 women had been followed, with a PID incidence rate of 1.6%. This rate is appreciably lower than the rate used by the government to justify their recommendation not to insert IUDs in young women with few children.

7. The Effect of Contraception on Sexually Transmitted Diseases (STDs)

Sexually transmitted diseases are a major cause of infertility in some parts of the world, especially parts of Africa. FHI has completed a pilot study of the prophylactic effect of the contraceptive sponge on transmission rates of gonorrhea, chlamydia, trichomonas and monilia. The study was a collaborative effort with the Venereal Disease Division of the Ministry of Public Health of Thailand. Two hundred fifty-five women, half of whom received sponges, participated and accumulated 575 woman-weeks of observation. The sponge reduced the incidence of chlamydia by 40%, and of gonorrhea by 10%. However, these estimates form minimal estimates of risk reduction because of compliance problems among the user group. The pilot study led to many protocol revisions and improvements, and after changes were instituted, the final phase began in March 1986.

A conference of fifteen STD experts from Africa and the rest of the world met in The Gambia in April 1986 to establish priorities for African STD work. This workshop is expected to yield a useful list of options for FHI to pursue STD work in the future as well as to help other organizations with priorities. A summary of the meeting's recommendations was published in The Lancet, and a full report of the meeting is in press in The African Journal of Sexually Transmitted Diseases.

8. Infectious Etiology of Ectopic Pregnancy

Prior infection of the fallopian tubes is an important risk factor for ectopic pregnancy. Salpingitis causes tubal scarring or dysfunction that may prevent fertilization or result in ectopic pregnancy due to abnormal transport of the fertilized ovum. Numerous types of bacteria can cause salpingitis; these include *Chlamydia trachomatis*, *Neisseria gonorrhoea*, genital mycoplasmas, and aerobic and anaerobic bacteria.

To investigate the relationship between chlamydia or other bacterial infection and ectopic pregnancy, investigators in Boston will perform a hospital-based case-control study. They will establish the prevalence of: 1) active infection of the fallopian tubes among ectopic pregnancy patients compared with matched patients undergoing post-cesarean section tubal ligation; 2) active infection of the endocervix among ectopic pregnancy patients compared with matched prenatal patients; and 3) serologic evidence of active (IgM) or previous (IgG) chlamydia infection among ectopic pregnancy patients

compared with matched prenatal controls. Data collection began in February 1986.

9. Conference on Smoking and Reproductive Health

Cigarette smoking influences several aspects of reproductive health from the well-being of the fetus to the development of reproductive cancers. An FHI-sponsored international conference on the effects of smoking on reproductive health took place in San Francisco on 15-17 October 1985. The conference summarized the effects of smoking on reproductive health, with an emphasis on new findings, to review smoking cessation efforts during pregnancy and materials, and to review public health policy. Co-sponsors included the Agency for International Development, the World Health Organization, National Institute of Child Health and Human Development, Office on Smoking and Health, Centers for Disease Control and the University of California at San Francisco. A book based on the conference has been completed and is to be published in Fall 1986.

10. Effect of Smoking Among Breastfeeding Women on Infant Growth

Using data from a non-randomized clinical trial of progestin-only contraception among breastfeeding women, the impact of smoking on infant growth after birth was evaluated. Despite having a mean birth weight of 242 grams less than infants of nonsmokers, infants of heavy smokers showed no catch-up growth during the first four months of unsupplemented breastfeeding. Women who smoked only during

breastfeeding (not during pregnancy) had infants with comparable growth to the growth of infants of non-smokers. These results were presented at the Conference on Smoking and Reproductive Health.

11. The Male Influence on Spontaneous Abortion

There is increasing evidence to suggest that male exposure to hazardous substances (usually in the workplace) can impair reproduction. A study was initiated in March 1985 that uses the Finnish hospital discharge registry and census data to examine the relationship between fetal loss and exposure to certain agents with recognized reproductive toxicity. The registry permits use of a sample of 73,000 exposed and 1.5 million unexposed men and has the ability to control for maternal history and exposure to substances associated with an increase in spontaneous abortion. The sample size permits reliable detection of as little as a 3% increase or decrease in the rates of fetal loss. The cohorts have been identified and linked, and preliminary analysis will be completed in Spring 1987. The crude analysis showed no association between paternal exposure and risk of spontaneous abortion. Our Finnish collaborators are proceeding with analyses which examine this association in occupational subgroups and control for the effects of other risk factors. The investigators have been given a no cost extension through June 1987 to complete these analyses and to evaluate the effects of maternal exposures.

12. Cohort Study of Oral Contraceptive Users

During this reporting period, FHI continued to collaborate with the Contraceptive Evaluation Branch of the National Institutes of Health in organizing a large cohort study in England to investigate the influences on health of low-dose oral contraceptives and other hormonal contraception (including the newly approved DMPA). This study is patterned on the first Royal College of General Practitioner's (RCGP) Oral Contraceptive study--a landmark prospective study that helped to establish much of our knowledge of the health effects of the pill. The new study, also from the RCGP, will include 100,000 women of reproductive age. FHI's contribution has consisted of technical and financial assistance with the pilot study and non-recurring initial costs, including computer support. The pilot study indicates that it is feasible to follow women as they move around the country and switch doctors; inclusion of these women will reduce the high loss to follow-up of the first study. Evaluation of computer hardware and software was completed in March 1986.

13. Cardiovascular Disease and Oral Contraception

FHI is collaborating with the Department of Community Medicine and General Practice, Radcliffe Infirmary of Oxford (UK) in a case-control study of young women with fatal myocardial infarction. This study began in early 1986. To date, 69 cases have been identified for the first three months of 1986; not all of these were able to be included in the study (for a variety of reasons). Information on contraceptive history and presence of other risk factors for

myocardial infarction are collected from surviving family members and the deceased's physician.

The association between myocardial infarction and stroke and use of combined high- or standard-dose (i.e. 50 ug or more of estrogen) oral contraceptives is well recognized. Since the first report in the early 1960s, this association has been confirmed by three major cohort studies and a large number of case-control studies. However, all research involves women taking oral contraceptives with relatively high doses of both estrogen and progestin. Today's pill formulations contain much lower doses of both hormones, and while the risk of cardiovascular disease associated with these formulations is thought to be lower, this has yet to be demonstrated.

14. The Effect of Condom Use on Mild Cervical Dysplasia

Richardson and Lyon found in a non-random, uncontrolled 1981 study that condoms were an effective means of treating cervical dysplasia: 98% of women with cervical dysplasia treated only with condoms for six months showed complete regression of the disease. No other study has been done to confirm these findings. FHI is collaborating with Juarez University in Durango, Mexico to test the efficacy and acceptability of this approach to managing dysplasia. Two hundred women with mild dysplasia will be allocated to a condom or control group and observed after three months for changes in the cervical dysplasia. This study started in August 1986.

C. Planned Projects

1. Clinical Trial to Manage the Side Effects of Oral Contraceptive Use

In Zacatecas, Mexico, an investigator has had success with managing certain side effects of oral contraceptives with Vitamin B₆. The primary purpose of this study is to measure the severity and rates of side effects associated with initiation of oral contraceptive use between the two study groups: women taking 150 mgs of Vitamin B₆ daily and those taking a placebo. The side effects of nausea, headache and irritability may be directly or indirectly ameliorated with therapeutic doses of Vitamin B₆ as used to manage similar side effects of early pregnancy. A less specific measure of the regimen's success will be a comparison of continuation rates between the two groups at three months.

2. Oral Contraceptives and Osteoporosis

Estrogen therapy is known to retard osteoporosis in menopausal women. Although bone loss is accelerated after menopause, loss actually begins well before. FHI is developing a study with the Chapel Hill Spine Clinic to determine whether the bone mineral density of premenopausal women in their 40s who have taken oral contraceptives is greater than that of women who have never used oral contraceptives. The bone mineral density of the lumbar spine will be measured by dual photon absorptiometry, and two sites on the distal radius will be measured by the single photon method. Information on other risk factors for osteoporosis and contraceptive history will be

collected by interview. The mean bone density of never-users of oral contraceptives will be compared with that of current and former users. This study will start during fiscal year 1987.

3. Presence of Human Papilloma Virus in Cervical Tumors

In collaboration with the Virology Division of the CDC and the Department of Pathology of the University of the West Indies (Jamaica), FHI will examine tissue from the cervical tumors of cases in our case-control study (described above). The tissue samples will be prepared at UWI, and examined for the presence of the HPV at the CDC; DNA typing will also be done at the CDC. A pathologist from UWI will assist with the work at the CDC.

4. Maternal Mortality

Building on its past experience in studying maternal mortality, FHI is developing studies in Haiti and in Kenya. Both will start with the obstetric ward and expand to all hospital wards and then to the community. This diverse approach should permit estimation of maternal mortality ratios and the degree of under-reporting associated with a single method approach to measurement. Both of these studies will be undertaken with Mission funds. The Haiti study will be done in collaboration with Columbia University.

5. Oral Contraceptives and Liver Cancer

Two recent studies published in Britain showed an association between hepatocellular carcinoma and oral contraceptive use. These two case-control studies confirmed an association which had been suspected for several years. In Britain and the United States hepatocellular carcinoma is extremely rare, and the association with oral contraceptives has almost no public health impact. In developing countries, however, it is much less rare. The prevalence of liver cancer in developing countries is attributed to the high prevalence of Hepatitis B infections as well as to aflatoxins in some food staples. Since the British studies excluded cases with evidence of exposure to HBV (which were very small in number) it is not known whether oral contraception promotes the development of liver cancer in women exposed to HBV, or if the effect is independent of HBV exposure. FHI is seeking a site in which to do a case-control study of liver cancer. Hong Kong is a possible site, since it has a high prevalence of both HBV exposure and oral contraceptive use, and has a tumor registry.

V. PROGRAM EVALUATION

A clinically satisfactory method of contraception can go unused because it is misunderstood, inappropriately used or poor methods may be overutilized. In all cases, success in family planning turns a subtle balance between the knowledge, enthusiasm or hostility of the provider and the needs of the consumer. When it comes to pregnancy spacing, the needs of the consumer are partly determined by current patterns of breastfeeding.

The Program Evaluation Division supports research in three key areas: family planning evaluation, maternal and child health/family planning, and natural family planning/breastfeeding. Some studies focus on the acceptability, use, and client satisfaction with family planning methods in non-clinical settings. Other studies evaluate the performance of delivery systems and the knowledge and attitudes of providers toward the methods they deliver.

One aspect of Program Evaluation's work relates to the individual freedom of choice - are the people having coercive pregnancies, because of the barriers that prevent them getting access to voluntary sterilization, or are they being unreasonably influenced by the financial compensation offered by some programs at the time of sterilization?

A. Family Planning Evaluation

Although many of FHI's family planning evaluation studies are tailor-made and one-of-a-kind, FHI has focused on several general areas: provider knowledge and attitude surveys; adolescent fertility surveys; surveys of male attitudes toward family planning; studies on access to sterilization; evaluation of different family planning service delivery systems; and demographic projects. Methodologies range from in-depth interviews and focus groups to hospital-based studies and large household surveys.

The evaluations are designed to provide information to improve service programs. The link between service providers and clients is especially crucial. Several studies assess the family planning knowledge and attitudes of providers (such as physicians) or commercial distributors. Other studies focus on accessibility of services, acceptability of new methods, program impact, and family planning needs, attitudes, and family planning knowledge and attitudes of special segments of the population (adolescents, males).

New initiatives include studies of acceptability of new methods, particularly NORPLANT[®], and studies of patterns of pill compliance in the general population.

1. Provider/Client Surveys

Throughout much of the developing world, oral contraceptives are generally acquired without first making a visit to a physician.

K tailers and community-based distributors play an important role in determining what clients know about this and other methods. Such information may affect how users cope with problems and in turn affect continuation rates and user satisfaction.

a) Honduras: Survey of CBD Distributors

In collaboration with the Asociacion Hondurena de Planificacion Familiar (ASHONPLAFA), a survey of distributors and promoters in the Honduras community-based distribution (CBD) program was carried out. Costs of data collection were paid for by the local AID Mission. A final report has been prepared. Results show that (1) a high percentage of distributors work in areas where contraceptives are not available from other sources, especially low-cost sources; and (2) training of distributors to recognize contraindications of the pill, to advise women with side effects, and to know the appropriate way to use family planning methods needs to be strengthened. A paper based on this study was published in the Boletin de la Sanitaria Panamericana, July 1986.

b) Honduras: Survey of Oral Contraceptive Purchasers

When a new source of supplies is added, it may gain customers who switch methods or sources or may attract new users. Point-of-purchase surveys can be used to evaluate the impact of new programs to provide contraception. Also, such surveys provide information on what purchasers of contraceptives know about contraception.

The Social Marketing Program of ASHONPLAFA has carried out a survey of purchasers of oral contraceptives at a sample of 27 pharmacies where Perla, the program's standard dose pill, is sold.

The purposes of the survey were: a) to determine the knowledge of OCs (including how to take the pill, expected side effects and what to do if one or more pills are skipped) among purchasers of oral contraceptives including Perla; b) to determine whether the social marketing program is attracting low- and middle-income women to use oral contraceptives (for example, are the characteristics of Perla buyers different from those of women buying other brands of OCs?); c) to determine previous contraceptive use of buyers and source of previous method (i.e., is the program attracting non-users, users of other methods or users of other brands of pills?); d) to determine the reasons for the visit to the retail outlet at which orals are purchased, purchasing patterns, travelling time and method of transportation to the outlet; and, e) to determine if buyers seek information about contraception from pharmacy staff and if they consider the pharmacist an important source of information.

Data collection was completed in May 1986. The total number of completed interviews was 2,231. Only 56% of purchasers were the actual users. Twenty-eight percent were men buying oral contraceptives for spouses and friends.

Since 1984, when Perla accounted for 20% of all orals sold in pharmacies, Perla has doubled its market share to 42%. The study found that Perla users are of a lower socio-economic status than the

users of other brands with less education and less comfortable homes (less electricity and fewer inside toilets).

There has been considerable switching of brands: 48% of Perla users compared with 37% of users of other brands used a different brand of orals before buying their current pill. About the same proportion of women in each group have never used another brand or a different method (45% of Perla users compared with 49% of users of other brands).

The users of the more expensive brands were more likely to have purchased their previous pill in the commercial sector (70%) compared with Perla users (41%). A quarter of the women buying Perla had obtained their previous pill from ASHONPLAFA's CBD program compared with 4% of the users of more expensive brands.

Preliminary results were presented at the American Public Health Association (APHA) meeting in Las Vegas, September 1986.

c) Nepal: Contraceptive Retail Sales Study

The Nepal Contraceptive Retail Sales (CRS) Company is a private company that began assisting governmental family planning activities in 1978 by bringing temporary family planning methods to couples through existing retail outlets (including medical shops, general shops and pan shops). The CRS program offers pills, condoms and foaming contraceptive vaginal tablets at very low cost. In 1984, the CRS company accounted for almost half (47%) of all condoms

distributed in Nepal, and more than one-fifth (22%) of all oral contraceptives. One of the components of the program is to assist in educating and motivating individuals to select and correctly use the appropriate CRS product for family planning.

In this study, a sample of retailers and consumers from a large number of urban medical shops which provide standard- and low-dose oral contraceptive and contraceptive foaming vaginal tablets was interviewed. Since the vast majority of medical shops selling pills and contraceptive vaginal tablets are in urban areas, the study focused on these areas. Knowledge, attitudes, correct and incorrect usage, and problems associated with specific CRS methods sold at medical shops were assessed for about 300 retailers and approximately 800 consumers of CRS products.

Fieldwork was initiated in late February 1986 and as of the end of March, interviews were completed with 761 consumers and 297 retailers. Data analysis took place from June-August 1986 and a preliminary report was prepared in September 1986. There will be a seminar on the survey findings in late October 1986.

Preliminary results indicate that consumers of the low-dose (and more expensive pill) are more educated than those buying standard-dose pills. The majority of CRS pill users did not use any method prior to using the CRS pills. Thus, it appears that a large share of CRS consumers are first time acceptors indicating that the CRS program may be increasing contraceptive use. About half of the consumers of CRS pills do not buy the product themselves. The program needs to

consider this in designing ads to attract clients. Less than one-third of pill consumers consulted a physician or received a health exam prior to taking the pill. Thus, in this setting the retailer is an important potential source of information about contraception.

d) Mexico: Promoter's Knowledge of Contraceptives

In Juarez, Mexico a survey of community-based distributors including those involved in recruiting women, men and young adults is underway. The first phase of the study used focus groups with providers. Insights gained from this study were used in designing the questionnaire for the second phase.

Ms. Rebeca Ramos visited FHI and with the assistance of Dr. Harrison McKay (FHI Consultant), two questionnaires were designed. One is being administered to female promoters and the second to young adult promoters.

One of the goals of this project is to determine whether or not promoters who have a thorough knowledge of the products they distribute are more successful at recruiting and maintaining clients than other promoters. Other factors such as follow-up visits to those who do not return for contraceptives and neighborhood meetings to recruit more users, may also affect the promoters' performance. This study will provide FEMAP with predictors of distributor performance and recommendations on how to improve training programs for promoters in order to raise contraceptive prevalence and improve continuation rates.

e) Nigeria: Survey of Physician Attitudes and Practices Regarding Modern Methods of Contraception

Especially in Africa, where contraceptive use is low and the medical profession is conservative or ambivalent about allowing non-physicians to provide contraception, it is important to obtain information about physician attitudes toward providing family planning. In Nigeria there is no organized family planning program, and physicians are the major providers of contraceptive services. This study, conducted by the Fertility Research Unit of the Department of Ob/Gyn, University College Hospital, Ibadan, assessed the attitudes and practices of Nigerian physicians regarding modern methods of contraception.

This study examined family planning attitudes and practices of 681 Nigerian physicians selected from cities in which large university teaching hospitals are located. About half of the physicians were themselves practicing family planning; the method of choice was the IUD. Obstetrician/gynecologists and general practitioners were more likely to provide methods to their patients than were other types of physicians. Many physicians were concerned about population growth and favored family planning, yet a substantial minority believed that family planning is foreign to the culture and that it promotes promiscuity. Many physicians were reluctant to promote family planning on a wide scale; many disapproved of non-physicians providing oral contraceptives or IUDs.

The final report has been completed and a paper entitled "Physician Attitudes: An Aid or a Barrier in the Provision of Family Planning Services in Nigeria?" was presented at the APHA meeting in November 1985. It was published in Studies in Family Planning in July/August 1986.

f) Brazil: Family Planning Advice of Physicians

Data from a contraceptive prevalence survey conducted in the State of Sao Paulo in 1978 showed that use of vasectomy was virtually nonexistent. Since that survey was conducted, a program to provide vasectomy services was begun by Dr. Marcos de Castro. In order to assess the potential for increased vasectomies, it is important to know what role physicians play in promoting this method.

Far from being a barrier to the promotion of vasectomy, the results of this survey indicate that physicians have positive attitudes regarding vasectomy. Thirty-eight percent of male physicians or their partners have been sterilized; of these, over 30 percent chose vasectomy. Vasectomies are performed by all urologists surveyed and by over 20 percent of obstetrician/gynecologists and surgeons. While performers of vasectomy are most ready to recommend vasectomy, other physicians are often more ready to recommend vasectomy than to recommend tubal ligation. Both vasectomy and tubal ligation are frequently recommended for older couples with three or more children. When either partner has a health or method related problem, sterilization for the person reporting the problem is most often

recommended. However, if a method is recommended for the other partner, the recommendation is for vasectomy rather than for tubal ligation.

A paper based on the study findings was presented at the annual meetings of the APHA in November 1985. A paper is being revised for publication in Studies in Family Planning.

2. Accessibility, Acceptability, and Effectiveness of Selected Methods

Sterilization is one of the two most prevalent methods in most developing countries. However, even in countries in which it is a common method, there may be barriers to its use. In Africa, where the prevalence of sterilization is low, programs to provide information and counseling may be necessary for women to overcome their fears and misinformation and adopt this method. Finally, information on long-term satisfaction provides a good measure of project success.

a) Honduras: Access to Sterilization

This is a continuing study of women's interest in and barriers to sterilization in Honduras. The first phase of the study was carried out at two hospitals in Honduras in 1980-1981. Results showed that fewer than half the postpartum women who expressed a desire for voluntary sterilization (42% in Tegucigalpa and 21% in San Pedro

Sula) actually obtained the operation at or within four months of delivery.

Since the original study was conducted, a number of factors changed that were expected to increase the number of sterilizations in Tegucigalpa. A final study conducted in the latter half of 1984 sought to determine the contribution of these factors to meeting the demand for sterilization.

The results are disappointing. While the rate of postpartum sterilization rose, the increase is small. New facilities are not being fully utilized. Services to facilitate interval sterilization are largely unused and unknown. The easing of age-parity requirements may make little difference in the short-run perhaps because the earlier guidelines were never fully followed. Over time, demand may increase as women begin to ask for a service for which they may now consider themselves "eligible" and as physicians learn that the age-parity guidelines have been changed.

b) Brazil: Access to Sterilization

In collaboration with the Pathfinder Fund, FHI developed a project in Brazil to analyze the factors that cause women, who say they are interested in tubal ligation and who make inquiries concerning the surgery, to fail to follow-through and get sterilized.

While approval is dependent mainly on demographic variables, especially age and parity, FHI found that follow-through by a woman

is related to her education and income. The steps that a woman must complete to obtain a sterilization also affect whether she ultimately undergoes surgery. Almost no women were scheduled for sterilization during their initial clinic visit. Women who were not scheduled because they lacked certain documentation were more likely to follow through than women who, in addition to lacking documentation, were asked to switch from an inefficient contraceptive method (or no method) to a more modern one. The lessons to be learned from this study provide useful information to programs in other countries that are concerned about maintaining high standards but do not want to discourage women in their efforts to be sterilized.

As a result of this study, the clinic has changed its procedures for scheduling sterilization surgery. Also, the documentation process has been simplified. The decision of CPAIMC to modify requirements for sterilization, some of which only existed to prevent sterilization of pregnant women, seems to demonstrate that CPAIMC administrators were unaware of the extent to which such requirements could discourage women from getting sterilized.

A final report was prepared and submitted to AID. This report has been widely circulated in Brazil. A paper was presented at the APHA meetings in November 1985 and a longer version was published in Studies in Family Planning, July/August 1986.

c) Nigeria: The Effect of FS Counseling on the Rate of Female Sterilization

The prevalence of female sterilization is very low in Nigeria. At the University of Benin Teaching Hospital (UBTH) in Benin City, Nigeria, few women get sterilized, possibly because of presumed opposition from their husbands or their own fears of complications of the surgery. This latter fear may be the result of inadequate counseling.

This study sought to determine the effects of counseling on the female sterilization rate, to study the effects of socio-demographic factors on the acceptance of female sterilization, and to assess the potential impact of the increase in demand on available facilities.

The study design is a randomized trial. The sample includes women of parity four or more who attended the prenatal clinic and delivered at UBTH. Completed forms were received at FHI from 509 women in the counselled group and 503 women in the control group. At delivery, 13% of women were sterilized in the counselled group and 3% in the control group. Dr. Alex Omu, the study director, visited FHI in October 1986 to work on data analysis.

d) Sri Lanka: Follow-up of Tubal Ligation Cases

USAID has a clear policy of not paying "incentives" for the acceptance of family planning. In 1980 the government of Sri Lanka, using non-AID funds, initiated a program that reimbursed all

individuals sterilized in Sri Lanka for costs (lost work time, transportation, etc.) associated with the operation. The amount paid has varied since the introduction of the program as has the response of the community. This study attempts to assess the effect of government-cash payments on the decision to accept sterilization and on long-term satisfaction with the method. It will provide information relevant to policymaking in Sri Lanka and elsewhere.

The investigators selected a sample of 1350 acceptors of female sterilization from the 16,301 women served by Community Development Services (CDS) in urban, rural and estate sectors from 1980 through 1983. The samples were stratified by date corresponding to the government incentive program so that comparisons in satisfaction could be made among groups receiving different payment amounts.

The analysis to date suggests that cash payments may have brought forward the time when a couple or individual accepted voluntary sterilization, but did not induce individuals into a decision they subsequently regretted.

A paper entitled "Incentives and Satisfaction: A Study of Female Sterilization Acceptors in Sri Lanka" was presented at the APHA meeting in November 1985. There were delays in receiving the final 600 forms which slowed down the data processing. These data have now been cleaned and analysis tables are being prepared.

e) NORPLANT® Acceptability Surveys

NORPLANT® is a new method of contraception and hence provides an opportunity for studying potential interest in the population. FHI's first NORPLANT® acceptability studies looked at acceptability among clinic populations.

As part of FHI's Clinical Trials pre-introductory studies of NORPLANT® in several countries, the Program Evaluation Division studied the factors that affect the acceptance of NORPLANT®. A NORPLANT® Acceptability Questionnaire that records information for all women considered to be potential acceptors of NORPLANT® was developed. Results will show reasons why women are interested or not interested in trying the method and what factors correlate with interest. The first clinic-based NORPLANT® Acceptability Surveys (NAS) were initiated in Nepal, Bangladesh, Nigeria and Haiti in 1985. Preliminary analysis is underway for some study sites. Tables and a report are currently under preparation. It might also be noted that questions on acceptability of NORPLANT® were also included in a rural household survey in Sri Lanka conducted in the Spring of 1986. Results should be available in early 1987.

f) Haiti: Condom Acceptability Study

The condom is an important method of family planning but one which is often ignored in family planning programs oriented towards women. However, partly because of growing concern with STDs, but also as a result of greater appreciation of the role played by men in the

fertility decisions made by a couple, interest in condoms seems likely to increase.

To look at issues relating to the acceptability of condoms, a study was designed to evaluate the effectiveness of a distribution program in the Cite Soleil district of Haiti's capital and largest city, Port-au-Prince. The project is assessing reasons for use and for non-use, and obtaining information on the sources of condoms used by men residing in the study area. It will be used to design effective approaches to increase condom use among Haitian couples who are not otherwise protected against unwanted pregnancy.

Client records maintained by the Cite Soleil family planning clinic in December 1985, showed a total of 901 acceptors of condoms in its two years of operation. Nearly one-fourth of these acceptors had received condoms (either at the initial or resupply visit) during the past three months. These individuals (50 percent of those who had not returned for resupply within three months, and 100 percent of those who had received condoms during the past three months) were interviewed in their homes by trained community health workers between February and August 1986. A second sample, numbering 600 individuals, was drawn from household listings in May 1986, to obtain information from those who had never used condoms. Field work is expected to be completed in October of this year.

Data entry and analysis for this investigation will be done at the Centre Haitiano-Arabe in Cite Soleil, with technical assistance from FHI. A final report for this study is expected in FY 87.

Preliminary results indicate very low continuation rates for condoms in this study site.

g) US: Comparative Study of the Today™ Vaginal Contraceptive Sponge with Traditional Use versus Use During the Fertile Phase

The TODAY™ sponge is a new barrier contraceptive for which FHI conducted initial clinical trials. A study involving the contraceptive sponge is being conducted through the Los Angeles Regional Family Planning Council (LARFPC) to compare the use of the contraceptive sponge at every intercourse with the use of the sponge during only the fertile phase as identified by the woman after training in the Fertility Awareness Method (FAM) of natural family planning. The design called for 200 volunteers to be randomized, 100 in each study group, to be followed for one year.

This study was hampered by recruitment problems and as a consequence, the number in each group was reduced. Only 53 women were finally admitted to the study. Twenty-five women were admitted to the Sponge-only group and 28 women to the group using the Sponge in conjunction with FAM. Currently, 15 women are in follow-up and 38 have been terminated from the study. Of the 38 women who were terminated, 5 women completed 12 months of follow-up, 6 women were discontinued because of pregnancy and the remaining 27 left the study for "other" reasons. Some women left because they did not trust the effectiveness of the method, while others left because they were no longer sexually active.

At this time, the admission data and the discontinuation data to date have been loaded onto the computer. The follow-up interviews will continue through February 1987. In February and March 1987, the follow-up data and the remaining discontinuation data will be loaded and ready for analysis.

h) Colombia: Pill Compliance

Methods currently in use, such as oral contraceptives (OCs), sometimes have disappointingly low use-effectiveness in the general population, possibly because providers give little or no instruction to acceptors, who then do not use the method correctly. Studies of user compliance, provider knowledge and client-provider interaction can yield practical information on how use-effectiveness can be increased.

For example, there are almost no data on the compliance patterns among women who accept the pill outside of a clinic setting. In many countries, poor compliance is not only directly related to method failure, but may be an important contributing factor to high discontinuation rates. One possible explanation is that women may not be taking pills correctly and, as a result, may experience unacceptable side effects which lead them to discontinue use. A 1985 study by Seaton in Bangladesh found very high rates of non-compliance among oral contraceptive acceptors in the Matlab district.

A study in Colombia is the first of what is anticipated will be a series of oral contraceptive compliance and continuation studies in

several countries. FHI is currently conducting a study of Compliance and Continuation of Oral Contraceptive Acceptors in Magdalena, Colombia. Magdalena is the only Department (State) in Colombia in which all rural health promoters are trained to provide oral contraceptives, making it an ideal site to investigate the oral contraceptive use of all clients of the Ministry of Health program for this prospective, longitudinal study spanning six months of pill use.

The primary purpose of the Colombia study, initiated at the request of the Ministry of Health (MOH), is to measure compliance and continuation of oral contraceptive acceptors in the context of the services they receive from the MOH rural health promoters. The project has four components: (1) An evaluation of the family planning training of the rural health promoters. The knowledge, attitudes and stated service practices of a recently trained group of promotoras will be compared with their previous levels, and with those of two groups trained at least two years earlier. (2) A series of five focus groups was conducted in July-August 1986, one with the rural health promoters, two with OC users and two with OC discontinuers, to obtain qualitative data on their perceptions, attitudes and beliefs about family planning and pill use. (3) A series of three interviews with new acceptors of the pill beginning in October 1986, asks women about their personal characteristics, their health and reproductive history; how they take the pill (using pill counts and a recall calendar) as well as their knowledge, beliefs and attitudes, and their perceptions of the service system. (4) There will be a final interview with the rural health promoters

evaluated earlier to explore their perceptions of the system and their clients. We will then compare their knowledge, attitudes and service practices with the contraceptive behavior of their clients. Data collection will be completed in FY 87.

3. Household Surveys (including Secondary Analysis)

To improve the delivery of family planning services, governments need information on the level and composition of services demanded and on the ability of the commercial and non-commercial sector to meet this demand. In estimating the need for services, it is important to recognize that the contraceptive mix appropriate for various groups will differ. Surveys of women, men and young adults provide data to plan and evaluate service delivery projects for these different groups.

Household surveys of women are an important source of information on contraception, breastfeeding and MCH care. They provide baseline data to show where and what type of services are needed. Multiple surveys can show the impact of programs that provide contraception, promote breastfeeding or immunize children. The first three projects involve data collection and analysis. The latter two projects support secondary analysis of data.

a) Honduras: Maternal and Child Health and Family Planning Survey,
1984

In 1984, a survey of 5500 households was conducted in Honduras to obtain information on both maternal and child health and family planning, including use and source of family planning, use of primary care facilities, breastfeeding and child mortality and other aspects of reproductive health.

The percentage of all women aged 15-44 in union that were contracepting increased from 27% in 1981 to 35% in 1984 (Tegucigalpa/San Pedro Sula, 56%; other urban areas, 45%; rural areas, 24%). Most of the increase was in female sterilization. The main source of oral contraceptives was ASHONPLAFA; the private sector and the Ministry of Health (MOH) were the other main providers. The main provider of sterilization was also ASHONPLAFA through its programs at the MOH and private hospitals.

The total fertility rate declined from 6.4 in 1981 to 5.3 in 1984. While the total fertility rate was almost unchanged in urban areas over the period 1981-84, it declined from 8.1 to 6.6 in rural areas.

The mean duration of breastfeeding increased by one month from 1981 to 1984 (from 15.2 to 16.2 months). The duration of breastfeeding increased more in urban areas (2.1 months) than in rural areas (1.3 months). The increase was greatest (2.6 months) for women in the highest education group.

The percentage of children aged 0-4 years who had been immunized increased substantially over the period 1981-84 with the largest increases for Polio (46% to 76%). The increase was larger in rural areas than in urban areas. By 1984, coverage for all immunizations was about the same in rural and urban areas.

A research dissemination seminar was held in July 1986. Participating organizations included the Ministry of Health, Management Sciences for Health, CONSUPLANE, ASHONPLAFA, UNICEF, PROALMA and FHI.

A research paper "Contraceptive Use and Fertility" has been written and, after in-house review, will be submitted for publication. Papers on immunization, prevalence and treatment of diarrhea and MCH services will also be prepared.

b) Honduras: Maternal and Child Health Survey and Family Planning Study, 1987

AID/Tegucigalpa has asked FHI to provide technical assistance in carrying out a 1987 MCH/FP Survey. Funds to carry out activities are being provided through a PIO/T.

The primary purpose of the 1987 Survey will be to update the information gathered from the 1984 Survey. Specifically, we will measure contraceptive prevalence, duration of breastfeeding, fertility among women 15-44 and infant mortality. Among children less than 5 years of age, the impact of health services will be

measured by immunization coverage, the prevalence and treatment of diarrhea and acute respiratory infections. In an effort to provide a more precise estimate of infant mortality, this survey will include 12,000 households--about double the number in 1984.

The agencies involved in the 1984 survey will also be carrying out the 1987 survey. An FHI consultant has been contracted to construct a sampling frame based on maps to be used in the 1988 Census. As before, the survey will be a multi-stage probability sample.

Questionnaire development will take place between September 1986 and January 1987. Field work is scheduled to begin in May or June of 1987.

c) Mexico: Combined Reproductive Risk and Contraceptive Prevalence Survey

Funds and technical assistance were provided to the Federation of Private Family Planning Associations in Mexico (FEMAP) to design and implement a Combined Reproductive Risk and Contraceptive Prevalence Survey in selected areas of the cities of Leon and Saltillo in the summer of 1984.

One of the main questions that the study addressed is whether resources should have been devoted to introducing a CBD program in Saltillo and Leon or if those resources could have been used more effectively elsewhere.

Contraceptive use is 50% or better for currently married women aged 15-44 in both cities, and in Saltillo a high percentage of women are using the most effective methods. In Leon, the more conservative of the two cities, use of the rhythm method is high. In both cities, while use of contraception is positively associated with education (especially if the rates are age standardized), use of orals is not associated with education. If education correlates strongly with income, we could confer that inability to pay for orals does not deter their use.

Although there is no clear evidence that use of the pill is discouraged by high cost, the FEMAP program does offer an attractive alternative in that it combines low cost without imposing lengthy waiting times. This combination could be attractive in drawing in new users.

Results of the study indicate that previous users of contraceptive methods, including program methods, have more negative perceptions or experiences than do current users. A high percentage of never-users also have negative perceptions. An important role of the program could be to provide adequate counseling to women with side effects associated with pill use and to provide encouragement to continue use if side effects prove to be of short duration or not severe. FEMAP could also provide education and better information to the many women who have never used the pill because of the fear of side effects.

The program could play an important role in raising contraceptive prevalence by providing methods to non-contraceptors. Among women

"in need", only 20-26% at any time could be considered potential acceptors; if all these women accepted the pill, contraceptive prevalence would increase from 59 to 61% in Saltillo and from 52 to 56% in Leon. However, a substantial percentage (22% in Saltillo and 26% in Leon) have never used contraception. Never-users of contraception are more likely than previous or current users to hold traditional perceptions about childbearing and contraceptive use. The FEMAP program can play a role in providing these women with information about the benefits of family planning.

Ms. Rebeca Ramos visited FHI several times and worked with FHI staff in preparing the project report. A final report is available in English and is being translated into Spanish for wider distribution in Latin America.

d) Philippines: Proximate Determinants of Fertility

FHI is funding a secondary analysis of data collected in four surveys carried out during the past two decades in the Philippines. The purpose of the analysis is to study the trends in and proximate determinants of fertility. The study is being carried out by the staff of the University of the Philippines (UPPI), where the project is based, and Professor John Casterline of Brown University, an FHI consultant. It commenced in November 1985. An initial visit to the Philippines was made by Dr. John Casterline in January 1986 to set up data files and develop the analysis plan with UPPI staff. Analysis of fertility trends and decomposition of these trends in terms of the proximate determinants (e.g., breastfeeding, marriage, contraceptive

use) were carried out in the Spring and Summer 1986. Dr. Casterline will make a final visit in October 1986 to analyze the study results and assist in the writing of the final report which will be completed by December 1986.

e) Thailand: Secondary Analysis of CPS III Data

In Thailand, as in many other countries, supplementary feeding is introduced early in lactation, decreasing the period of postpartum amenorrhea and increasing the need for early resumption of contraception. The third Contraceptive Prevalence Survey (CPS III) collected detailed information on infant feeding practices, postpartum amenorrhea and contraceptive use which can be used to study the relationships among these variables.

This project funded secondary analyses of these data by Drs. John Knodel and Peerasit Kamnuansilpa. Their analysis suggests that many Thai women appear to be following a reasonable strategy for initiation of contraception postpartum. A significant number had an immediate postpartum sterilization. Of the remainder, most waited until menses to resume contraception. Rates of initiation (of contraception) are unusually high at and immediately following the time at which menses resumes, strongly suggesting that the return of menses is an important stimulus for postpartum contraceptive use. Few women started using oral contraceptives during the first few months postpartum and most of these continued to breastfeed for several months. The proportions of Thai women exposed to risk of

unwanted pregnancies for any extended period of time postpartum is modest.

Although there were some limitations of these data, the results are both consistent and convincing. It would be interesting to know whether women in other developing countries are following similar "strategies".

The final report was submitted to FHI by Drs. Knodel and Peerasit and a shorter paper was then submitted to Studies in Family Planning. FHI distributed copies of the final report to researchers in the area of breastfeeding.

4. Surveys of Young Adults

In many places, rapid urbanization has led to the breakdown of many of the traditional norms concerning sexuality and fertility, and premarital pregnancy among adolescents has become a serious national concern. Surveys of young adults are usually the first source of objective information on a group whose problems need to be recognized in the design and implementation of programs to improve reproductive health at the national level.

a) Nigeria: Sexual Behavior, Contraceptive Practice and Reproductive Health Survey of Young Adults

In the context of a high and increasing incidence of unwanted pregnancy among Nigerian adolescents, a survey of 1800 never-married residents of the Ibadan area of Oyo State, aged 14 to 25 years of age, was conducted by the Family Planning Unit, University College Hospital, Ibadan. The purpose of this investigation was to learn about perceptions and practices relating to reproductive health. Findings showed that a substantial proportion were sexually active, and that despite comparatively high contraceptive prevalence among such individuals, many were still engaging in regular sexual relations without contraceptive protection. Nearly half the secondary and university students and two-thirds of those not currently enrolled in school had been pregnant. Among respondents who had been pregnant, almost all reported that they had electively terminated their pregnancies. These findings, as well as a discussion of existing and needed reproductive health care services for young adults in Nigeria, are included in the study's final report, which has been distributed to health providers and policy-makers in Nigeria.

A revised version of that report (Nichols et al., "Sexual Behavior, Contraceptive Practice and Reproductive Health Among Nigerian Adolescents") was published in the March/April 1986 issue of Studies in Family Planning.

b) Liberia: Reproductive Health Knowledge, Sexual Behavior and
Contraceptive Practice Among the Young Adult Population

In response to a request from the Medical Director of the John F. Kennedy Memorial Hospital Maternity Center in Monrovia, FHI participated with the Liberian Ministry of Health and Social Welfare in the design and implementation of a community-based survey in 1985 in Liberia's capital to ascertain the reproductive health needs of its young unmarried population. The study found a substantial unmet need for reproductive health knowledge.

Following the preparation and distribution of a final report of the study's principal findings, a two-day workshop in Monrovia was held in September 1985 to share the results with representatives of Monrovia's medical, educational, legal and religious communities, as well as international donor agencies. During the past year, a paper based on the final report for this study has been written and will be submitted for publication to Studies in Family Planning. In addition, the questionnaire used in Monrovia has been adapted for subsequent FHI-supported studies in Zimbabwe and The Gambia.

c) Mexico: KAP Survey of Young Adults

The Center for Orientation of Adolescents (CORA) in Mexico City provides a variety of services to young adults in two areas of the city. Interviews were conducted with approximately 1,500 men and 1,750 women from a randomly selected household sample of the areas where CORA is active. The field work was initiated in March and

concluded in August 1985. Data entry and editing were coordinated in-country by the Mexican Academy for Medical Demography. Data analysis began in October 1985 at the CDC in Atlanta.

This survey is the first large effort of its kind in Latin America.

Some of the findings include:

- a) 13% of women 15-19 years and 39% of women 20-24 reported that they have had premarital sexual intercourse. These figures for males were 43% and 86%, respectively;
- b) of the unmarried respondents who are currently sexually active (sex in the last month), 75% of the females and 82% of the males reported using contraception;
- c) almost half of the sexually active females reported using rhythm (42%) followed by oral contraceptives (19%) and the IUD and injectables (11%) each. Sexually active males also reported rhythm (29%) as their most used method.
- d) for unmarried men and women, the primary source of contraception is the private sector whereas for the married, the government is the primary source;
- e) the preferred family size is two for both young men and women;
- f) 78% of the women and 73% of the men have had a sex education class in school;
- g) only about a quarter of each group could correctly identify at what point in the menstrual cycle a woman is fertile.

Results of the survey will be used to develop and improve information and service programs which seek to reach adolescents who have concerns about reproductive health.

Papers were presented at the American Public Health Association in November 1985, and the First International Conference on Adolescents in Oaxtepec, Mexico, in December 1985. Additional presentations were made at the Population Association of America (PAA) and the US-Mexico

Border Health Association, both held in April 1986. The final report in Spanish and a summary version in English should be ready by December 1986.

d) Zimbabwe: Reproductive Health Survey of Young Adults

This project funds a survey of young adults in Harare, the capital of Zimbabwe. Approximately 1600 women and 800 men in the age group 14-24 are being interviewed. The survey includes both married and unmarried women but only unmarried men. Fifty enumeration areas were selected and within each enumeration area, a cluster of 100 households was selected.

Originally it had been intended to use 21 as the upper end of the age range but it was found during the listing that very few women 21 and under were married. As a consequence the design was modified to include 22-24 year olds.

Data collection is underway and will be completed in October 1986. Coding will be completed in November 1986. Ms. June Tsodsai, Chief Youth Advisor in the Zimbabwe National Family Planning Council will visit FHI in the Spring of 1987 to work on the final report which will be available in FY '87.

e) Gambia: Technical Assistance to Survey of Young Adults

In 1983 the Gambia Family Planning Association (GFPA) expressed concern that the Gambia had a significant problem with unwanted

pregnancies among adolescents. The Gambia Reproductive Health Survey of Young Adults will be conducted in two of Gambia's nine government districts. Approximately 800 young men and 1600 young women between the ages of 14 and 24 in the Greater Banjul area will be interviewed. Information will be collected on young people's attitudes and behavior regarding dating, marriage, sexual activity, contraception, childbearing, and problems facing young people in the Gambia such as unwanted pregnancy and sexually transmitted diseases.

The goal of the study is to provide data to the GFPA to enable it to develop, evaluate, and improve programs targeted to meet the needs of young adults for information and services in the area of reproductive health and family planning. Questionnaires were pretested in August. Field work will be initiated in November 1986.

5. Surveys of Men

a) Ghana: Analysis of Male Attitudes Survey

Family planning services in Africa have traditionally been targeted towards women despite the fact that men sometimes play a dominant role in determining family size and in the choice and use of contraceptives. Both male and female sterilization are poorly accepted in most parts of sub-Saharan Africa, especially in rural areas.

Knowledge of, attitudes towards and use of contraception among Ghanaian men were explored in this survey of 168 men randomly

selected from a computer-generated list of households in rural Accra (population 16,000). Particular attention was given to attitudes towards male and female sterilization.

Nearly three-quarters of the men interviewed approved the use of contraception but only 8% of these men or their spouses were currently using modern contraceptives. Almost 80% of men correctly explained that female sterilization permanently prevents a woman from having any more children. However, only 2% of men correctly understood male sterilization. After the interviewers described both female and male sterilization to all interviewees, 63% of men said they would be willing to consider sterilization for their wives and 33% sterilization for themselves after completion of their family size.

b) Nigeria: Male Attitudes Study

Existing local and national family planning activities in Nigeria, as well as the many studies which have been conducted over the past decade on contraceptive attitudes and practices, have usually been focused on women. However, in a male-dominant society such as currently exists in Nigeria and many other developing countries, the attitudes and prejudices of men may be important in fertility control as they are in other areas of health care delivery.

For this reason, and to assess the acceptability of community-based contraceptive service delivery programs for adult men, a survey is being conducted among males aged 18 to 60 years of age in Benin City

and three surrounding rural villages. Male respondents will be asked their achieved and intended family size, attitudes toward child spacing in general, and knowledge and use of specific contraceptive methods.

During the period covered in this report, the study questionnaire was drafted, pretested, revised, male interviewers (recent graduates of the University of Benin Teaching Hospital Nursing School) were recruited and trained during a site visit by FHI's technical monitor, and field work initiated. Household interviewing is expected to continue through December 1986, at which time coding and data entry will be done at the University of Benin Institute of Computer Science. A final report is expected in early 1987.

B. Maternal and Child Health/Family Planning (MCH/FP)

In many developing countries, the health benefits of family planning still need to be documented and publicized. Although maternal and infant mortality rates continue at unacceptably high levels, due at least in part to pregnancies that occur too early, too late, or are too closely spaced, family planning programs, particularly in Africa, have not yet gained wide acceptance and are low in government priorities for health care. In such settings, FHI is conducting pregnancy monitoring studies and surveys of the causes and consequences of illegal abortion, studies of maternal mortality, and infant and child mortality and morbidity, all of which attempt to assess unmet needs for family planning.

1. Pregnancy Monitoring Studies

Most developing countries have come to realize that health for all cannot be achieved simply by increasing the number of hospitals and health care providers. Throughout sub-Saharan Africa, poor and deteriorating economic conditions emphasize the need for comprehensive health and family planning policies. In times of economic austerity, policymakers and economic planners are looking for ways to achieve better utilization of existing resources to provide health care. In most Sahelian countries, hospitalization for pregnancy-related reasons currently makes up the largest portion of care needed by and provided to women. These services also constitute a substantial proportion of all hospital-based health care. Decreasing the risks associated with early, late, numerous or closely spaced pregnancies is a serious concern among those involved in the delivery of health care. Birth spacing as a health measure for both mothers and their infants is thus becoming an increasingly accepted concept in many African countries.

During the period covered by this report, data collection was completed at previously initiated projects in Senegal and Ivory Coast. The collection of infant mortality data continues at a third site in Zaire. Site visits by FHI technical monitors were made to review project implementation, and to work with in-country collaborating investigators in planning the analysis of data collected and the reporting and dissemination of findings.

During FY 87, final reports for these studies will be prepared and disseminated to appropriate audiences at both policymaking and service delivery levels, as well as to collaborating organizations and funding agencies. A regional conference has been proposed for late 1987 to enable investigators in these three countries to present and compare their major findings and their implications, and to outline courses of action to improve the delivery of obstetric care services in sub-Saharan Africa.

Research findings from each of the country projects will be shared with government policymaking officials, health care providers, and international donor agencies. The broad goal of this program is to assist in the design of appropriate service delivery and training programs to improve maternal and child health. Areas to be addressed through the findings of these country studies include better utilization of limited medical personnel, hospital facilities and traditional birth attendants (TBAs), improved prenatal screening, and more effective counseling and services for birth spacing.

a) Senegal: Obstetric Surveillance and Determinants of Mortality to Women of Reproductive Age in the Sine Saloum Region

To gain a better understanding of factors affecting maternal and child health in a largely rural region of Senegal, this project was designed to collect information on obstetric care and the determinants of mortality to women of reproductive age in the Sine Saloum region. Approximately 8500 deliveries over a period of one year have been monitored in a representative sample of health

facilities in the project area. Information is available from village level health huts, health posts, sub-regional health centers and the regional referral hospital. Data on obstetric history, prenatal care, referral status, delivery and pregnancy outcome have been recorded by health care providers trained in the collection of data.

In a second phase of the project, initiated in FY 86, deaths occurring to women of reproductive age in the project area were investigated by a trained interviewer to determine the cause. Institutional deaths were investigated both in the health institution and at the place of residence of the deceased. Attention is being given to deaths resulting from pregnancy or childbirth. Because of the passive nature of the reporting system for deaths occurring in the community, substantial underreporting--particularly in the more remote rural areas--is likely to have occurred. Based on current estimates of age-specific mortality, information on as many as one half of the deaths to women of reproductive age was not received at the central statistical office of the Medical Region, and thus not available for the study interviewer to follow-up.

During the period covered by this report, data have been received and are presently being tabulated at FHI and at the Bureau National du Recensement in Dakar, using microcomputer facilities provided under a separate FHI subagreement.

The results of this study will provide policy-relevant information on the relationship of family planning services and primary health care

and maternal and child care activities in the region. In addition to addressing a series of research questions about pregnancy-related care and outcomes in the Sine Saloum, this project will help to reinforce the health service statistics through the design and implementation of a uniform reporting system for obstetric care that can serve as a model for the entire country.

b) Ivory Coast: Pregnancy Care Surveillance in Abidjan

Ivory Coast, like its neighbors, has given priority to improving the health of its people, in particular that of mothers and children. However, the contributions that high fertility and inappropriate pregnancies (too early, too late, too closely spaced) make to maternal, infant and child mortality are not well understood by policymakers. Less is known about the details of pregnancy and childbearing in West Africa than in any other part of the world. Existing evidence points to high rates of perinatal, neonatal and maternal morbidity and mortality. There is also anecdotal information from Cote d'Ivoire of a growing incidence of illegal abortion, particularly among adolescents. What proportion of scarce health resources go to treating these young women for complications, what degree poorly-performed illegal procedures contribute to pregnancy-related morbidity and mortality and how the numbers might be reduced are all unknown.

This project collected data on a representative sample of women hospitalized for pregnancy-related care in the capital city, Abidjan, over a 15-month period. Special attention was given to studying

referral patterns from the eleven maternity centers of the city to the two major referral hospitals. Data on over 16,000 deliveries were collected and computerized and preliminary data tabulations completed. A final report is in preparation. Two seminars at the end of the analysis period will present results to Ivoirien staff who participated in the study and to policymakers to elucidate priorities in improving pregnancy-related care and pregnancy outcomes. The data will serve as a basis for developing service programs addressing priority needs.

c) Zaire: Traditional Birth Attendants (TBAs)

This project involves the collection of data on women hospitalized for pregnancy-related care at the major referral hospital in Karawa over a two-year period. In addition, because most maternity care is provided in the home by TBAs, this project included the development and implementation of a registry system, based on oral reports, to collect data on home deliveries attended by TBAs. Information from the registry, along with concurrent information gathered on institutional deliveries at the hospital, will provide a more complete picture of the factors that affect maternal and perinatal mortality in Karawa, and provide information for the ongoing AID-sponsored TBA training program there. Special attention is being devoted to studying TBA referral patterns. In addition, an estimate of the rate of perinatal and infant mortality is being made and causes of infant death determined for the home deliveries by following up those infants over an 18-month period.

Data collection on home and hospital deliveries has been completed. Follow-up data collection on infant mortality will continue throughout 1987.

Preliminary findings of this study ("Affecting Perinatal Outcomes Among Hospital Deliveries in Karawa, Zaire") were presented at the 1986 Annual Conference of the National Council for International Health. In addition, a poster session entitled "Traditional Birth Attendants (TBAs): Filling the Need for Better Health Statistics" was presented at this Conference using data collected in this investigation.

2. Maternity Care Monitoring (MCM) Studies

In addition to FHI's work in monitoring pregnancy outcomes in Senegal, Ivory Coast and Zaire, studies have been conducted in other locations. A hospital-based study in Haiti and MCM investigations in the Middle East and in other locations in sub-Saharan Africa have been completed during the period covered by this report. A number of consultant reports and publications have been prepared; others are in preparation. Finally, a monograph summarizing FHI's experience in MCM in sub-Saharan Africa has been completed, translated into French and disseminated to appropriate audiences internationally.

a) Haiti: Maternity Care Monitoring (MCM)

This maternity care monitoring study proposed to collect data on a systematic sample of deliveries during a 12-month period in eight hospitals/maternalities in the Western Region of Haiti.

Field work for this study was completed in December 1985.

Information was collected on more than 5,500 deliveries in eight hospitals. However, because data collection was either irregular or stopped in some centers, only data from the University Hospital, the Carrefour Hospital and the St. Catherine Laboure Maternity in Cite Soleil could be analyzed. All of these centers are in Port-au-Prince. For these centers, consultant reports have been prepared and translated into French, and will be presented to the Direction de l'Hygiene Familiale et de la Nutrition (DHFN), the government organization which is responsible for maternal and child health. After a review of the reports by investigators and officials of the DHFN, a one-day seminar will be held in early 1987 to identify problems and recommend action that will improve obstetric outcomes and reduce morbidity and mortality.

b) Maternity Care Monitoring (MCM in-house)

The overall aim of the MCH study area is to assist in insuring the most cost-effective use of the limited resources available to improve maternal and infant care and to document the need for improved family planning services by drawing attention to the expressed wishes of women for access to contraception.

Several papers based on the analysis of information collected on 22,000 women delivering at the University Hospital in Zaria, Nigeria, a project which was partially funded by FHI, were published (for example, Harrison, KA, "Childbearing, Health and Social Priorities: A Survey of 22,774 Consecutive Hospital Births in Zaria, Northern Nigeria", British Journal of Obstetrics and Gynecology, 92, Supplement No. 5, 1985).

Other papers based on Maternity Record or Pregnancy Wastage Record data are in press or were published in the last twelve months: "Hospital Maternal Mortality Risk by Cesarean and Vaginal Deliveries in Two Less Developed Countries - A Descriptive Study", International Journal of Gynaecology and Obstetrics; "Hospital Deaths in a High Risk Obstetric Population: Karawa, Zaire", International Journal of Gynaecology and Obstetrics; and "Delivery Type and Neonatal Mortality Among 10,749 Breeches", American Journal of Public Health.

c) Obstetric Care in Africa (Monograph)

Under previous MCM subprojects, FHI has conducted studies in twenty-three centers in sub-Saharan Africa to obtain information on obstetric care and family planning. Results of these studies have been used to prepare a monograph Reproductive Health in Africa: Issues and Options, that discusses the following topics: maternal mortality, antenatal care, obstetric practice, family size, fertility intentions, breastfeeding, contraceptive use and postpartum family planning. The English version has been translated into French. Printing and distribution were completed during this reporting year.

3. Pregnancy Wastage Studies

Deliberate termination of pregnancy in developing countries is often a direct consequence of the limited knowledge and non-availability of effective contraceptive methods among the sexually active population. In addition to posing a major health problem, the hospitalization and treatment of patients with complications resulting from illegally induced abortion consumes a substantial portion of scarce medical resources and adversely affects other branches of medicine.

FHI has provided technical and financial support to two recently completed studies of pregnancy wastage. Results have been used to impress upon health policymakers and service providers the contribution safe and effective contraceptive services can make to reducing the number of unwanted pregnancies.

a) Zaire: Multi-center Pregnancy Wastage

A hospital-based study of the social determinants and medical consequences of pregnancy wastage was conducted in 1983 at ten medical centers located in three regions of this central African nation. Under the direction of the Comite National des Naissances Desirables (CNND), the study documented the incidence and nature of complications associated with pregnancy wastage requiring hospitalization and estimated the level of contraceptive knowledge and use among women whose pregnancies were interrupted.

During the 18 months of data collection (November 1982 - April 1984), a total of 2,465 women were admitted to the ten participating centers for treatment of medical complications following abortion. At a minimum one-fourth of the total abortions had been illegally induced, frequently with resulting fever, infection, bleeding and lesions/lacerations requiring medical attention. Thirteen patients died as a result of these complications.

A report, "Determinants and Consequences of Pregnancy Wastage in Zaire: A Study of Patients Requiring Hospital Treatment in Kinshasa, Matadi and Bukavu", has been prepared and distributed in conjunction with the CNND and research investigators at several of the participating centers. The goal is to impress upon Ministry of Health officials and private service delivery programs the critical importance of contraceptive services in reducing the incidence--and associated economic and human costs--of unsafe and illegally procured abortions throughout Zaire. This report has been translated into French and is being distributed to appropriate agencies and individuals in Zaire by the CNND. CNND staff plan to prepare additional pamphlets and other informational materials based on the results of this study, and to travel to CNND regional offices to conduct small seminars emphasizing the importance of family planning as a means of avoiding unwanted pregnancies and their consequences. Several papers based on the findings of this study and their implications are planned for FY87. They will be prepared for both English and French-language journals.

b) Bolivia: Pregnancy Wastage

This subgrant funded a multi-center study of women hospitalized for complications associated with illegally induced and spontaneous abortions at 11 hospitals in five cities in Bolivia.

Over a 12-month period, beginning July 1983, socio-demographic, family planning and clinical information was recorded. Based on this study, it was estimated that at least 23% of the 4371 abortions were illegally induced. Almost 1% of the patients died. The women who deliberately terminated their pregnancies tended to be younger, nulliparous and not in union, compared to those with spontaneous abortions. Of the illegally induced cases, 65% were induced by Medically Trained Practitioners (mostly by curetage), and 35% by non-MTPs (mostly by inserting a foreign object). The higher a woman's education, the more likely she was to seek out a trained practitioner. Women whose abortions were induced by curetage were less likely to experience fever and lesions, but had longer hospital stays.

Sixty percent of those women hospitalized with complications resulting from induced abortion reported they did not use a contraceptive method during the month they became pregnant and nearly half of these gave as their reason a lack of knowledge. After medical treatment, 77% planned to use contraception, the IUD being their most frequent choice. Results show the need to improve the delivery of family planning services in Bolivia.

In April 1986, the results of this investigation were presented to the Bolivian Society of Obstetrics and Gynecologists. FHI staff have submitted a paper based on the final report to the Bulletin of the Pan American Health Organization.

c) Ghana: Pregnancy Wastage Study

In Ghana, induced abortion is recognized as a major cause of maternal mortality. An earlier FHI sponsored study of abortion experience among obstetric patients at the Korle-Bu Hospital, Accra, Ghana, showed that one-third of women with only one previous pregnancy reported that the pregnancy had ended in induced abortion.

This study examined the complications of pregnancy wastage at the Korle-Bu Hospital in Accra, Ghana. Korle-Bu Hospital is the teaching hospital and the principal referral hospital in the capital city of Accra.

Data were collected on 1,882 women admitted to the Korle-Bu Hospital for treatment of complication of spontaneous abortion and illegally induced abortion over a one-year period. Seventeen percent of the women had clinical or other evidence of illegally induced abortion. These women had more complications and used more hospital resources, compared to women with spontaneous abortion. The death-to-case rate in the induced abortion group was 39.6/1000 compared with no deaths in the spontaneous group. Although women with illegally induced abortion constituted only 2.4% of pregnancy-related admissions to the hospital, they accounted for 31% of the deaths. Hospital based

studies such as this have a number of limitations such as under-reporting of induced abortions, and lack of representatives of the general population. However, this type of study provides the only available indication of the magnitude of pregnancy-related morbidity and mortality in countries such as Ghana. The findings from this study are due to be published soon.

4. Maternal Mortality Studies

The reduction of deaths associated with pregnancy and childbirth is an important goal of many public health programs, particularly in developing countries, where overall mortality is high and maternal deaths constitute as much as 20 to 25 percent of all deaths to women of reproductive age.

With FHI technical and financial assistance, studies of maternal mortality under the Program Evaluation Division are underway in the Sine Saloum Region of Senegal, as part of the pregnancy monitoring investigation described above, and in the Giza Governorate of Egypt. In addition, FHI is supporting the secondary analysis of data collected on maternal deaths in earlier Senegalese studies and in The Gambia.

The overall objective of these studies is to identify the causes of reproductive age mortality as a first step in the development and delivery of health care services to reduce the number of deaths from those causes thought to be preventable. A secondary objective is to show that, despite the attendant publicity concerning the health

risks of various modern methods of child spacing, the relative risks of contraception compared with pregnancy and childbearing in developing countries are very low.

a) Egypt: Giza Maternal Mortality Study

A recent study of reproductive age mortality in the Governorate of Menoufia in Egypt found that the maternal mortality rate for that governorate was 28 times higher than the maternal mortality rate for the United States in 1981. The results of the Menoufia study have been used by President Mubarak in setting policies for health care in Egypt.

This study seeks to determine the incidence and causes of maternal deaths in the Governorate of Giza, Egypt. Information is being collected on all maternal deaths occurring in the Giza, Imbaba and Osim health sectors during a twelve month period. The deaths are expected to be registered at the local health bureaus, whether or not they occurred in a hospital.

The study objectives include the establishment of an effective system for locating maternal deaths, identifying maternal deaths that are currently preventable, determining the factors associated with maternal mortality and creating a profile of high-risk women. Household interviews began in August 1986 while hospital data collection began in September 1985.

Once maternal deaths are identified, trained interviewers (social workers) visit the household of the deceased and interview family members about the circumstances surrounding the maternal death and the symptoms the deceased woman manifested prior to her death. A medical panel is assessing the specific causes of death from the family interviews. Additional information is being collected for maternal deaths occurring in hospitals and is being compared with the results of the home interviews of family members of the deceased.

During the first ten months of data collection, 104 maternal deaths were identified and interviews with family members completed.

Data collection for this study will be completed in late 1986. In addition to addressing a number of important research questions on factors related to maternal mortality in Egypt, this project will also help to improve the health service statistics system through the design of a uniform reporting system for maternal deaths. Information will be used to design public health measures that will reduce the frequency of maternal deaths occurring in the home and in hospital settings throughout Egypt.

b) Senegal: Support to ORSTOM for Secondary Analysis of Data
on Maternal Mortality

Maternal mortality in rural Senegal is thought to be nearly 70 times higher than in developed countries. Maternal death is a serious hazard for Senegalese women, who average 7.4 births over their reproductive lives.

In the whole of sub-Saharan Africa, data on maternal mortality and its determinants and implications are scarce. This three-year project is a systematic attempt to collect data on deaths related to childbirth and to bring together a spectrum of demographic, sociological, nutritional and medical information obtained from households in a small rural area of Senegal.

The activities of the project include secondary analysis of two existing data sets: one for the Sine Saloum Region of Senegal, and the other for women and children attending a health center.

The questionnaire was designed to study the determinants of mortality among women of reproductive age. Data collected and analyzed thus far indicates that approximately 50% of all deaths to women of reproductive age can be attributed to maternal causes. ORSTOM estimates that the maternal mortality ratio in the region is about 8.9 deaths per 1000 deliveries. Similar results have been reported in a study in nearby Gambia. These are among the highest levels of maternal mortality studied anywhere. Data collection is now complete and ORSTOM researchers are analyzing the data, and will submit a report on this work during FY 87.

5. Infant Health

During the past year, FHI has provided technical and financial support to investigations of the role of non-medically trained workers in identifying and referring high risk pregnancies and

infants to reduce both perinatal and infant morbidity and mortality. In locations as diverse as Brazil and Thailand, studies with traditional birth attendants (TBAs) and village health workers (VHWs) are providing program-relevant information to increase their effectiveness in providing services in areas where the number of physicians is limited. Also supported was a secondary analysis of data collected in India to show the impact of birth spacing on the health and survival of children.

a) Brazil: Obstetric Care in the Northeast

The great majority of the world's maternal deaths occur in developing countries and the majority of these deaths involve deliveries attended by TBAs. The program of the Maternidade Escola Assis Chateaubriand (MEAC) directed by the late Dr. Galba Araujo has been unusually innovative and effective in training and supervising TBAs to ensure safe deliveries.

This study obtains information on the referral and deliveries of all TBAs working in a rural area of the State of Ceara and the survival status of infants over an 18-month period.

Data collection was initiated in May 1984 and for one year, questionnaires on home and hospital deliveries were completed for all residents for the county of Trairi. During the study period, 1,692 births were reported.

Of the 1,198 women attended by TBAs, 13% were referred. Referral was higher for women 35 or older and for primiparas. Also, women with at least three years of education were more likely to be referred. Referral was also higher for women who had antenatal care, some antenatal pathology or a suspected malpresentation.

Follow-ups are being conducted at six weeks, six months, one year and 18 months to determine the infant and mother's survival status, feeding practices and contraceptive use. All babies but seven have at least one follow-up form. When a child dies, a physician interviews the mother to determine the cause of death. Records for 125 infants who died have been collected. Half of those infant deaths appear to be linked to diarrhea and dehydration.

As one might expect, higher neonatal and perinatal mortality rates were observed among the patients referred to the hospitals than among the infants delivered at home. The stillbirth rate for the 1,211 births delivered at home or referred was 36 per 1,000 births; perinatal mortality was 53 and neonatal mortality was 27.

Although not statistically significant, mortality was lower for babies of primiparous women who delivered at the hospital than at home and for women with a malpresentation or complication of labor at the hospital than at home. Reporting problems may have reduced the statistical significance of hospital intervention.

The training and use of TBAs in conjunction with a medically-oriented system of maternity care and the review of causes of infant deaths is

an innovative accomplishment that will attract study and attention as an example for other parts of the world.

A paper on this study, "Delivery and Pregnancy Outcomes in a Rural Community in Northeast Brazil", was presented at the 1986 APHA meeting.

b) Thailand: Follow-up of Infants in Sukhothai Province

By providing information on the rate of infant and early child mortality and the factors associated with survival, this study will provide the Ministry of Public Health in Thailand with information useful for designing programs to reduce mortality and promote contraception.

Data on all infants included in a study of obstetric deliveries in Sukhothai Province, in north central Thailand, are being collected at 1, 3, 6, 9, 12 and 18 months after delivery. An infant monitoring form, completed by a Village Health Volunteer (VHV), provides information on pregnancy and contraceptive status of the mother, infant and child mortality, and infant feeding and weight if the child is alive. If the child has died, an Auxiliary Nurse Midwife (ANM) from a health center interviews the mother concerning symptoms the infant experienced, medical help received, medication used, infant feeding patterns and immunizations. Funding covers the design of data collection instruments, the collection of data, analysis, preparation of report and papers, and dissemination of information.

Data collection began in April 1985. It is evident from examining preliminary data that not all births have been included in the study population. Before the data can be analyzed, a more accurate count of births needs to be done. This activity is now being carried out by the Thailand Fertility Research Association (TFRA).

Current plans call for a TFRA staff member to visit FHI in FY 87 to analyze data from the admission record and at least one follow-up.

c) India: Birth Spacing and Infant Growth

This project supported secondary data analysis done by Professor Ron Gray of Johns Hopkins University using data from the Narangwal Project. Anthropometric and pregnancy history data were utilized to examine the association between intervals preceding and succeeding the birth of 2,442 index children and their subsequent growth in weight and height. Subjects were followed prospectively to age 36 months. As subjects entered observation at different ages, a separate analysis was applied to a cohort with recorded birthweight. To preclude confounding of the intervals by adverse pregnancy outcome of the preceding sibling or of the index child, intervals analyzed were selected for survivorship.

Short (≤ 17 months) preceding intervals were associated with increased risk of low birthweight, particularly among males, and with persistent, though small, weight deficits through age 36 months. In

general, significantly increased mean weight increment was associated with longer (≥ 36 months) preceding intervals.

For succeeding intervals, risk of malnutrition was examined for each age of the index child by whether or not the mother had conceived the succeeding sibling. Short succeeding interval length was not associated with any marked weight or height deficits. Results suggest, however, that first born index children may be more vulnerable to the effects of an early subsequent conception. Further, the combined effect of short pre-and post-intervals is to put the index child at increased risk of malnutrition.

Throughout this analysis, the small number of index children with short preceding or succeeding intervals made difficult the task of demonstrating a statistically significant association between adverse birth spacing pattern and poor growth of the child. Consequently, what the investigators have observed is probably not a major public health problem in this population.

d) Egypt: Extent and Attitude Toward Female Circumcision

Circumcision is a common surgical procedure performed on young females in some African societies, the Arabian peninsula and parts of Malaysia and Indonesia. In Egypt, recent studies have indicated a comparatively high prevalence, particularly among less-educated women.

Egyptian clinicians feel that circumcision may be the most frequently practiced surgical intervention on females in that country. Even when done under antiseptic conditions by trained medical practitioners, it can be associated with physical, psychological and sexual complications. In order to assess attitudes toward and complications resulting from female circumcision in Egypt, sample surveys of both circumcised and non-circumcised women were undertaken at Ain Shams University, Cairo, under the direction of Dr. Maher Mahran.

During the period covered by this report, data from these surveys were analyzed by FHI, and requested tabulations prepared for and sent to the study consultant, Dr. Laila Kafafi, in Cairo. A report on the findings of the surveys, and their implications for the reproductive health of Egyptian women, will be prepared during FY 87.

Future Plans: Family Planning Evaluation and Maternal and Child Health/Family Planning

FY 87 will be a period of reordering the goals of the Program Evaluation Department's work in reproductive health. Both governmental support for and individual interest in family planning have been increasing in many African countries, so that there is less need to undertake studies designed to sensitize policymakers to the need to introduce contraception. On the other hand, as family planning programs become established, new needs arise for the evaluation of their activities in order to make them as culturally acceptable and effective as possible within the limited resources

available. Below are listed several new areas the Program Evaluation Division will be pursuing in the coming year.

1. Long-Acting Steroids

Several studies focusing on both the demand and the supply side of the market are planned. In order to make decisions about where to put resources when developing new methods of contraception, it is important to know what users want. Do they want an injectable to protect them for a month or an implant that will provide protection for several years? Clinic-based surveys will be carried out to provide this information. In one possible design, potential users of long-acting steroids will view a presentation of different methods, possibly a slide-tape show, at the conclusion of which they will be interviewed concerning their preferences.

Use of contraception is also influenced by the methods that providers think are the best ones since they are likely to influence consumers to choose what they think is best. Studies will be carried out to determine, for the various long-acting steroids in development, which methods the providers think have the best market potential. One possible approach is to develop presentations for providers which inform them about the new technologies and then question the providers about their assessments of the potential of the method among their clients.

NORPLANT[®] pre-introductory clinical trials are now being conducted throughout the developing world. Questions concerning acceptability, counseling, management of side effects and removal in the case of dissatisfaction need to be addressed. FHI anticipates starting several studies to address these issues. Funding through a PIO/T will be used to conduct a study in Bangladesh and it is anticipated that this will be the first country in which programmatic issues in the delivery of NORPLANT[®] will be addressed. If funding through other Missions becomes available, additional studies will be started.

2. Pill Compliance

FHI has initiated one study of pill compliance and continuation in Colombia and is seeking other sites to replicate and extend this study. This new study design is increasing the scope of previous studies by looking at reasons for and implications of non-compliance. Although not all the studies will be identical, the studies will have combinations of three components: focus groups to examine the general knowledge and perceptions of users and discontinuers of OCs; interviews with acceptors to ascertain their perceptions about the method and their pill-taking behavior and, where possible, objective recording of use; and interviews with providers to determine their knowledge of OCs, delivery practices, and strategies to increase method acceptability and compliance. An FHI consultant is also trying to develop a simple device which automatically records when a pill is removed from the packet.

3. Thailand: Macro and Micro-Economic Aspects of FP Use

FHI received funds from the AID Administrator's Office, PPC, to support research on whether rapid fertility decline has resulted in economic benefits for Thai families and for the national economy. Two proposals have been received and are under review. One describes a study to be conducted by the Institute for Population Studies at Chulalongkorn University with the technical assistance of Dr. John Knodel. Using qualitative and quantitative approaches, it would try to assess whether Thai families who have limited themselves to two children feel they have benefitted economically compared to families with four or more children. The second proposal came from the Thailand Development Research Institute. This project has three components: household component (secondary analysis of fertility, family planning and economic data), demographic projections of population sizes if fertility had not declined rapidly, and computer modeling of the Thai economy using different population growth scenarios. FHI plans to hold a workshop, probably in early 1987 to review these proposals and to "brainstorm" on research needs and strategies on this important topic.

4. Kenya: Project Development

A number of projects in Kenya which would involve the Program Evaluation Department have been proposed. These would be funded through a PIO/T with AID/Nairobi. Some cost sharing arrangement would be made ranging from bilateral payment of field costs to full payment of all FHI costs. An arrangement has not yet been worked out, so projects to be funded have not yet started.

5. Bangladesh Projects

Through a buy-in from the USAID Mission in Dhaka, FHI has received funding which includes Program Evaluation studies in Bangladesh. A project development visit will be made in early FY 87 to assess what studies are needed and to work with the Bangladesh Fertility Research Programme (BFRP) on possible designs.

6. Honduras: Social Marketing of Condoms

As noted above, with support from AID/Tegucigalpa, a survey of buyers of orals in pharmacies in Honduras was carried out. ASHONPLAFA has asked FHI to be involved in a similar project but focusing on condoms. The social marketing program (under the auspices of ASHONPLAFA) recently introduced the condom, called Guardian. The survey would provide data - the characteristics of buyers of Guardian as compared to other condoms and on whether the program is attracting new users, and the main reasons for purchasing condoms instead of another method because they reduce the risk of STDs, they are convenient, etc.

7. Africa: Reasons for Discontinuation of Contraceptive Use

In recent years, substantial efforts have been made to enroll new acceptors in government and privately supported family planning programs in developing countries. Some of these efforts have been successful. However, many women who receive a temporary method such as oral contraceptives following an initial screening and counseling

visit do not return for resupply. In the absence of community-level outreach programs, program managers are unable to learn the causes of poor compliance and discontinuation.

FHI is currently developing studies of Contraceptive Users and Dropout Characteristics in Senegal and Zaire, using local mission funding. Collaborating organizations are the Projet Sante Familiale in Dakar, and the Bureau National du Recensement in Senegal. In Zaire, the collaborating organizations would be Tulane University and the Comite National des Naisances Desirables (CNND).

Of particular interest in these studies will be factors which can be influenced by the counseling given to clinic clients or to the general population as part of Information, Education and Communication (IE&C) activities.

C. Natural Family Planning/Breastfeeding (NFP/BF)

FHI initiated studies in natural family planning with the creation of a NFP research unit in 1982-1983. The NFP Advisory Committee, meeting for the third time in the Spring of 1986, has played an important role in assessing needs and setting research priorities. To forge a better integration of NFP with FHI's research activities on other methods of family planning, an NFP/BF unit was established in 1985 as one of three units in the newly-created Program Evaluation Department. By 1985, the FHI NFP/Breastfeeding program had become the largest single research program of its kind in the AID portfolio.

In 1986, FHI has continued to support basic research, programmatic research, and surveys on the use-effectiveness of natural family planning methods in the general population. The vaginal aspiration technique FHI pioneered with Dr. Schumacher continues to be tested by other groups and FHI is continuing the development of Home Assay Kits with Dr. Brown. FHI's programmatic research creates awareness about the function, acceptability and potential impact of NFP programs. Considerable emphasis is also put on the dissemination of findings. Many of the NFP/Breastfeeding activities are being coordinated with the AID funded NFP project at Georgetown University, Washington, DC.

FHI's work in NFP/BF is guided by the conviction that no single method of family planning is socially, culturally or psychologically acceptable to all couples wanting to control their fertility. No method of family planning is "perfect". Therefore, a cafeteria approach to family planning, in which NFP is one of the methods

available, is desirable to provide choices for couples making decisions concerning fertility control. FHI encourages family planning agencies and organizations to incorporate NFP into their standard programs. At the same time, FHI believes that those practicing NFP have the right to information about or referral to other methods of family planning. FHI believes that NFP should be promoted on its own merit rather than emphasizing the disadvantages of other methods of family planning. FHI has been working closely with programs offering NFP only as well as multi-method programs.

FHI has long recognized the importance of breastfeeding as a natural method of child spacing. In many developing countries, breastfeeding prevents more pregnancies than all other forms of contraception combined. This is in addition to the nutritional and protective health benefits breastfeeding provides for infants. There is, however, evidence of declining duration of breastfeeding among particular groups of women in developing countries. Some countries may have to increase contraceptive use just to keep fertility constant, if breastfeeding continues to decline. FHI's work is directed toward measuring the child spacing effects of breastfeeding as well as studying ways to enhance this effect.

NFP Advisory Committee:

The NFP/BF Advisory Committee met for the third time 21-22 April 1986 at FHI. Special attention was given to completed and ongoing breastfeeding research and on reviewing a strategy for future research in breastfeeding as a child spacing method.

1. Research to Improve NFP Methods

a) Canada: Study of the Relationship of Cervical Characteristics to Mucus and Temperature Symptoms among Experienced NFP Users

With FHI support, SERENA Canada conducted a secondary analysis of NFP charts of women experienced in cervical self-examination. The analysis addresses the temporal relationship between the cervical changes found by self-examination and the vulvar mucus and waking temperature signs at the end of the cycle's fertile phase. The findings demonstrate that cervical changes are good indicators of the actions of estrogen and progesterone since they correspond well with the peak mucus symptom and temperature shift. Fairly large intra-woman variations were observed which may be the effect of a learning curve. Comparisons between women above and below 40 years suggest that the cervical signs are not impaired with age. The final report is available and publication is planned.

b) US: Secondary Analysis of Chilean Data on NFP and Breastfeeding

Dr. Alfredo Perez has gathered data on more than 400 breastfeeding women in Santiago, Chile who practiced the Billings Method. These data are being analyzed by Dr. Miriam Lubbok at Johns Hopkins University. She is exploring the associations of signs and symptoms of NFP with infant feeding behaviors. This analysis should help refine the role of NFP symptoms in lactating women and their value in predicting the return of fertility. Information on the efficacy of

the Billings Method in this special population will also be obtained. Publications of the results should be of interest to the NFP community, lactating women and family planning professionals.

c) Multi-Center: Study of NFP Use by Breastfeeding Women in Selected Countries

FHI initiated the first setting of a multi-center study of NFP use among breastfeeding women with SERENA, Canada. During the reporting period, Drs. Suzanne Parenteau-Carreau, Anna Flynn and Barbara Gross, the Principal Investigators, met at FHI to finalize the protocol and obtain consensus on the operational definitions to be utilized during data collection and analysis.

Breastfeeding mothers who are experienced NFP users are recording their mucus symptoms, basal body temperature, cervical position (in some cases), and infant feeding information on a daily basis. Daily urine samples and serial ultrasonography (in some cases) will reveal the time of onset of ovarian follicular activity and first postpartum ovulation. The data analysis will be oriented toward finding the simplest NFP rules to predict the onset of fertility in the breastfeeding women, and to determine the role of breastfeeding in the occurrence of the NFP symptoms. The two other sites (Birmingham Maternity Hospital, United Kingdom and Westmead Hospital, Australia) were initiated by mid-1986 with support from the Institute for International Studies in NFP at Georgetown University.

d) Australia: Development of Home Assay Kits for NFP Users

FHI is providing core support to Professor James Brown at the University of Melbourne for the purpose of manufacturing and field testing enzyme immunoassay home test kits for predicting and detecting ovulation. In this project, the kit will be made available to normally cycling NFP users and to women whose mucus patterns are difficult to interpret (e.g., breastfeeding and pre-menopausal women) and to teachers while they are instructing new clients. The kits are intended to improve a couple's confidence while learning and using NFP, as well as to improve the effectiveness of NFP. The current subagreement supports the manufacture of a prototype spectrophotometer adapted for home use, and includes designing and creating the die from which at least the next 50 meters will be produced.

2. Evaluation of NFP Service Programs

a) Peru: Introduction and Evaluation of an NFP Project in Lima

This project is designed to provide answers on how much effort, in human and financial resources, is required to set up a NFP service program in a developing country and how many people, at what cost, will use such a service and with what effectiveness.

A total of 278 couples were enrolled in NFP instruction through the Asociacion de Trabajo Laico Familiar (ATLF) by the end of the recruitment phase. A total of 4,979 people attended information meetings about the NFP service during the recruitment period. These

meetings typically included about 15-20 couples each. The enrollment period is now finished, as well as the instruction period, and all couples are either in active follow-up, have completed a 12 cycle follow-up, or have discontinued. Fifty-eight percent of the enrolled couples have discontinued, about one-half during the early part of the training period.

Several important findings have emerged; the following six factors were positively associated with the likelihood of remaining in the program:

- . age of the woman
- . length of marriage
- . number of living children
- . age of youngest child
- . amount of participation of male partner in learning and using the method
- . the woman (or couple) was recruited as part of a group (e.g., woman's club) rather than as an individual.

The educational level of the couples in the study was concentrated at the primary school and secondary school years of completion. But those who completed only primary school had a greater likelihood of staying in the NFP program than those who completed both primary and secondary school. The median income of those who are currently in the program was slightly greater than those who discontinued.

An admission report has been completed. Training summary data and initial discontinuation data are loaded and cleaned. Data from the final follow-up interviews will be sent to FHI by the end of the year. A site visit by Dr. Harrison McKay, FHI Consultant, took place in September 1986 and a status report on the project was submitted by him to FHI.

b) Bangladesh: CARITAS Service Statistics Project

FHI supported a project to analyze service statistics of the CARITAS (a voluntary Catholic social service organization) NFP program in Bangladesh. Since 1976, CARITAS has provided training to, and collected data from, 2,453 eligible women in 13 districts of the country. The NFP program has 29 centers including one in Dhaka. FHI provided support to a local research agency, the B-SMERT Corporation, to process the service statistics and to assist CARITAS in improving the service statistics system. The results showed that most of the clients were new users of contraception. While in the initial years most of the users were of Catholic origin, the proportion of non-Catholics increased in recent years. About one-third of the total users were illiterates and had an average of four children living. Results from this contract were presented at the International Federation for Family Life Promotion (IFFLP) Meeting in Ottawa in June 1986. Perhaps the most significant contribution of this project was to help CARITAS set up an efficient data recording system.

c) Egypt: Evaluation of a NFP Program

A small retrospective study was undertaken in Egypt to examine the characteristics of those who entered a Billings program to determine which couples completed the six month training period and used the method successfully and which couples did not. In this project, procedures were developed for locating and interviewing people trained in the past to determine the feasibility of research in continuation and effectiveness rates. A description of couples already trained was compiled and stratified according to the couple's family planning intentions and the incidence of pregnancy. The final report of this project has been submitted to FHI and a publication is being prepared.

d) India: Technical Assistance to Develop a Training Plan for the Indian Council of Medical Research Project: Multicenter Field Trial of Billings Ovulation Method

FHI supported the consultancy of Dr. Mary Thormann to prepare a research training plan for a NFP study. The study itself will identify, recruit, and enroll a minimum of 500 couples (and preferably 700) who meet selection criteria in each of six study centers - located in Dindigul (Tamil Nadu), Bangalore, Jaipur (2), Kanpur, and Patna. The study will be a prospective two-year investigation of the acceptability and use-effectiveness of the Billings Ovulation Method and determination of its feasibility for use in a developing country. The principal co-investigators will be Drs. Catherine Bernard, Badri Saxena, Indian Council of Medical

Research (ICMR), and Mr. R. N. Gupta (ICMR). Dr. Thormann submitted a copy of the training plan to FHI.

e) US: Analysis of Baseline and Follow-up Data from NFP Programs in Five Countries

The purpose of this study was twofold: 1) to analyze baseline socio-demographic data on natural family planning acceptors in five countries and 2) to assess continuation and use-effectiveness among these acceptors. Reports on these data have been prepared. They provide a better understanding of the associations between socio-demographic variables and NFP use and continuation, and allow international comparison of five programs (in the US, Kenya, India, Korea and Bangladesh). Data on approximately 200 consecutive NFP acceptors in Billings Ovulation method programs in each of these countries were analyzed by Dr. Miriam Labbok of the Department of Population Dynamics, the Johns Hopkins University.

Dr. Hanna Klaus initiated the study and data collection while the Johns Hopkins University was responsible for data analysis and write up. Preliminary results were presented at the Ottawa IFFLP Congress in June 1986. Data from India and the US were inadequate to make any assessment of pregnancy. The data from Bangladesh, Kenya and Korea show that higher education was associated with lower pregnancy rates controlling for both age and country. Previous pill use was associated with lower pregnancy rates even when the same controls were applied.

f) Kenya: Evaluation of Two NFP Programs and Technical Assistance

Two NFP studies in Kenya were initiated in July 1986. The first project in Nyeri/Othaya District will: (1) investigate the similarities and differences of long- and short-term users of the Ovulation Method, (2) assess the efficacy of methods practiced among long-term users and, (3) examine economic, demographic and socio-psychological motivational factors associated with low and high degrees of efficacy of NFP methods practiced in Kenya.

The second project is being carried out in Meru Province, a district with a population of nearly one million. NFP was introduced and has been actively pursued under the auspices of the Diocese of Meru. Kenya Catholic Secretariat (KCS) has prepared a list of 1000 couples who have been trained in NFP (mostly OM), 450 of whom are believed to be continuing users. The project involves a baseline survey and follow-up of continuing users to determine the efficacy of the method practiced.

About 550 and 1,000 NFP ever-user women will be interviewed in Nyeri and Meru, respectively. The field work, which is currently underway, is expected to be completed in mid-December. Data analysis will begin in March 1987.

FHI continues to provide limited technical assistance for the Pathfinder Fund supported NFP project in Kenya. The project introduced NFP educational services at the Kenyatta National Hospital and seven Maternity hospitals. This project is undertaken in

collaboration with the Kenya Medical Research Institute in Nairobi. It is the first time NFP services have been offered as part of family planning service delivery in Kenyan Government hospitals. The project has trained nurses in these national hospitals in NFP teaching methods.

g) Mexico: Prospective Study of the Use Effectiveness and Continuation Rate of the Ovulation Method of Natural Family Planning in Metropolitan Mexico City

There has been a lack of objective information on the use effectiveness of natural family planning (NFP) in Mexico. It has been recognized that there are some Mexican women of childbearing age who, for a variety of reasons, consider themselves unable to use available contraceptive methods but who might employ a modern natural family planning method if it were shown to be effective. The lack of scientific data on NFP in Mexico has allowed biases to develop that have limited access to NFP for women who might elect NFP as a method of fertility control.

This subcontract funds a prospective study of the use effectiveness of the Ovulation Method/Natural Family Planning (OM/NFP) as it is taught by the Centro de Enseñanza e Investigación de la Planeación Natural de la Familia (CEIPLAN). The study will measure use effectiveness and continuation rates among women attracted to NFP in Mexico City. An effort will also be made to evaluate the impact of undesired pregnancies on users of the method, with respect to their future use of the method, the outcomes of the pregnancies, and user's attitude toward the pregnancies. In addition, the study will attempt to identify

reasons for dropping out of training and the successful or unsuccessful use of the NFP method. The study will enroll 500 couples in the training phase with the goal of having 350 couples entering the use effectiveness phase. After receiving training and achieving "autonomous status", couples will be followed for 13 menstrual cycles to assess the effectiveness of the method, and the rate of continuation of its use.

h) Mexico: Scientific Consulting to the CEIPLAN Prospective Use Effectiveness Study of NFP in Mexico City

The Academia Mexicana de Investigacion en Demografia Medica (AMIDEM) will provide an ongoing consultancy throughout the course of the above prospective use effectiveness study of NFP in Mexico City. AMIDEM is a research organization that enjoys scientific credibility in the field of human reproduction and maintains very extensive links with national family planning policymakers in Mexico. The scientific consulting provided by AMIDEM will facilitate the potential for policy impact and assure the scientific credibility of the prospective use effectiveness study.

The project will begin recruitment of patients during the first quarter of FY 87.

i) Nepal: Technical Assistance to SATA and FPA NFP Projects

With assistance from the Swiss Association for Technical Assistance (SATA), the Ministry of Health of the Government of Nepal initiated a

small NFP project in a rural district in the early 1980s. The NFP project was implemented as part of the Integrated Hill Development Project.

By mid-1985, about 700 acceptors had been taught the use of the Dorairaj NFP approach. The life-table annual failure rate was about 8%. This rather low failure rate is suspected to be associated with relatively older women practicing the method. FHI has provided limited technical assistance to this study.

The Family Planning Association of Nepal has recently initiated an NFP project as part of its delivery of other family planning services. If requested and if funds are available, FHI will provide assistance with data analysis.

j) US: Development of NFP Evaluation Forms

With the Johns Hopkins University and IFFLP, FHI is developing simplified forms and manuals to evaluate pre-existing as well as new NFP programs. The form to be used for the evaluation of a pre-existing program includes screening, teaching, use-effectiveness and discontinuation items. This instrument will permit the efficient evaluation of retrospective data.

A second set of forms is being developed for new NFP programs. This set includes four instruments, one each to measure acceptability, teaching, use-effectiveness and discontinuation. These forms are designed for prospective data collection.

The forms were reviewed at the Ottawa NFP Research Workshop. FHI plans eventually to have the forms and manuals available in three languages (English, Spanish, and French) and to develop a micro-computer package to process the forms and produce a set of standard tables.

k) NFP Research Methodology Workshop

As recommended by the NFP Advisory Committee, FHI sponsored a NFP Research Methods Workshop as part of the 4th World Congress of the International Federation for Family Life Promotion (IFFLP) in Ottawa, Canada, 23 June - 3 July 1986. The objective of the workshop was to create a pool of NFP program managers who are capable of identifying potential NFP research areas in their respective countries and are able to work with funding and technical assistance agencies in designing and carrying out NFP research projects. The workshop, which was co-sponsored by FHI, IFFLP, WHO and the Johns Hopkins University, was attended by 22 participants from 17 countries.

l) Indonesia: NFP Study (Three NFP Approaches)

A prospective multicenter trial of three NFP methods in Indonesia was initiated in July 1986. The main objective of this project is to evaluate the teaching, learning and use-effectiveness of three NFP approaches: 1) the Ovulation (Billings) Method, 2) the modified mucus method and 3) a mix of the two methods. The project is carried out in five locations in Indonesia where there are ongoing NFP

programs. The implementing agency is PERDHAKI (Voluntary Health Services Association of Indonesia).

3. Surveys to Assess NFP Knowledge and Use

a) Multi-Center Physicians' Knowledge Attitude and Practices (KAP) Study Regarding NFP in Selected Developing Countries

Since NFP receives uneven acceptance around the world and because physicians are often the leaders of social acceptance of family planning methods, FHI supported a study which explored the knowledge, attitudes and behavioral intentions of physicians toward NFP. This KAP study was implemented by the Institute for Population Studies at the University of Exeter, UK and took place in Mauritius, Peru, the Philippines and Sri Lanka.

In-country principal investigators (PIs) conducted pilot interviews or focus groups with small numbers of providers. Then they attended a meeting at Exeter with Institute staff and designed a cross-cultural KAP questionnaire based on those interviews. Quota samples of 100 suitable respondents were selected within each country and interviews were conducted by the PIs. They prepared summary reports of the results and reconvened to refine their country's reports. At this second meeting, they prepared a cross-cultural report and finalized a model questionnaire that can serve as a tool for subsequent researchers in other countries.

The findings suggest that the amount of NFP knowledge a physician has and the physician's overall attitude toward a particular method (i.e., whether a method is good, useful or scientifically sound) can predict a physician's willingness to provide services, seek information, and in essence, encourage his/her patients to use (or not use) a method. Knowledge and the religiosity of the physician were particularly important in the Philippines. The findings of the study were presented at the IFFLP World Congress in June 1986. The Institute for Population studies has submitted to FHI four country reports, the summary report, the review of the literature, the guidelines for the data analysis and report writing and the revised final questionnaire. Several papers for publications are in preparation.

b) Sri Lanka: Traditional Contraceptive Survey

In several countries, the untutored use of the "rhythm" method and "traditional" methods of family planning is widespread. Between 1976 and 1981, the proportion of contraceptive users using these "non-program" methods increased from approximately 15% to more than 25% in Sri Lanka. This increase has generated a high degree of curiosity among family planning program managers and policymakers in Sri Lanka. In order to determine whether these practices have a demographic impact, and whether they suggest a latent demand for NFP services, FHI is currently supporting two family planning survey projects in Sri Lanka.

The first project, with the Department of Census and Statistics, involved following up a national sample (both urban and rural) from the 1982 Contraceptive Prevalence Survey. The basic purpose was to investigate the reasons for the increase in the use of "non-program" methods. The first part of the project, which involved in-depth interviews to identify local and folk expressions used to refer to "non-program" methods of family planning, is completed. A paper based on this work has been submitted to Studies in Family Planning. The findings of the first phase were utilized to develop the survey questionnaire.

Survey fieldwork began in early March 1985 and was completed in May 1985. More than 2,300 women of reproductive age and 577 of their husbands were interviewed. A seminar to highlight preliminary findings of the study was held in May 1986. The final report is currently under preparation and review and is expected to be printed in early 1987. The report includes eight chapters covering such topics as knowledge and misconceptions about modern and traditional family planning methods, contraceptive use, switching and discontinuation, and husband and wife communication and decision-making in family planning matters.

c) Sri Lanka: Rural Family Planning Survey

The Family Planning Association of Sri Lanka (FPASL) has completed the field work for the Rural Family Planning Survey which measures the use-effectiveness of various family planning methods, including traditional and natural methods. A newly developed methodology uses

retrospective data (up to three years preceding the survey date) to estimate use-effectiveness of each family planning method (individual as well as combined methods). Approximately 3,300 rural women were interviewed. Community level data were also collected.

The data are being analyzed both at FHI and at the FPASL. The preliminary findings show that while the correct knowledge about the fertile and infertile phases in the menstrual cycle is low, over two-thirds of the women using a natural method were found to have used more than one method at a time. The survey has collected very high quality data. Several important papers are expected to be produced based on this survey.

d) Sri Lanka: Trends in Natural Family Planning Use

A significant and unexpected rise in current use of traditional contraception among currently married women of childbearing age was observed from results of the 1975 World Fertility Survey and the 1982 Contraceptive Prevalence Survey conducted in Sri Lanka. FHI supported a project with the Carolina Population Center of the University of North Carolina at Chapel Hill to investigate possible factors that led to the apparent increase in the prevalence. The analysis examined the effects of survey differences on measurement of fertility control and changes in the components of traditional contraceptive use--marriage, pregnancy exposure, overall use, and method choice. In particular, delayed marriage patterns over this period were hypothesized to alter the marital duration composition of the 1982 sample, thereby influencing the type of family limitation

practices. The large increases in traditional contraceptive use observed among those subgroups composed predominantly of newly married women became only small or moderate when standardized by marital duration. Decomposition analysis indicated that increased fertility control among women at risk of pregnancy, as opposed to preference for traditional over modern methods, accounted for the bulk of the observed rise. The report concluded that the rise in traditional contraceptive use was due to compositional changes in its components as well as measurement differences between surveys.

A second set of analyses will examine determinants of natural method use in the 1982 survey using a multinomial logit model where the probability of using a natural versus modern method is modelled as a function of various background and motivational variables. This will enable a closer investigation of the factors influencing some women to use traditional as opposed to "modern methods", including the role of birthspacing motives.

Two papers based on this project are planned to be submitted for presentation at professional meetings and for publication.

e) NFP Review Paper

At the request of the Demographic Data for Development (DDD) Project of Westinghouse Health Systems, FHI prepared a monograph entitled Periodic Abstinence in Developing Countries: Update and Policy Options. The paper contains new information on prevalence levels of periodic abstinence methods, use-effectiveness and psychosocial

issues. A final section describes program and policy considerations for family planning policymakers and program managers in developing countries. A description of selected countries where periodic abstinence is popular is appended. The monograph was published by the DDD Project of Westinghouse in June 1986. It was widely reviewed and should make a major contribution to information dissemination about periodic abstinence. About 500 copies were distributed at the IFFLP meeting in Ottawa in June 1986. Additional copies were produced and distributed by Westinghouse in the Fall of 1986.

4. Breastfeeding Studies

Family planning programs have given insufficient attention to breastfeeding, which is a major means of birth spacing in many developing countries. It is both a natural method of birth spacing and highly significant to the welfare of the infant. FHI's research addresses the birth spacing effect of breastfeeding and how it can be maximized.

a) US: Breastfeeding Trends in Developing Countries

Despite the widespread impression that breastfeeding is plummeting throughout the developing world, there is remarkably little research on breastfeeding trends: FHI is supporting a project, being carried out at Brown University, to analyze breastfeeding trends over the last decade in selected developing countries.

A set of sixteen developing countries was identified in which at least two nationally representative surveys in the last decade gathered comparable information on breastfeeding and other aspects of reproductive behavior. These surveys cover a diverse set of nations in three continents. In each case, the first of the pair of surveys is part of the World Fertility Survey and the second is a Contraceptive Prevalence Survey. Comparable data from the two time points can be used to establish the feeding patterns in effect in each country at those times.

Dr. Sara Millman, Principal Investigator of the study, presented findings from 12 developing countries at the IFFLP Congress in Ottawa, 23 June-2 July 1986. Declines in breastfeeding were evident in five countries (Thailand, Taiwan, Panama, Korea and Malaysia). Three countries showed no change (Mexico, Dominican Republic, and Sri Lanka) while four showed increases in breastfeeding (Guatemala, Jamaica, Jordan, and Singapore). Further analysis of the data is underway.

b) Philippines: Infant Feeding Trends

This project supported secondary analysis of breastfeeding data from two surveys conducted over a ten-year period in the Philippines. Results showed the proportion of women who breastfed declined by five percentage points over the period 1973-83. The mean age of the infant at which breastfeeding ceased increased slightly. Most increases or decreases in the duration of breastfeeding were seen during the second year of the infant's life.

The declines in the proportion ever breastfed occurred mainly because of factors associated with social change, namely increased education, electrification and urbanization, and a reduced number of jobs in the traditional sector. Increases in the length of breastfeeding among those who ever breastfed were the net result of two conflicting patterns. Increased urbanization, shifts in the occupational composition of women, and residence in Mindanao (the center of extensive social unrest during this period) were associated with decreased duration, while there was a large and unexplained effect resulting from structural-behaviorial factors which was associated with a large increase in duration of breastfeeding. A paper for policymakers has been prepared by the principal investigator, Dr. Barry Popkin, and is under revision.

c) Multi-Center Longitudinal Study of Breastfeeding and Return to Fertility in Selected Developing Countries

This study follows a small group of breastfeeding women from delivery through ovulation and compares them to non-breastfeeding controls to determine the effect of breastfeeding patterns on the timing of ovulation. The aim is to provide guidelines that individual women can follow to determine when to initiate another family planning method.

Centers in four countries are involved in this study. Pramongkutkiao Hospital in Bangkok, Thailand and the Instituto de Investigacion Cientifica in Durango, Mexico have completed the study, and several

findings appear below. Data from the Assiut University Hospital have been collected and are being queried at this time. Data collection is in progress at the National Research Institute for Fertility Control in Karachi, Pakistan.

The data from Mexico and Thailand have clearly documented the contraceptive effects of breastfeeding, and in particular the effect of breastfeeding frequency. The frequency of breastfeeding per day, night and 24 hours was similar in both sets of women during the week of the first ovulation (i.e. a mean of nine breastfeeding episodes per 24 hours with a range of 0-15 episodes). This similarity of breastfeeding frequency occurred despite the great difference in median duration until first ovulation, at five months in Mexico and nine months in Thailand.

Similarly, small proportions of women in both settings ovulated prior to all three of these events: the initiation of supplementation, vaginal bleeding or menses, and the three-month birthday of the child. Some of the early ovulations observed probably had defective luteal phases, and so the risk of conception before any of these three events is very low. Among the controls, under comparable conditions, 40-50% were ovulatory.

A series of reports and publications from this study is being prepared. The first paper from the Mexico data, "Preliminary Observations on the Return of Ovarian Function among Breastfeeding and Postpartum non-Breastfeeding Women in a Rural Area of Mexico" was published in the Journal of Biosocial Science Supplement in late

1985. The second paper from this data, "Breastfeeding and the Return to Ovulation in Durango, Mexico" is in final preparation for submission to the American Journal of Obstetrics and Gynaecology. The third and fourth papers to come out of this study are in the data analysis stage.

d) Philippines: Effect of an Education Program on Breastfeeding Practices and Duration of Postpartum Amenorrhea in a Rural Area

FHI is supporting a prospective study with Silliman University in Dumaguete, Philippines, in which pregnant women are being taught guidelines for maximizing the nutritional and contraceptive benefits of breastfeeding. A control group of mothers not exposed to such teaching is also being monitored. The duration of postpartum amenorrhea and patterns of infant feeding will be compared between the group receiving the educational program and the control group. During this reporting period, the education program was designed, data collection instruments were pre-tested, staff were trained, pregnant women were recruited, and study subjects were instructed and followed up. The study team has developed and tested educational modules on breastfeeding practices that may enhance the postponement of a menses such as breastfeeding on demand, breastfeeding at night, etc. They have printed attractive posters and other materials. Monthly follow-up data are being collected at this time. All 135 study subjects were recruited and half have completed followed up, having experienced two postpartum menses.

e) Indonesia: Breastfeeding and the Modern Health Sector

The purpose of this project was to collect information to assist hospital administrators and perinatal care providers (i.e., obstetricians, pediatricians, nutritionists, nurse-midwives and nurses) to establish a "rooming-in" system throughout all hospitals in Indonesia. The project identified the nature and extent of needs, problems and obstacles related to implementing a new policy for rooming-in. The specific objectives were: to assess the attitudes about breastfeeding and rooming-in and knowledge about the infant health and contraceptive effects of breastfeeding, of perinatal care providers, hospital administrators and mothers who enter hospitals for delivery; and to investigate the current hospital policies and practices regarding rooming-in and infant feeding.

Three papers based on the results of the study were presented at the Conference of Hospital Administrators held 8-15 May 1985 in Jakarta and were well received. A set of resolutions, based on the survey findings, was passed at that conference and were recommended to the Department of Health for implementation.

Based on the needs, as assessed by this survey, the AID Mission in Jakarta has expressed interest in supporting the development of a training program for the management of breastfeeding and rooming-in in Indonesian hospitals. Study findings were also presented at the Congress of OB/GYN for Asia and the Pacific held in September in Colombo, Sri Lanka and at the World Congress of OB/GYN in Berlin,

15-21 September 1985, as well as at NFP meetings in the USA and Canada (IFFLP meeting, Ottawa).

The final report of the project was published in Jakarta in the form of a monograph. The first drafts of additional papers have been completed. FHI expects to publish them in two international journals.

f) Breastfeeding as a Child Spacing Method: A Pamphlet for Program Managers and Physicians

Many family planning managers and physicians are skeptical that breastfeeding makes a major contribution to child spacing for the individual woman. This pamphlet reviews research findings on the effectiveness of breastfeeding, compared with other methods used in the postpartum period. It reviews research that has attempted to predict returning fertility and will suggest guidelines that breastfeeding women can use to decide when they should stop relying on breastfeeding as a child spacing method. This project is being done with other organizations (the WHO, IPPF, and Georgetown University). The final version may be available by the end of 1986 with production and distribution in 1987.

Future Plans: Natural Family Planning/Breastfeeding

a) Philippines: Effectiveness of NFP in a Multi-Method Setting

The Family Planning Organization of the Philippines now provides, through its affiliate network, a variety of family planning methods for spacing and limiting family size. It has included calendar rhythm but not modern NFP methods. The organization would like to upgrade its NFP services and then compare use-effectiveness, continuation, client satisfaction, and cost effectiveness of five "temporary" methods: NFP (probably the Ovulation Method), pills, injections, spermicides and condoms. Five affiliates will enroll the first 40 acceptors of each of these five temporary methods. Clients will be followed up for one year. The current plan is for Georgetown University to fund the first part of the project, upgrading NFP services, with FHI to support the evaluation phase. Realistically, FHI's part will not start until FY 88.

b) Effect of an Education Program on Breastfeeding Practices and Duration of Postpartum Amenorrhea

A rural breastfeeding study is underway in the Philippines that is evaluating the impact of an educational program promoting intensive breastfeeding on the postpartum amenorrheic period. This study will be replicated in an urban area of the Philippines. FHI recently obtained local funding for in-country field costs in the Philippines. The urban Philippine study has been approved by AID/Manila and the Population Commission (POPCOM) and will start 1 December 1986. It

will be conducted by staff of the Philippine General Hospital with assistance of an epidemiologist from the Institute of Public Health, University of the Philippines.

VI. FIELD DEVELOPMENT AND TRAINING

The Field Development and Training Division (FDT) has as its primary objectives the development of research capabilities and skilled investigators in priority countries through training and institutional development programs; the transfer of contraceptive technology to developing countries; and the dissemination of research findings and information through publications, workshops, seminars and support for collaborating investigators to attend international conferences. A fellowship program established in 1984 enables collaborating researchers to spend several months at FHI working on a project of their choice. In addition to providing funding and staff support for these activities, FDT plays a major role in providing field support to the other research divisions, including the identification and development of projects, coordination of the field approval process through local governments and AID Missions, study monitoring as needed, and coordination of international travel.

Activities during this reporting period are separated into the following areas: institutional strengthening; training; transfer of contraceptive technology; and information dissemination.

A. Institutional Strengthening

1. Support to Family Health Research Centers (FHRCs)

Support to six maturing FHRCs and several newer organizations remains the major activity sponsored by FDT. The FHRCs vary in focus, structure, and level of development depending on the socio-political environment in each country, and on the duration of FHI involvement with these programs. FDT's goal for each of these programs is to develop competent, well-managed and securely funded institutions capable of designing and implementing research to meet a variety of needs in their own countries. The following section describes each program and the development activities underway with FHI support through a core subagreement, as well as summarizing other FHI contract activities being carried out by the FHRCs.

a) Bangladesh Fertility Research Programme (BFRP)

The Bangladesh Fertility Research Programme (BFRP) has probably the most extensive network of centers and clinical investigators of any of the Family Health Research Centers. It has historically been the primary coordinating body for clinical trials research in Bangladesh and has recently been recognized by the Ministry of Health and Family Planning as the gateway for introduction of new contraceptive methods into the country.

The BFRP was established in 1976 as a quasi-governmental research organization funded by FHI. It operates under the guidance of an

Executive Council chaired by the Secretary of the Ministry of Health and Family Planning. The BFRP coordinates a network of 35 participating hospitals, clinics, and researchers, and has a core administrative staff responsible for planning, implementing, and monitoring research.

During this reporting period, studies were underway at twelve different centers. Subcontract studies included three 200-case pre-introductory NORPLANT® trials, and a non-comparative study of the progestogen-only pill, Exluton. A comparative study of Triquilar and Marvelon was initiated; a comparative study of oral contraceptives with versus without iron will begin in November.

Studies supported under the core support subagreement included a double-blind comparative study of three oral contraceptives; two comparative studies of oral contraceptives supplemented with and without vitamins; a comparative IUD study of TCu 380A versus ML 375; two comparative studies of the Cu 200 IUD with and without vitamin supplements; and a long-term follow-up of female sterilization cases. A new study of prophylactic antibiotics with female sterilization is being designed for implementation later this year.

Dr. Halida Akhter joined the BFRP as Executive Director in February 1986, after nearly 8 months without a full-time director. Dr. Akhter immediately began to re-train the BFRP staff and upgrade their skills. An FHI biostatistician visited in May to provide an update for the staff in clinical trials research methods. A routine of weekly staff meetings and a monthly "brown bag" lunch program

featuring visiting and local experts have been initiated. A brochure describing BFRP activities and a newsletter with research news were printed, and the organization's personnel policies were updated. In September, a second deputy director (research) was hired. He and one other staff member will attend a workshop on research methods for community family planning programs in Bangkok in November-December.

During this reporting period, planning and arrangements were completed for a clinical trials research methods workshop. The workshop, to be held in early October in Cox's Bazaar, will be attended by 25 mid-level physicians who have some experience and/or interest in research. Two FHI staff will teach the course. This workshop will be the first opportunity for Bangladeshi investigators to receive formal training in research methods for clinical trials studies.

Early in FY'87, the data processing capability of the BFRP will be enhanced when a TI-351 microcomputer is installed and staff are trained by FHI experts. Many doors will open for the BFRP when it can process its own data and even contract to process data generated elsewhere. In-house data analysis will become possible for the first time, rather than having to send all data to FHI for processing. Shipment of the computer has been delayed for several months due to difficulties in obtaining clearances, but is expected in December. FHI staff will install the computer and train staff in early 1987.

b) Egyptian Fertility Care Society (EFCS)

The Egyptian Fertility Care Society (EFCS) is a voluntary organization affiliated with the Egyptian Medical Association. Founded in 1974 with a membership of over 260 medical specialists, the EFCS works closely with the Egyptian Ministry of Health (MOH), the National Population Council (NPC), the Egyptian Society of Ob/Gyn and the Egyptian Family Planning Association.

Internationally, the EFCS has maintained working relationships with FHI, WHO, PIACT, AVS, JHPIEGO, USAID and other organizations. The EFCS has been recognized by officials of the National Population Council as the research wing of the Egyptian National Population Program.

FHI began support for the EFCS in October 1980. The purpose of this ongoing support is to develop an independent research institution through training and research assistance. The current subagreement concentrates on clinical trials, information dissemination, and individual training and workshops. All projects are designed to expand knowledge of the safe, effective and acceptable usage of family planning methods; increase the knowledge and skills of the EFCS staff; and expand the research capabilities of the EFCS through the motivation and training of a large network of medical collaborators.

In order to further improve EFCS's data processing and analysis skills, FHI donated a Texas Instruments microcomputer in August 1984.

FHI has continued to provide required follow-up and training under the current subagreement.

In August 1986 the EFCS was designated by the National Population Council as the research agency to manage and coordinate a three year bilaterally funded NORPLANT® project in Egypt (see Section on Transfer of Contraceptive Technology-Egypt-NORPLANT® Support). This project will strengthen the EFCS by giving it additional experience in coordinating large scale research projects. It will assist in developing the EFCS's funding base and increase staff and computer capabilities, adding to the financial stability of the organization.

During 1985 and 1986, the EFCS conducted the following activities:

Institutional Development

- Two Clinical Trials Workshops were held in Cairo
- The Executive Director and the Program Officer attended a Family Health Research Center (FHRC) Coordination Meeting in Chiang Mai, Thailand.
- The EFCS sponsored a joint annual conference with the Egyptian Society of Gynaecology and Obstetrics in July 1986. This is a meeting of research investigators of the Ob/Gyn Society, decision makers from the Ministry of Health, the National Population Council and other interested professionals. Its purpose is to distribute information and results of clinical research studies from both Egyptian and international projects.

Research Activities

- A comparative study of the TCU 200 versus the ML 250 versus the Lippes Loop C was continued at five university hospitals. This project will be completed in February 1987.
- A maternity care monitoring study was extended to two more university hospitals and one Ministry of Health hospital

(1 January 1986 - 31 December 1987). This expansion is intended to test the feasibility of expanding maternity care monitoring to all hospitals in Egypt.

- A comparative study of the oral contraceptives Triovular® versus Ovrall® versus Nordette® involving 2,400 cases randomly assigned and divided among eight centers was initiated.

Over the same period EFCS assisted in the following projects under separate subcontracts:

- Began management and implementation of \$2.2 million, three-year multicenter NORPLANT® research projects under the overall administration of the National Population Council.
- Published a "Fertility Care Bulletin".

During the coming year the following activities are planned:

- Continuation and expansion of the MCM study at two additional university hospitals and a MOH hospital
- Continuation of the ongoing Three-way IUD study
- Continuation of the Comparative Three-way Oral Contraceptive Study (Triovular® versus Ovrall® versus Nordette®)
- Clinical Trial Workshops will be held on a yearly basis
- A MCM meeting is scheduled for December 1986 and an EFCS investigators meeting will be held in June 1987
- The Data Analyst will receive advanced training at a local university and at FHI in Spring/Summer 1987
- The Data Collection Coordinator will receive further training at FHI in early 1987
- The publication of the "Fertility Care Bulletin" will continue
- Follow-up training for staff using the microcomputer will take place in October 1986
- Development of a Five Year Plan of Operations will be finalized.

In addition to the above-listed activities, core support will indirectly support the following projects:

- The international management firm of Deloitte Haskins and Sells (DH&S) will meet at the EFCS in Cairo to assist with improving financial management
- The analysis of data from an injectable contraceptive study funded by the WHO will continue

- A comparative study of the Copper T 380A versus the Copper T 200C will continue
- Processing and analysis of data will begin for hospital deliveries at three hospitals participating in the Giza Maternal Mortality Study (under special subagreement from FHI).

With FHI support the EFCS has been able to grow as a research institute of national prominence. With greater diversification of funding and strengthened ability in financial management/planning the EFCS is making in-roads towards financial independence and institutional autonomy. The current two year agreement became effective as of 1 January 1986.

c) Indonesia Fertility Research Coordinating Board (BKS PENFIN)

Since January 1979, FHI has provided financial and technical assistance to the BKS PENFIN, a private, non-profit fertility research organization located in Bandung, Indonesia, and composed of 14 (originally 12) member centers that are Government University teaching hospital departments of Ob/Gyn. The BKS PENFIN was established to serve the research needs of the Indonesian national family planning program. With FHI assistance, the BKS PENFIN has conducted a wide range of contraceptive clinical trials, maternity care studies and other reproductive health research. It has conducted numerous training activities and conferences to upgrade the clinical research skills of Indonesian physicians while disseminating widely the results of the BKS PENFIN studies.

As both the capacity of the BKS PENFIN centers to do clinical research and the capacity of the Secretariat at Bandung to coordinate

such research (including data processing, analysis and computer skills) have increased, so too has the BKS PENFIN's ability to attract research work from various sources. The BKS PENFIN uses its own Texas Instruments TI-352 Microcomputer (provided by FHI in 1984) and has access to a mainframe computer in Bandung. A TI-1 Microcomputer provided in 1982 has been transferred to BKS PENFIN's center in Yogyakarta.

Several FHI contract studies have recently been initiated by the BKS PENFIN, including a 3,000 case evaluation of the TCu 380, a 300 case study of the Filshie Clip versus Tubal Ring (via laparoscopy), a 100 case evaluation of the FEMTEST device, and a 320 case study of oral contraceptives with and without iron supplements. All of these are multicenter studies, coordinated by the BKS PENFIN. Other studies, funded by non-FHI sources, are also continuing, and new ones are planned. BKS PENFIN is trying to maintain a diversified program of research including both contraceptive and reproductive health components, with a correspondingly diversified range of funding sources. Also, BKS PENFIN will make its data processing facilities available under subcontract to another non-government organization, PERDHAKI, that is conducting an FHI study of three NFP approaches.

A top priority over the past year has been to strengthen the BKS PENFIN's financial management systems. In 1984, FHI announced its intention to gradually phase-out its core support funding of the BKS PENFIN and other FHRCs. The BKS PENFIN's FY 86 core support budget reflected this policy, and their FY 87 budget is reduced further. Future levels of core support will continue to decline (about 20-25%

per year), but FHI will seek to contract with the BKS PENFIN to conduct both FHI strategy studies and Indonesian programmatic research. As core support funding is phased out, FHI and all other funding sources for BKS PENFIN studies will be asked to pay a fair share of the BKS PENFIN's organizational costs. FHI has contracted with the accounting firm Deloitte Haskins & Sells (DH&S) International to provide technical assistance to the BKS PENFIN (and other FHRCs) in establishing the systems necessary for managing multiple contracts with full direct and indirect cost allocation and recovery.

A two week visit by two DH&S consultants in August 1986 provided in-depth assistance in appropriate budgeting and accounting procedures. An operating year (1 January - 31 December) was adopted, and a BKS PENFIN organizational accounting manual was developed, based on a draft which had been prepared by the BKS PENFIN's accountant. The final English translation is now in process. It is expected that these new procedures will be initiated during October - December 1986, so that a consolidated 1986 financial report and 1987 organizational budget can be prepared. It is recognized that some current research contracts do not provide for indirect administrative cost recovery, and the BKS PENFIN may not be able to renegotiate these. The continuing, though reduced core support from FHI will help to cover such unreimbursed costs. It is also recognized that this transition is administratively complex; the BKS PENFIN seems to be making solid progress in becoming more business-like and independent as an organization.

d) Family Planning Association of Sri Lanka (FPA/SL)

The Family Planning Association of Sri Lanka (FPA/SL) is a non-governmental organization providing clinical services, motivating potential acceptors and supplying contraceptive products. After nearly ten years of clinical trials collaboration with FHI, a Family Health Research Center was established within the Research and Evaluation wing of the FPA/SL in late 1983. The current subagreement marks the third year of funding for this project.

During this reporting period, activity has focused on four areas: clinical trials research, network development, research training and report writing. Subcontract clinical trials of NORPLANT® involving 565 women (including 75 cases under a research contract with Leiras Pharmaceuticals and 90 cases recently added) are ongoing at the FPA's two clinical sites in Colombo and Kandy. Two new subcontract studies were undertaken: a 300-case comparative study of the oral contraceptives Triquilar and Lo-Femenal, and a 300-case comparative study of the IUDs TCu 380A and Multiload Cu 250. The latter study is being implemented by an FPA staff physician who received training at FHI's Research Methods Workshop in Singapore in July 1985.

A second physician who attended that workshop is the FPA's first collaborating investigator. This physician, who works at the Faculty of Medicine in Galle, has also initiated a comparative study of the IUDs TCu 380A and the Multiload Cu 250, under the supervision of the

FPA. Staff at the Galle center were trained in data collection methods by FPA staff.

A research methods workshop based on the curriculum materials used at the Singapore workshop was held in Colombo in May 1986. In addition to an FHI biostatistician, the workshop was led by FPA staff and three Sri Lankan physicians also trained by FHI in Singapore. Over 30 physicians from various specialties and organizational affiliations attended, and because of their favorable response, a second workshop is planned for spring of 1987.

Reports published during the period include "Knowledge and Attitudes about Reproductive Health among Youth in Sri Lanka" and "Considerations in Improving Follow-Up in Clinical Trials", both of which were written by Dr. Sriani Basnayake, Medical Director of the FPA/SL. The former report was disseminated to newspapers and television stations in Colombo and generated a number of press reports and editorials in the local media relating to the need for sex education courses in the schools. A more detailed study of a larger population has recently been initiated. The latter report has been used as a resource for FHI research methods workshops in Panama and Bangladesh.

FHI staff also assisted Dr. Basnayake in the analysis of clinic records and editing of her paper, "Depo-Provera Use in Sri Lanka: Acceptor Characteristics, Continuation and Side-Effects".

Studies underway with subagreement funding include "Attitudes Toward Vasectomy" (report being finalized), "Follow-up of Female Sterilization Acceptors" (follow-up in progress), and "Infertility Study" (data analysis underway).

Other studies conducted under contract to FHI include a survey of oral contraceptive pill safety (completed in February) and a large Rural Family Planning Survey (analysis ongoing). The latter will provide information relating to acceptability, satisfaction, and reasons for continuation and discontinuation of family planning methods.

The FPA/SL's TI-352 microcomputer has been used continuously almost from the day it was installed in July 1984. The computer programmer trained at FHI resigned in August; her replacement is learning to work with the TI system. With a computer programmer and two data processors, the FPA/SL has attained a high level of proficiency, and uses the computer for various management purposes as well as research. The FPA/SL is exploring purchase of an IBM PC-AT to supplement the TI-352.

The FPA/SL devoted considerable energy in the winter to develop a Five-Year Plan providing a framework for management, research, and funding strategies. The plan reflects the gradual decline of FHI core support funding and its replacement with funds from other sources. The plan was submitted to the Ministry of Plan Implementation and AID/Colombo, both of which have approved the intended directions of the organization.

As part of the staff development process, the FPA/SL sent a research assistant to train with the Egyptian Fertility Care Society (EFCS) in August for ten days in order to learn skills and systems related to monitoring and supervising centers in a research network.

In addition to the ongoing work described above, the FPA/SL plans to expand their NORPLANT® caseload by 500 cases under a contract with FHI. They will also fund two female sterilization follow-up studies with funds from the subagreement. Two investigators trained at the spring research methods workshop will be chosen to undertake this study using the same protocol used for the FPA's ongoing study on the topic.

e) Sudan Fertility Control Association (SFCA)

The SFCA has received assistance from FHI beginning in 1979. Since that time this FHRC has established itself as a national organization for research in family planning and maternal and child health. Membership in the SFCA has grown to more than one hundred, mostly obstetrician-gynecologists and other physicians interested in family planning. Plans are underway to expand SFCA activities into areas outside of Khartoum. The SFCA places major emphasis on the development of its clinical trials capability in order to determine safe, effective and acceptable methods of family planning for the Sudan. To achieve geographic and organizational expansion the SFCA emphasizes training, workshops and projects that will expose members to new learning experiences in regional research projects.

FHI subgrants have provided financial and technical support aimed at developing the SFCA's skills and resources, meeting core administrative costs, and funding specific research studies. SFCA has also received financial support from AID/Khartoum and AVS. AID is supporting a Model Family Planning Clinic that is utilized by the SFCA as a research center.

To expand their data processing and analysis skills the SFCA will receive from AID an IBM PC-AT computer within the coming year. AID will also provide software for research and management capabilities. FHI will, in turn, train SFCA staff to use the computer.

During 1985 and 1986 the following activities were conducted:

- The Model Family Planning Clinic began operation at a new location in Khartoum in August 1986. Average patient intake is 30-40 patients per day for a variety of reproductive health services
- The Annual Scientific Meeting of the Sudan Fertility Control Association was held in February 1986
- A multicenter oral contraceptive study has been initiated
- A retrospective study involving the cause and treatment of infertility has been initiated at Soba Hospital.

During the same period SFCA researchers worked on the following activities under separate subcontracts:

- A survey in Khartoum of the perception of the safety of oral contraceptives
- An oral contraceptive comparison study, Triquilar versus Lo Femenal, was initiated
- A progestogen-only pill study is in the final follow-up phase
- A maternity care monitoring study in Port Sudan Hospital

- An IUD comparative study (TCu 380A versus TCu 200) was initiated in Port Sudan Civil Hospital to be completed in February 1988.

The following activities will be initiated in the coming months:

- A study evaluating the impact of health education on infant and maternal health and the acceptance of family planning
- An evaluation of a training program in family planning for a group of senior midwives
- A focus group study on the knowledge, attitudes and practices of modern, traditional and natural methods of family planning in Sudan
- A clinical trials workshop is scheduled for Kassala, a city in the Eastern Region of Sudan, in November 1986.

SFCA is entering a phase of diversification of funding in order to gain greater autonomy in the field of research. The planned visit of the Deloitte Haskins and Sells team will greatly facilitate this new phase of development. However, the drought that has affected large sections of the country and recent political problems have restricted movement into the country as well as within the country. These problems may hamper development planning and technical assistance visits over the coming months.

The current two-year agreement became effective on 1 March 1986 and will extend until 29 February 1988.

f) Thailand Fertility Research Association (TFRA)

The TFRA was established with FHI assistance in 1979 to serve as a national center for research in support of the National Family Planning Program (NFPP) of Thailand. The TFRA is a private, non-

profit organization that operates within the administrative structure of the Ministry of Public Health (MOPH) in Bangkok, and therefore enjoys a close two-way relationship with the NFPP. As such, it is uniquely situated to enlist and coordinate capable researchers from both the private and public sectors--including centers serving small towns and rural populations. The TFRA's network consists of physician researchers from each of the country's medical schools and from numerous MOPH hospitals and MCH centers all over Thailand. The TFRA's close association with the MOPH also assures that research findings will reach relevant policymakers.

Successive FHI subgrants since 1980 have provided financial and technical support aimed at developing the TFRA's skills and resources, meeting core administrative costs, and funding specific research studies. The MOPH has also provided significant core support in the form of office space, transportation and personnel, and, since October 1983, it has also assumed the direct study costs for the Sukhothai Province Maternity Care Monitoring (MCM) program, formerly supported by FHI. The TFRA has also conducted clinical trials with funding from private pharmaceutical companies and has initiated three major studies under separate contracts with FHI. Final approval has been obtained for a study with funding from AID (bilateral funds), although the funds have not yet been released by the Thai Government.

The TFRA has made good progress in developing its data processing and analysis skills. In June 1986, the TFRA's Data Collection Coordinator, Ms. Mukda Tadrudtong, visited FHI for four weeks of

training in microcomputer use and data management. Emphasis was placed on developing her SPSS skills, particularly to assist TFRA in the analysis of MCM data from Sukhothai Province. Training was provided at FHI on the same Model TI-352 microcomputer that the TFRA uses at their own facilities in Bangkok.

During this reporting period, work continued on the following studies:

- Comparative study of mini IUDs: Minigravigard versus Nova T versus ML Short (follow-up stage)
- Comparative interval female sterilization study: Filshie clip versus tubal ring via laparoscopy
- Comparative interval female sterilization study: Filshie clip versus modified Pomeroy technique via minilaparotomy
- IUD perforation study (in analysis stage).

In addition, the TFRA has conducted several studies under separate contracts with FHI and other funding sources. The studies include:

- Infant health follow-up in Sukhothai (FHI)
- Postpartum sterilization by nurses (FHI)
- Progestogen-only pills for lactating women (FHI)
- Perception of pill safety survey (FHI-Completed)
- Follow-up study of Uttradit IUD campaign (AID)
- Eugynon versus Microgynon 30 (Schering)
- Ovral versus Marvelon (Organon)
- MCM research in Sukhothai (Ministry of Health).

Core support contributes to the TFRA's ability to carry out effectively both subagreement and other contract studies. As FHI's core support is gradually phased out, the TFRA will increasingly seek core support from the Thai Ministry of Public Health. Allocable cost reimbursement as part of their grants and contracts from all sources will provide for some of the core support needs. A visit to Thailand in March 1986 by FHI's financial management consultants from Deloitte Haskins & Sells International provided an in-depth assessment of the TFRA's current systems and needs for future assistance in this area if the TFRA wishes to adopt a consolidated financial management

system. The TFRA's leadership has indicated that they will review their options for replacing FHI core support over the next several months, with assistance from FHI's financial management consultants. It is expected that at least one DH&S consultant will visit the TFRA for two days in November 1986 to review these options and possible plans for further FHI assistance.

g) FHRC Directors Conference

From 2-7 March 1986, the Second Family Health Research Centers Directors Conference was held in Chiang Mai, Thailand. The theme of the conference was long-term planning, and focused on developing skills to enable FHRCs to plan for institutional and research strategy development including options for obtaining funding from multiple sources as FHI implements its plan to reduce core funding. The meeting also provided an opportunity to review progress on a number of issues introduced at the first FHRC conference in September 1984. A two-day scientific session provided each FHRC an opportunity to present and discuss research implemented through its program. The conference was hosted by the Thailand Fertility Research Association (TFRA) and was attended by 13 leaders (three from TFRA, two from the other FHRCs- in most cases the chief policy person and the chief program manager) of the FHRCs in Bangladesh, Egypt, Indonesia, Sri Lanka, Sudan and Thailand.

FHI Attendees included the Director of FHI's Field Development and Training Division (which coordinates FHRC activities), the three FDT program coordinators for the FHRCs, the FDT coordinator for African

programs, and the Director of FHI's Clinical Trials Division. In addition, two consultants from the accounting firm of Deloitte Haskins & Sells International attended to provide special financial management input.

The first half of the week was devoted to discussions of planning and management issues, and the second half concentrated on scientific issues. Session topics in the latter included NORPLANT® Studies, Social Determinants of Contraceptive Use, Voluntary Sterilization, Pregnancy Outcomes and Postpartum Contraception, Systemics, and Intrauterine Devices. Speakers were asked to focus on the "process" (conceptualization, methodology, policy implications, and information dissemination) rather than only citing results of their research. This emphasis made the presentations a good learning forum for replicating successes and avoiding the failures in other centers.

The conference received very positive comments by participants in the post-conference evaluation.

h) Technical Assistance from Deloitte Haskins and Sells (DH&S) to the Family Health Research Centers

Two years ago FHI embarked on a program to phase out core funding to the more mature Family Health Research Centers over a five year period. It is FHI's goal that at the end of this period the six major FHRCs (in Indonesia, Thailand, Sri Lanka, Bangladesh, Egypt and Sudan) will be able to stand on their own as research institutions

capable of designing, managing and implementing research to meet the needs of their countries. An integral part of this transition to a self reliant status is the strengthening of financial management capabilities of these institutions. They must be able to plan for future needs, obtain financial support to carry out their program, have a workable system to recover costs from research contracts and be able to demonstrate fiscal accountability to prospective donors.

Under a subagreement from FHI, Deloitte Haskins and Sells (DH&S) International is providing technical assistance the FHRCs need to strengthen their financial management capabilities. During fiscal year 1986, phase I of this project was completed. It covered the planning of the proposed technical assistance. During this phase, DH&S collected information both from FHI and the FHRCs on current systems and capabilities in financial management and monitoring. A plan for the next phase was designed, reviewed and finalized. It included the development of a shell for a generic accounting system and the design of a manual that will be customized for each FHRC during the implementation Phase II.

Toward the end of the fiscal year, Phase II was initiated to provide technical assistance and training to implement the new system.

The Indonesian FHRC was the first to receive training to implement the new accounting system. A manual for the BKS PENFIN was developed and is being finalized. It is being written both in English and in Bahasa. The generic system has been customized for the BKS PENFIN

and it is expected that full implementation of the new accounting system will be in place at the beginning of the calendar year 1987.

Initial visits to the Thailand and Bangladesh FHRCs have also been conducted to assess the current capabilities and prepare for implementation of the new financial system expected during fiscal year 1987.

A visit to the Sri Lanka FHRC reviewed the system already in place. It is similar to the one proposed by the DH&S consultants. The assistance provided to the Sri Lanka FHRC included a small amount of consultation and recommendations to refine current FPA/SL systems.

2. Other Technical Assistance and Development Activities

As resources permit and as interest and absorptive capacities allow, FDT has initiated small institutional development programs in other countries -- Mali, Niger and Brazil. At present these research funding and technical assistance programs are small, but thriving. A small institutional grant has also been provided to a program in Mexico. FDT has also continued support for developing data processing capability within the FHRCs and other programs. Progress in each of these programs is described as follows:

a) Technical Assistance to the AMPPF/Mali

FHI technical assistance to the Association Malienne pour la Protection et la Promotion de la Famille (AMPPF) was begun in 1981

and is being continued through a new two year subagreement. An analysis of the clinic records of the AMPPF and 30 MCH centers initiated under the previous subagreement is being completed and shows the increasing demand for family planning services, especially among young men and women. The growing proportion of clients who use the MCH centers demonstrates the decentralization of services and the possibility for the AMPPF to address other needs of the family planning program: research, IEC and services. FHI has agreed with AID to act as the lead assistance agency with AMPPF on the full range of activities this agency is likely to undertake.

The AMPPF has completed two surveillance studies: one of women who use the IUD and the other of OC users. The IUD study showed a high number of expulsions. As a result, a workshop was held to retrain providers in IUD insertion techniques and the proper storage of IUDs. The OC study has just recently been completed and the data are being analyzed. The research assistant at the AMPPF has provided regular supervision of the surveillance studies being carried out at other MCH centers in Bamako. Completed forms are channeled through him for review and corrections before being sent to FHI.

The AMPPF will play an important role in the recently signed bilateral project; the Association will be responsible for the family planning IEC component of the project. Likewise, it will participate with the Sahel Institute and FHI in preparing baseline statistics to evaluate the impact of the project. Through the bilateral project, funds will also be made available for a needs assessment that will examine the development of the AMPPF through its nearly 25 years of

service and, in its evolving role, assessing how the Association can contribute most effectively to the growth of the national family planning program.

b) Niger: Technical Assistance to the CNSF

The Centre National de Sante Familiale (CNSF) is the principal government agency providing family planning services in Niger. During a 1985 national conference on family health and development in which FHI participated, the Ministry of Health requested FHI's technical assistance to the CNSF to strengthen its research capabilities and increase its visibility as the leading national institution in family health and family planning. A series of activities was presented and approved to be carried out during a two-year period. This project provides funding for the technical assistance required by the CNSF to implement their program of activities.

Presently, the CNSF, in collaboration with FHI, is conducting an oral contraceptive surveillance study that follows 200 women using the most frequently prescribed combined pills - Stediril and Minidril. This study will determine acceptability of the two different pills by evaluating side effects and continuation rates.

The results of a study of Vanguard Acceptors of Family Planning Services that was carried out at the CNSF and completed at the beginning of FY'86 are being written in a final report. The report will focus on clinic activities in the provision of family planning

services as well as the socio-demographic and obstetric characteristics of the clients, and will discuss means of improving service delivery and important groups to be targeted.

Plans are being made to hold an applied research methodology workshop in Niger in February 1987. The objective of the workshop is to teach participants the fundamental skills in developing and carrying out research projects. Simple research projects will be developed by the participants during the workshop and then submitted to various donors for funding. Through this workshop a network of investigators who will work together to develop research strategies appropriate to their country will be established. The CNSF will coordinate the implementation of these projects, thus increasing its visibility as the principal government agency for family planning activities.

c) Brazil - ABEPF

Since 1982, financial and technical support has been provided to the Brazilian Association of Family Planning Entities (ABEPF) of Rio de Janeiro, Brazil. The project seeks to strengthen ABEPF's clinical research capabilities by funding a full time data collection/research coordinator (DCRC). Currently ABEPF is coordinating a 1,200 case FHI-funded progestogen-only pill clinical trial. This multicenter research project, managed by the DCRC, is providing ABEPF with an organizational experience to implement and coordinate clinical research studies among its affiliates.

The multicenter progestogen-only pill study is nearing completion. It is anticipated that 12-month patient follow-up will be completed by January 1987.

During the period covered by this report, FHI has concentrated on building a larger institutional understanding of the issues associated with the implementation and coordination of multicenter clinical research. FHI provided the impetus and financial support for a meeting of ABEPF investigators participating in the multicenter trial to review the progress being made by ABEPF in developing an institutional research capacity. Several important issues were discussed in this meeting and a more detailed strategy was developed to facilitate the strengthening of ABEPF's clinical research program.

d) Mexico: Computerized Service Statistics System

During this reporting period, FHI provided funds to the Mexican Federation of Private Family Planning Associations (FEMAP) to improve their institutional capability to utilize service statistics in the evaluation of research activities. The project was designed to meet the need of FEMAP for accessing service statistics for both research and programmatic purposes, in addition to permitting a more systematic evaluation of its own programs. The computerization of FEMAP's service statistics is a key step in the successful implementation of a planned project within the Juarez CBD program to determine factors affecting "promoter" productivity. This project will relate the "promoter's" background characteristics, knowledge of

contraceptives and community activities to recruitment success and continuation rates.

This project is now nearing completion. The service statistics program should be fully operational by early FY 87.

e) Microcomputer Training and Development

Highlights for this reporting period consist of four basic areas:

1. New Microcomputer Installations
2. Follow-up Visits to Existing Microcomputer Sites
3. Software Development
4. In-house Microcomputer Related Training and Documentation.

1. New Microcomputer Installations.

A new microcomputer installation is currently being planned for the Bangladesh Fertility Research Programme (BFRP). This installation has been planned for some time, but was delayed pending the appointment of a new Executive Director of the BFRP as well as a decision as to what hardware was to be installed there. The decision was made to go ahead with the equipment originally designated for the BFRP, a Texas Instruments Business System 352 with 256K bytes of main memory, two workstations, two printers (one standard 810 and one letter quality printer for word processing), and mass storage devices consisting of one 1.2 megabyte floppy disk and one 17 megabyte Winchester disk. As some time has elapsed since the installation was

originally planned, the various components have been tested and certain of them sent to TI for servicing, to assure that all parts are in working order upon arrival in Bangladesh. An export license for the TI BS352 was applied for in January of 1986 and received at FHI 12 March 1986. Preparations for the designated computer room have been reviewed, including electrical current, proper grounding, air conditioning and flooring. An installation trip by FHI staff, originally planned for June 1986, is still pending, awaiting import approval by customs in Bangladesh.

2. Follow-up Visits to Existing Microcomputer Sites

During the past year, follow-up visits were made to: Colombo, Sri Lanka; Bangkok, Thailand; Dakar, Senegal; and Bandung, Indonesia. Additional follow-up visits are planned for Egypt and Senegal in October 1986.

A follow-up visit was made to the Family Planning Association of Sri Lanka in December 1985. The primary purpose of this trip was to assess the progress of the FPA since the installation of a TI Business System 352 in July 1984 and to determine future needs in the areas of training, software and additional hardware. The trip included a review of the actual usage of the computer to date, along with suggestions and recommendations on how to use it more effectively and efficiently, and the installation and training in the use of the Oral Contraceptive Clinical Trials software package and a data entry program designed for use with extremely large data collection instruments. Time was also spent reviewing surveys the

FPA is currently conducting in order to recommend best use of the computer for related data entry and analysis.

A follow-up visit was made to the Thailand Fertility Research Association in December 1985. The primary purpose of this trip was to install and train in the use of the Oral Contraceptive Clinical Trials Software package and to review the progress and use of the TI BS 352 by the TFRA staff. Time was also spent going over systems operation and the importance of data management on the machine.

Another follow-up visit was made to the TFRA in May 1986. The TIPE word processing system and the DX10 Recover Volume Space (RVS) command were installed on the BS 352. The Microgate 931 package that will allow an IBM PC or PC compatible computer to be connected to the TI as an additional terminal was also installed. Additional training and assistance with specific software packages and the operating system, DX10, was also provided.

A follow-up visit was made to the Bureau National du Recensement in Dakar, Senegal, in March 1985. The primary purpose of this trip was to assess training absorption, utilization of both hardware and software and additional training in systems operations and management. The Oral Contraceptive Clinical Trials software package was also installed, and BNR staff trained in its use. The BNR is also interested in the acquisition of additional hardware, and the possibilities of expansion of the current system as well as communication with IBM hardware was explored. An additional follow-up is planned for October 1986, when the Microgate 931 communications package will be installed.

A follow-up visit was made to the BKS PENFIN in Bandung, Indonesia in May 1986. The new Oral Contraceptive Patient Summary (OCPS) clinical trials software package was installed and training was provided in its use. Training for and installation of the RVS command and the TIPE word processing system was also accomplished. The TI BS352 system was reconfigured to allow for operation in case of main disk drive failure, and the Microgate 931 package was installed. New computer staff members were evaluated for their current knowledge of the computer system, and for their potential in providing continued support to the BKS PENFIN research staff. Discussions were also held with the BKS PENFIN management staff to help them to determine the data processing and analysis needs of the organization.

A follow-up visit to the Egyptian Fertility Care Society in Cairo is scheduled for October 1986. Specific tasks to be accomplished at that time include installation and training of the OCPS clinical trials software package and the Microgate 931 communications package. Assistance will be provided in reviewing hardware and software options to be purchased for analysis of the NORPLANT[®] study to be conducted by the EFCS.

3. Software Development

Software developments during this reporting period consisted of the following:

- a. New system software for the Oral Contraceptive Patient

Summary Questionnaire was completed. It is a complete package and includes data entry, invalid code and range checks, consistency checks and standard tables.

- b. Modifications were made to all of the other FHI Clinical Trials packages to incorporate the new OCPS system and to facilitate user interaction.
- c. Modifications were made to the FS and IUD Clinical Trials programs to allow tables to be run prior to completion of data entry of all acceptors in the study.
- d. A new data entry program was written to allow for extremely large data collection instruments to be entered onto the TI Business System computers for data analysis. This program was developed specifically for the Family Planning Association of Sri Lanka.
- e. The table specifications for the Maternity Care Monitoring system are currently being reviewed by the research staff at FHI. Any modifications the researchers agree should be made will be incorporated into the existing software, if warranted after an assessment of the cost.
- f. Modifications were made to the Maternity Care Monitoring System tailored to the MCM program at the Egyptian Fertility Care Society to incorporate differences on the EFCS forms.

4. In-house Microcomputer Related Training and Documentation

Training was provided at FHI for Dr. Soeprapti Thaib, the Senior Program Officer of the BKS PENFIN during her visit in October 1985. Dr. Soeprapti received an overall orientation to microcomputers and their potential in research and administrative applications. She was also given an introduction to the TI BS352 and each of the software packages currently available on it.

Ms. Mukda Takrutong of the Thailand Fertility Research Association received training at FHI in June 1986. Her training included a review of the FHI developed clinical trials software systems and other utilities, and concentrated on the intensive use of SPSS for the analysis of data sets on the TI BS352 system.

In-house training is also scheduled for Ms. Susanty of the BKS PENFIN in November 1986 and Ms. Pattaka of the TFRA sometime this winter. Ms. Susanty's training will consist primarily of an overall orientation to the TI BS352 computer, the DX10 operating system, and each of the FHI developed utilities and clinical trials software packages. Ms. Pattaka's training will more closely mirror that of Ms. Mukda. She will concentrate on the analysis of TFRA collected data which she will bring with her. Ms. Pattaka will be using SPSS on the TI system for the data analysis so that the process can be duplicated for other studies using the computer facilities at the TFRA.

Training is also planned for Mrs. Kumudini Abeysooriya, the new computer programmer at the Family Planning Association of Sri Lanka. This training is tentatively planned sometime in the late winter of 1987.

A new Users Guide for all FHI-developed software currently available on the TI Business Systems computers was produced. This manual includes documentation for the Clinical Trials Package, the Data Analysis Package, Lifetable Analysis, Data Entry, Random Allocation, Sample Size Determination and the Select program. A summary of the DX10 copy commands was produced, along with examples of when to use what command.

Based on the follow-up visits to the various microcomputer sites, two in-house workshops to be held at FHI for advanced users are being considered:

- A. Advanced system concepts, to include more in depth data management techniques and possibly system generation
- B. FORTRAN-78 on the TI Business System to include working with core limitations and the use of overlays.

Also, based on the follow-up visits, the interest of some sites in hardware expansion and in the interests of increased IBM compatibility, a communications package to enable the TI BS to be linked to IBM PCs and compatibles was purchased. The Microgate 931 software package will enable an IBM PC or PC compatible computer to

be connected to the TI BS352 as an additional terminal, and also allows for transfer of data between the two machines. This software package has already been installed on the TI systems in Thailand and Indonesia, and will be installed in Senegal and Egypt in October 1986.

B. TRAINING

1. Training in Research Methods

To enhance the research skills and capabilities of collaborating investigators and to develop and expand the number of highly skilled researchers in FHI's international network, support is provided for research training workshops. During this funding period, the following research training activities were implemented:

a) Clinical Trials Training Curriculum Development

Regional and national clinical trials workshops are an ideal way to meet clinical trials training needs in the developing world. FHI's new Clinical Trials Research Methods curriculum was successfully implemented for the first time in a one-week workshop in July 1985, in Singapore. That workshop was aimed at training and working with 12 new Asian investigators from Sri Lanka, Nepal, Malaysia and the Philippines. All of these 12 participants have subsequently initiated FHI supported clinical trials or have been involved in further training of other investigators in their own country. Following the Singapore workshop, minor modifications were made to

the curriculum and an outside professional review was carried out under contract with consultants in Mexico, who also translated the finalized materials into Spanish. Subsequent workshops using this standard curriculum have been conducted by FHI in Egypt (December 1985 and August 1986) and Panama (August 1986). In addition, a workshop was conducted in Sri Lanka by the FPA/SL (May 1986) with more limited FHI technical assistance.

Based on both outside and in-house review of the training materials and our experience in the several workshops to date, some final revisions and corrections were incorporated and a camera-ready final version of the four modules was prepared for printing or reproduction as needed. The Spanish version is also being revised and finalized and a French translation has been commissioned.

A workshop will be conducted in Bangladesh in October 1986 for BFRP investigators. Another Asia regional workshop with emphasis on training of trainers from the BKS PENFIN and TFRA in addition to some new investigators from Malaysia and Philippines is tentatively planned for early 1987, possibly in Singapore again in collaboration with the National University.

b) Panama: Clinical Trials Research Course

A workshop on Clinical Trials Methods for Contraceptive Research was held in conjunction with the School of Medicine, Department of Obstetrics and Gynecology of the Universidad de Panama, on 21-26 July 1986. Seventeen trainees were selected from applicants from Mexico,

Peru, Brazil, Colombia, Venezuela and Panama to participate in this event. The workshop trainers used the standardized curriculum developed by FHI for the Singapore workshop. The trainers included two FHI staff members who were involved in the development of the curriculum materials; two consultants, including one from Mexico who participated as a trainer in the course on research methods for reproductive epidemiology in Durango; and an FHI investigator from Chile with ample experience in FHI's clinical trials research program.

The event was a success in terms of the objectives it set out to achieve. Participants used the knowledge that they acquired during the course to prepare and present protocols for consideration and funding. These protocols are being reviewed at FHI and it is expected that funding will be provided for most of them.

c) Development of an Analysis Curriculum for Clinical Trials

In support of its international network of investigators, FHI is preparing standardized training materials for the analysis of data from clinical trials of contraceptive methods. The materials are being designed for use in a course of four to five days, intended mainly for current or potential researchers and/or their research assistants who are interested in doing their own analyses.

Investigators who desire a more complete understanding of the analysis process will also be appropriate students. The format of the training materials will be a set of essentially self-instructional modules designed to present step-by-step instructions

for analysis of data from contraceptive clinical trials. FHI specialists in biostatistics and clinical trials are developing the content. A primary target for use of these training modules will be the core staff and investigators who make up the Family Health Research Centers. The first training course using the materials is planned for the summer of 1987.

d) Mexico: Epidemiologic Training

FHI has just completed the third in five years of technical assistance to an epidemiologic training program implemented by the Instituto de Investigacion Cientifica of the Universidad Juarez, Durango, Mexico. Under a five-year grant from the UNFPA the Instituto trains investigators to conduct epidemiologic studies in the area of reproductive health, with emphasis on benefits and risks. A third three-week workshop is scheduled for November 1986 to train ten physicians from Mexico who are associated with the research group, the Mexican Interuniversity Group for Epidemiologic Research in Reproductive Health (GIMIESAR). GIMIESAR was spawned by the experience of the training project. It is based in Durango, and the members are some of the alumni of the first two workshops. GIMIESAR is designing a maternal mortality study for several states in Mexico and has been selected by WHO to help with an epidemiologic investigation of oral contraceptives.

2. Contraceptive Technology Workshops

Physicians and other health providers are not only a key resource for carrying out biomedical research activities; they influence the provision and acceptance of family planning services in a number of ways. In countries where contraceptive service and research are in the early stages of development, they are an important target audience for training in contraceptive technology. Three contraceptive technology workshops held in the current reporting period and one other planned for the next reporting period are described below.

a) Pakistan: Contraceptive Technology Workshop

FHI provided support to a three-day workshop entitled "Reproductive Health and Contraceptive Technology in Pakistan" which took place in Lahore, 28-30 April 1986. FHI support included sponsorship of the international speakers/resource persons, consultant honoraria and all educational materials utilized in the workshop. The Pathfinder Fund (Boston) covered all in-country costs.

The Government of Pakistan's Population Welfare Division identified a need to update physicians and family planning service providers in contraceptive technology and family planning practices. The workshop addressed this need as well as provided a forum for discussion among service providers, policymakers, and clinical researchers.

The objectives of the workshop were:

1. To provide an update for physicians and family planning providers (both urban and rural) in recent developments in contraceptive technology, contraceptive distribution and selected issues in reproductive health;
2. To respond to an identified need and priority of the Population Welfare Division of the Government of Pakistan with the hope and intent to build this cooperative relationship in terms of future collaborative research in Pakistan;
3. To discuss the current Pakistan population program and identify mechanisms by which service providers can contribute to it more effectively;
4. To help identify future directions and needs that the Pakistan population program should address;
5. To develop a FHI strategy for contraceptive biomedical research (particularly in the area of introduction of contraceptives new to Pakistan, eg., NORPLANT[®] subdermal implants and copper IUDs including the TCu 380A IUD).

FHI sponsored three international speakers/resource persons and two staff to attend this workshop.

b) Niger: Contraceptive Technology Workshop

As part of the series of activities to be carried out in collaboration with the Centre National de la Sante Familiale, FHI conducted a Contraceptive Technology Update Workshop in Niamey, 24 February - 1 March 1986. With 22 Nigerien physicians participating, the workshop focused on updating the physicians' knowledge of the latest research findings for different contraceptive methods and discussion of the risks and benefits of contraception relative to another pregnancy. A final report is on file.

Recommendations by the participants were to integrate family planning services into all maternal and child health activities and undertake research studies to examine the risks and benefits of contraception.

A 200-case surveillance study of oral contraceptive users is currently underway in response to the workshop recommendations.

c) Mexico: 2nd International Course on Family Planning, Population and Maternal Child Care

Support was provided to the Academia Mexicana de Investigacion en Demografia Medica (AMIDEM) for a two week course on family planning program administration, medical demography, contraceptive methods and maternal/child health. The participants developed skills to create family planning programs and to interpret demographic changes, vital statistics and the demographic and social impact of family planning programs. They received information about institutional and community resources; integration of family planning services within community and institutional health services; orientation of new acceptors to make informed choices in the use of contraceptives; and evaluation of family planning programs at all levels of the medical triage, in both the urban and rural setting. The course took place 12-23 May 1986.

Participants included 15 physicians from the Mexican Social Security Family Planning System and 10 physicians from other private and public sector family planning programs in Latin America. The content of the two week course consisted of 75 hours of theory and 45 hours of field visits and observation of surgical procedures, including IUD insertions. The implementation of this project is seen as an opportunity to aid in the development of AMIDEM as a Mexican training center.

d) Bangladesh Contraceptive Technology Update

In June 1986 the Bangladesh AID Mission agreed to "buy-in" to FHI's cooperative agreement to fund a contraceptive technology update workshop in Dhaka. FHI, in collaboration with the Bangladesh Fertility Research Programme (BFRP), is inviting 3-4 international experts (including FHI President Dr. Malcolm Potts) and many local experts to address an audience of 150-200 leading policymakers and family planning physicians during the two-day conference. The early November conference will include such topics as risks and benefits of modern contraception, oral contraceptives, male and female sterilization, NORPLANT[®], injectables, and contraception for breastfeeding women. The conference will be an opportunity to update the audience on contraceptive advances, dispell misconceptions about the risks of modern contraception, and discuss incorporation of new contraceptive technology into the national family planning program. Planning for the workshop began during this reporting period.

C. SUPPORT FOR CONFERENCES, SEMINARS AND EXPERT MEETINGS

FHI believes that international meetings, conferences and seminars are a useful way to generate research ideas, discuss major issues and share research findings. FDT provides support for many of our international colleagues to attend and participate in such meetings. During this reporting period FDT supported a number of conferences, seminars and expert meetings.

a) Research Advisory Committee for Latin America

The inaugural meeting of FHI's Latin America Advisory Committee (LAAC) took place at FHI on 19-20 May 1986. The meeting brought together a group of experts from Mexico, Brazil, and Colombia. The meeting was organized to accomplish the following goals:

1. To identify the most effective strategies for meeting regulatory requirements of specific Latin American countries for the evaluation and introduction of new contraceptive products
2. To serve as an institutional mechanism to maximize the effectiveness of FHI's research program in the evaluation and introduction of new fertility regulation methods.

The LAAC meeting was extremely useful for FHI. The meeting permitted an open exchange of information and an opportunity for discussing the salient issues relating to the evaluation and introduction of new contraceptive technologies. Discussions provided information that will be useful in the development of strategies designed to facilitate the contraceptive introduction process in the Latin American region. Most important of all LAAC developed the concept of the local approval and manufacture of specific new contraceptive technologies

Follow-up activities to the LAAC meeting have already begun and preliminary soundings in Mexico suggest that ways may exist to accelerate the introduction, approval, manufacture and distribution of related contraceptive methods. FHI plans to organize another meeting of LAAC during FY 87.

b) Sexually Transmitted Diseases (STD) Expert Meeting

FHI sponsored an Expert Meeting on "Sexually Transmitted Diseases in Africa" in Banjul, The Gambia, 28-30 April 1986. The meeting was attended by recognized experts from the US, Europe and Africa to review STD research conducted in Africa and to define FHI's options for pursuing such work.

At the meeting a series of recommendations was formulated to provide a comprehensive overview of research needs which might be addressed by FHI or other funding agencies, i.e., (a) to study the relationship between contraceptive use and STDs, (b) to integrate family planning and STD services and evaluate the effect of the integration on maternal and infant mortality and morbidity and subsequent rate of infertility, (c) to emphasize intervention efforts coupled with evaluation in some specific areas, such as gonococcal ophthalmia neonatorum and congenital syphilis. The Lancet published an editorial summarizing the expert group's recommendations in July 1986 and the meeting's proceedings, in their entirety, are scheduled to be published in a special issue of the African Journal of Sexually Transmitted Diseases (September 1986).

c) Mexico: Adolescent Reproductive Health Conference (CORA)

The recognition of young adults as an integral part of social and health programs is an increasing trend in Latin American health circles. The numerical and proportional growth of this age group and their reproductive behavior has led to increasing levels of concern.

Complications of pregnancy are among the five leading causes of death for young female adults in all subregions of Latin America and the Caribbean.

During FY86 FHI provided funding to the Centro de Orientacion para Adolescentes, A.C. (CORA) in Mexico for an "International Conference on Reproductive Health Among Young Adults". The Conference permitted an exchange of programmatic information, research priorities and political strategies among health professionals working with young adults in the region. The conference program was divided between the topics of research, services and educational materials. A compendium of presentations will be published that will provide government and health planners with information on young adult reproductive health programs in a variety of Latin American settings.

The conference also generated some concrete research ideas for development on high priority studies in the area of reproductive health for young adults.

d) Mexico: AIBIR Conference

Support was provided to the Mexican Academy of Research in Reproductive Biology (AIBIR) for their Eleventh Annual Meeting, held 3-5 April 1986. The annual symposium included sessions on "Advances in Contraceptive Technology", and "NORPLANT[®], Development and Outcome". FHI was represented at the meeting by Dr. Albert J. Siemens, Director of Clinical Trials, who delivered a paper entitled "Advances in Contraceptive Technology". The meeting provided an

opportunity for FHI to discuss our new research directions in reproductive health and contraceptive technology with our Mexican colleagues, as well as with other international health research organizations.

e) Pregnancy Monitoring Workshop

This activity was cancelled due to lack of funding.

f) Support for Conference Travel

FDT also provided support for many of our international colleagues to attend and participate in international meetings and conferences.

The meetings were attended by the following individuals:

1. American Public Health Association, Washington, D.C.,
17-21 November 1985
 - Dr. Serge Armand, Port-au-Prince, Haiti
 - Dr. Jacqueline Polynice Pierre-Louis, Port-au-Prince,
Haiti

2. Third International Seminar on Microcomputer Applications in
Health Services, Perugia, Italy, 5-15 November 1985.
 - Karen Johnson Lassner, Rio de Janeiro, Brazil

3. American Fertility Society, Chicago, Illinois, 30 September-
4 October 1985.
 - Dr. Ricardo Rueda, Jr., Bogota, Columbia

4. American Association of Gynecologic Laparoscopists Annual Meeting, Anaheim, California, 19-23 November 1985.
 - Dr. Jose Moreno Arosameno, Panama City, Panama

5. Interregional Meeting on Prevention of Maternal Mortality, Geneva, Switzerland, 11-15 November 1985.
 - Dr. Nanta Oaumkul, Bangkok, Thailand

6. Third Latin American Congress on Family Life Education, Caracas, Venezuela, 16-20 June 1986.
 - Dr. Anameli Monroy de Velaso, Mexico City, Mexico

7. Society for the Advancement of Contraception, Chicago, Illinois, 23-26 September 1986.
 - Dr. Harith Hamad Ali, Khartoum, Sudan

8. First South American Congress of the Society for the Advancement of Contraception (SAC), Quito, Ecuador, 21-25 July 1986.
 - Dr. Roger J. Lara Ricalde, Mexico City, Mexico
 - Dr. Alvaro Narvaez, Mexico City, Mexico

9. Philippine Pediatric Society Annual Convention, Metro Manila, Philippines, 2-6 June 1986.
 - Dr. Benjamin Sachs, Boston, Massachusetts

10. Carter Center Seminar on Emerging Health Problems: A Global Consultation, Atlanta, Georgia, 27 April-1 May 1986.
 - Dr. Haryono Suyono, Jakarta, Indonesia

11. "Family Planning, Nutrition, and Primary Health Care for Africa: Program Design, Management, and Evaluation", Columbia University Seminar, New York, New York, 2-27 June 1986.
 - Dr. Arkia Doucoure, Bamako, Mali

12. Second Annual SHDS-WHO/AFRO Applied Research Conference, Abidjan, Ivory Coast, 27 April-2 May 1986.
 - Mr. Abdou Tounkara, Bamako, Mali

D. TECHNOLOGY TRANSFER

While all FDT activities (institutional development, training, conferences and information dissemination) enhance the transfer of contraceptive technology to programs in LDCs, two major efforts are underway to introduce specific methods through research and to put in place the mechanisms to increase the contraceptive choices available to families in the developing world.

- a) Involvement of Private Sector Physicians on Voluntary Surgical Contraceptive in Mexico

This project has provided financial support for the development and implementation of training courses on voluntary surgical

contraceptive procedures and techniques of tubal occlusion for private physicians in three centers in Mexico. Fifty-four physicians have been trained in minilaparotomy and are currently providing services to women in private sector clinics in Oaxaca, Veracruz and Tijuana. All of the participants received a minilaparotomy kit donated by AVS after completing the training.

The training component of this project was a precursor to an evaluation research project designed to monitor the surgical performance of these newly trained physicians. Each procedure performed during the first year after training is being evaluated. The data are being collected and analyzed by FHI. To date over 700 cases have been collected. All admissions are expected to be completed by 6 October 1986 with follow-up of for final cases continuing until January of 1987.

The analysis will attempt to evaluate the role of the private sector physician in the provision of surgical contraceptive services in the three locations involved in the project. It will also seek to examine the relative vigor of the private sector surgical contraceptive services in the three participating centers. The safety, efficacy, and feasibility of short-term surgical contraceptive training courses as well as the trends in the learning curve for the physicians will be evaluated by analyzing data for all cases performed by the trainees.

FHI believes considerable potential exists for involving private physician in voluntary surgical contraception. Such sources are

likely to be cost effective, culturally acceptable and, as the consumer will always pay part or all of the cost, will be free of accusation of coercion.

b) Egypt - NORPLANT[®] Support (Long-Acting Contraceptive Steroids)

This three year research program is being conducted in Egypt by medical institutions and physicians under the directions of the Program Implementation Bureau of the National Population Council (NPC) and Family Health International (FHI). In order to facilitate management, coordination and planning for this extensive project the National Population Council asked the Egyptian Fertility Care Society (EFCS) to have direct administrative control over the NORPLANT[®] project. In July 1986 this project was shifted to the EFCS Offices.

The project has several components: a large scale program of training and introduction designed to assess the performance of NORPLANT[®] implants across a broad spectrum of providers; a detailed program of clinical research aimed at providing guidance to physicians and regulatory agencies regarding appropriate clinical management; a large-scale prospective cohort study to evaluate the relationship between NORPLANT[®] implants and potential sources of morbidity and mortality; a program of small acceptability studies designed to indicate patterns of acceptability in various sectors; and a post-marketing surveillance scheme to monitor rare adverse events.

Mr. Peter Miller, FHI's Program Director, arrived in Cairo, Egypt in late January. He currently has an office and support staff at EFCS. Mr. Miller will coordinate and facilitate activities of the involved agencies and organizations in support of this project.

E. SHARON CAMP FELLOWSHIP

The Sharon Camp Fellowship Program was established at FHI in 1984, to enable 1-2 collaborating researchers each year to spend approximately six months in residence at FHI working, with the benefit of FHI facilities and collegial support, on a project of mutual relevance and interest.

The second Fellow, Dr. Nabil Younis, from Al-Azhar University, Cairo, Egypt, is currently in residence at FHI, for the period July-December 1986.

Dr. Younis' primary project at FHI is to write a family planning program manager's manual for use in Egyptian clinics. If time permits, he also hopes to develop a brief contraceptive methods reference for Egyptian physicians and residents based specifically on Egyptian data available at FHI; and he hopes to complete some secondary analysis of a FHI sponsored vaginal tablet study he conducted previously.

F. INFORMATION DISSEMINATION

Research is useful only to the extent that its results are shared with the individuals and programs who provide family planning services, make program and policy decisions and further define the needs for research. A number of FDT activities support dissemination of FHI research findings to appropriate audiences around the world. This program of information dissemination includes specific publications such as FHI's newsletter, network; support for journal subscriptions for LDC investigators and programs; and through a new effort to make scientific literature on contraceptive research more useful and accessible to non-scientists who nevertheless are instrumental in the provision of family planning services.

a) International Journal of Gynaecology & Obstetrics

An important part of Family Health International's information dissemination strategy includes the distribution of subsidized subscriptions to the International Journal of Gynaecology & Obstetrics to members of the FHI network. During this fiscal year, 522 subscriptions were provided to research collaborators who depend regularly on the medical information the Journal contains to update their knowledge on the latest contraceptive methods and techniques. Letters of appreciation were received from many recipients thanking FHI for the valuable subscriptions.

FHI staff met in March with the new editor-in-chief and the managing editor to gain a better working knowledge of the various aspects

associated with the production of the Journal. The meeting created a stronger working relationship between FHI and IJGO. This led to increased collaboration on editing articles for publication. The total number of articles for which FHI provided editorial assistance this year was 12.

b) network

The spring issue of network, FHI's quarterly newsletter, was published in May with a focus on African pregnancy surveillance and immediately "sold out". To meet the increased demand for copies of the newsletter, the print run of the summer issue, on FHI's 15th anniversary and the Pill, was expanded to 4,000 copies. New attention has been paid to graphic elements in the newsletter to emphasize important points discussed in the articles. To reduce costs and streamline circulation of the newsletter, work was started to update FHI's mailing list for network.

The Information Management Committee chose four themes for the next year of network: 1) the contraceptive needs of breastfeeding women, 2) IUDs, 3) information dissemination, and 4) long-acting contraceptives. Work on the fall issue of the newsletter is well underway with the help of a new journalism intern from UNC's School of Journalism.

c) network IN SPANISH

Many of the individuals and programs in FHI's network are in non-English speaking areas of the world. To strengthen information dissemination to these colleagues, the first edition of network en espanol went into press in January. The articles published in this twelve page annual issue were a selection of regionally relevant articles published in the last five issues of network in English.

Distribution to more than 1300 Latin American investigators, clinicians and physicians, and to various health and family planning organizations was completed in early February. So far, responses to a survey questionnaire mailed separately have been extremely favorable. Plans for the next issue are underway. It is expected that articles published in the second issue will be written especially for the Spanish version of network and the possibility of having a Latin American scientist as a guest author is being explored.

d) network IN FRENCH

During this reporting period approval was obtained from AID to publish an annual 12-page French edition of network, in order to better serve French-speaking readers from Africa and Haiti. Articles were selected, re-edited, and translated, and the first issue of the new network en français has just been published. The Publications staff has worked to develop a French-language mailing list for the new publication.

e) Other Information Dissemination Activities

FHI is a treasure house of information of contraception and sterilization, while studies (above) have shown some methods of family planning, such as OCs, are grossly misunderstood. FHI, like several other cooperating agencies, attempts to get findings and accurate information to the media in the USA and worldwide. During 1986 a formal system to disseminate FHI research findings to the U.S. was established.

This system, along with increased personal contacts with news organizations, has resulted in coverage of FHI research over the Cable News Network, CBS-TV, US News and World Report, USA Today, the Los Angeles Times/Washington Post News Service, the Associated Press, the Detroit Free Press, Medical Tribune, national women's magazines, including McCalls, Modern Bride, Good Housekeeping and Essence, numerous state newspapers across the country and local newspapers, including the Durham Sun and Raleigh Times.

In family planning preempting alarmist reports is as important, or more important, than placing informative pieces. A major effort to provide a realistic perspective on the 1986 publication of papers on OCs and hepatocellular carcinoma was highly successful in preventing imbalanced reports and alarming headlines. After extensive contact with the media only one US newspaper - the Philadelphia Inquirer - covered the story and it did so in a responsible manner.

A larger mailing on an FHI study, "Oral Contraceptives and Life Expectancy" resulted in coverage by local radio and television stations, local newspapers, the Associated Press, and the New York Daily News. Publicity about the Latin American Advisory Committee meeting resulted in coverage by a local public radio station, a local newspaper and Voice of America.

With proven success in the U.S. media, the information dissemination program has begun to concentrate on efforts to disseminate information on FHI research internationally.

An interpretive article on maternal mortality, one of the topics chosen for dissemination efforts by FHI, was given to the Bangladesh Fertility Research Program and the Egyptian Fertility Care Society for use in their information dissemination programs. A similar FHI article has been accepted by South magazine, and FHI visitor Dr. Barbara Kwast was interviewed about maternal mortality by Dateline Africa, a national radio program.

FHI has arranged to have interpretive materials picked up over People News/Features Service, reaching 150 publications and over 600 newspapers, radio stations and television stations in developing countries. Additional outlets include a health advice column in the Indian Hindi press and a similar column in Bengali in West Bengal and Bangladesh.

The publications staff has begun preparations to run the press office at the World Bank's Safe Motherhood Conference, 10-13 February in Nairobi, and will take that opportunity to widen information dissemination efforts in Africa. To this end, international mailing lists are being updated and developed for both the ob/gyn community and journalists in developing countries. Other Information Education Communication (IEC) projects have been examined, and FHI continues to develop a resource base of French- and English-language publications that would be useful to this new international audience.

f) SPANISH TRANSLATIONS

During this last reporting period, work was completed to translate, print and distribute two publications in Spanish. The first was a series of five articles published by the Centers for Disease Control on the risks and benefits associated with hormonal contraception: "The Food & Drug Administration and Medroxyprogesterone Acetate"; "Long Term Oral Contraceptive Use and the Risk of Breast Cancer"; "Oral Contraceptive Use and the Risk of Ovarian Cancer"; "Oral Contraceptive Use and the Risk of Endometrial Cancer; and "The Noncontraceptive Health Benefits from Oral Contraceptive Use". The first four articles were published in the Journal of the American Medical Association and the fifth one originally in English in Family Planning Perspectives. Our colleagues in Latin America have responded enthusiastically to this publication, and have expressed their praise for the timely publication of information which sheds light on a very controversial issue in countries around the world. The second publication is a manual of Tubal Occlusion via

Minilaparotomy, published in Mexico in 1979 by Dr. Mario Domenzain and the Instituto de Nutricion. Distribution of both publications throughout Latin American centers, schools of medicine and clinics continued during this reporting period. So far, over 2,000 copies have been distributed.

Work was also completed in the translation of a document to be used by our Panamanian investigators in an epidemiology research project. In addition, during this reporting period, work was completed in the translation and editing of the curriculum materials developed by FHI to be used in research methodology workshops under our transfer of technology strategy. These materials will be provided to Latin American researchers who have expressed an interest in including them in their university curriculum and to those who are interested in repeating this type of workshop locally.

G. MONITORING OF COMPLIANCE WITH AID REGULATIONS

During this reporting period, FHI established a documentation system and engaged a consultant to monitor compliance with new AID regulations for core funding to programs in less developed countries. Findings from site visits in March and April to programs in Indonesia and Sri Lanka indicated that these programs remain in compliance with the AID regulations.

VII. MANAGEMENT

The structure of FHI and its major divisions remained unchanged during the reporting interval. The computerization of financial records and other aspects of administration has continued satisfactorily. A Scientific Projects Committee meets monthly and a Scientific Committee quarterly. There were 121 FHI employees as of 30 September 1986.

a) Board of Directors

The Board of Directors held two meetings:

Spring meeting: 15-16 June 1986, FHI and Chapel Hill, NC

Annual meeting: 28-29 September 1986, Research Triangle Park, NC

At the annual meeting, the Board authorized the establishment of a satellite office in the vicinity of Washington, DC.

The three incumbent Directors were reelected for three-year terms (1986-89):

Dr. Torrey Brown, Secretary, Department of Natural Resources for the State of Maryland;

Dr. Sharon Camp, Vice President, Population Crisis Committee, Washington, DC;

Mr. Donald Collins, President, International Services Assistance Fund, San Francisco, California.

The following Corporate officers were appointed at the annual meeting:

Dr. Roger Short, Chairperson
Dr. Torrey Brown, Vice Chairperson
Dr. Malcolm Potts, President/COO
Mr. John Ganley, Executive Vice President
Gen. Alexander Andrews, Secretary
Mr. Fred Coe, Jr., Treasurer.

The following Directors were appointed by the Board as observers (1986/87) to FHI's external advisory committees:

Drs. Torrey Brown and Pramilla Senanayake, Protection of Human Subjects Committee;

Drs. Arthur Christakos and Pramilla Senanayake, Technical Advisory Committee;

Dr. Sharon Camp, Latin American Advisory Committee.

b) Protection of Human Subjects Committee (PHSC)

Three meetings of the Protection of Human Subjects Committee (PHSC) were held at FHI on 15 November 1985, 21 March 1986, and 13 June 1986 to review 44 research proposals, inclusive of amendments and those for expedited review.

Two members rotated off at the end of the calendar year: Dr. Mary Jane Gray, an obstetrician/gynecologist, of Student Health Services at the University of North Carolina at Chapel Hill and Dr. Kay Omran, an obstetrician/gynecologist, with the George Washington University Health Plan, Washington, DC.

Mr. Robert R. Price, the legal representative of the Jordan, Price, Wall, Gray and Jones law firm of Raleigh, NC, was reappointed for a second three-year term.

Two new members were appointed as public health representatives for three-year terms:

Elizabeth Mann, MD, Associate Professor, Department of Anesthesiology, University of North Carolina's School of Medicine and the Director of Clinical Services for the Department of Anesthesiology at North Carolina Memorial Hospital at Chapel Hill. From 1972-76, she was affiliated with the University of Virginia Medical Center as the Assistant Professor of Anesthesiology. She is licensed as a medical doctor in North Carolina and Virginia and is the author/co-author of several publications related to the field of anesthesiology.

David A. Savitz, PhD, Assistant Professor, Department of Epidemiology, University of North Carolina's School of Public Health, Chapel Hill. Prior to affiliating with the University of North Carolina, Dr. Savitz served five years as Assistant Professor, Department of Preventive Medicine/Biometrics at the University of Colorado School of Medicine. While at the University of Colorado, he directed the epidemiology program for the community health section, chaired the Comprehensive Examination Committee, served on the Appointments/Promotions and the MS in Preventive Medicine Admissions Committees. Dr. Savitz has conducted a number of investigative research projects and has published extensively in the epidemiology field.

The operating and administrative procedures for the protection of human subjects were audited by the Food and Drug Administration (FDA) in December 1985 and resulted in three recommendations:

- 1) The PHSC's Operating Guidelines should be specific in defining the frequency of periodic and continuing review of research projects.
- 2) The PHSC's Operating Guidelines should provide procedures for identifying and handling research projects which may require more frequent review than once a year.
- 3) The PHSC should establish procedures for allowing direct communications between the clinical investigators and the PHSC.

To comply with the first two FDA recommendations, the PHSC adopted measures to decide the frequency of review when reviewing research proposals with the Committee's decisions being cited in the minutes record.

To comply with the third FDA recommendation, Rose De Buysscher, an Assistant Program Coordinator of the Field Development and Training Division, has been appointed to the PHSC, increasing the committee composition from nine to ten. This represents the first time that a member of the FHI staff has been appointed to the PHSC. The Committee's FHI staff representative will be responsible for direct communications between the PHSC and the clinical investigators.

The PHSC's Operating Guidelines have been revised to reflect the adopted measures.

An article reviewing the issues facing a US based IRB with worldwide responsibilities has been prepared for publication.

c) Technical Advisory Committee (TAC)

The Technical Advisory Committee (TAC) held its annual meeting at FHI on 10 July 1986. Dr. Benjamin Sachs (obstetrician/gynecologist and perinatologist) rotated off the committee, having completed a three-year term. Three committee members were reappointed for a second three-year term:

Linda Atkinson, PhD (physiologist), a reproductive health consultant residing in Portola Valley, California;

Willard Cates, Jr., MD, MPH (epidemiologist/internal and preventive medicine physician), Director, Division of Sexually Transmitted Diseases, Centers for Disease Control, Atlanta, Georgia;

William Droegemueller, MD (obstetrician/gynecologist), Chairman, Department of Obstetrics/Gynecology, University of North Carolina's School of Medicine, Chapel Hill.

Three new members were appointed for three-year terms to fill residual vacancies from last year:

Michael John Kennedy Harper, PhD, ScD (reproductive biologist), Chief, Division of Reproductive Research, Department of Obstetrics/Gynecology, University of Texas Health Science Center, San Antonio, Texas;

Judith P. Rooks, CNM, MS, MPH (nurse midwife/epidemiologist),
Kaiser Center for Health Research, Portland, Oregon;

Rochelle N. Shain, PhD (social scientist), Associate Professor,
Department of Obstetrics/Gynecology, University of Texas Health
Science Center, San Antonio, Texas.

d) Expert Meetings

Sixteen expert scientists field were assembled 11-12 December 1985 to explore potential research and development leads in spermicides. Of the seven identified classes of compounds, two appeared worthy of pursuit as potential spermicidal agents. The formulation and delivery system were considered as important as the spermicide. Initial research with propranolol revealed that the delivery system greatly influenced the effectiveness of the spermicide in vitro. Attention was also given to combining agents with a number of different actions on sperm into a common formulation, ie, surfactants, enzyme inhibitors, sperm immobilizers and substances that might affect cervical mucus.

Ten of the leading scientists in zona pellucida research were assembled for a workshop at Baylor College of Medicine in Houston, Texas, 22-24 February 1986, to accelerate basic research in isolating/identifying potential zona immunogens which may lead to the development of an antifertility vaccine. Suppression of fertility in mice has been demonstrated by passively immunizing them with

monoclonal antibodies specific to the mouse zonae pellucida. Infertility in marmoset monkeys has been achieved by actively immunizing them with whole porcine zonae pellucida; however, there were difficulties in maintaining antibody titers in these animals. Work is in progress to identify a basic functional protein fragment from the zona pellucida which will elicit sufficient antibody response to inhibit fertility without causing any damage to the ovaries or endocrine systems. The scientists expressed pleasure in being assembled to unify the terminology, to exchange ideas and to refine approaches for isolating/screening zona pellucida proteins.

A multidisciplinary group of 16 experts in sexually transmitted diseases (STDs) from Africa, Europe and the United States was assembled in Gambia, 28-30 April 1986, to formulate priorities for STD research and control in Africa, which has an alarmingly high incidence of STDs and their sequelae, most notably infertility. Many African countries are becoming alert of the STD public health menace; however, due to deteriorating economies they are unable to provide the technical and financial effort necessary to attack the epidemic. The recognized consequences of STDs seriously affect a country's public health economy and development.

Thirty-six scientific experts were assembled in Toronto, Canada, 30 June 1986, for a sperm antigen workshop to examine 56 monoclonal antibodies (MABs) from 15 different laboratories. Twenty-two MABs had one or more antifertility effects. Two were active against the acrosome and six against mature sperm. Some of the MABs, but not all, cross-reacted with other tissues. Monoclonal antibodies' effect

on fertility was assessed by the hamster egg test, in vitro fertilization in the mouse, mucus penetration, and sperm agglutination.

The Facilities Management Subcommittee of the Board is reviewing options for accommodation when the lease on FHI's current building expires in 1988. The Board has established a Program Subcommittee to review long-term directions and likely funding patterns for the institution.

The following table lists expenditures for the period covered by this report.

Expenditures

1 October 1985 - 30 September 1986

Salaries & Fringe Benefits	\$2,000,024
Service Centers	461,557
Consultant & Professional Fees	203,997
Contracted Labor	20,198
Travel - domestic	101,186
Travel - foreign	644,449
Supplies - office	26,526
Supplies - medical	71,064
Printing & Reprints	56,020
Medical Equipment	4,694
Freight	14,045
Dues & Registration Fees	13,409
IJGO Subscription	19,792
Other Purchased Services	100,227
Keypunching	28,470
Other Expenses & Bank Service Charges	57,646
Data Purchases	302,108
Subcontracts	1,914,975
General and Administrative Costs	<u>1,971,029</u>
TOTAL	\$8,011,416

VIII. FUTURE PLANS

With a successful Fiscal Year 1986 behind us FHI moves into the new reporting period, optimistic that there will be significant progress in a number of areas but concerned by the rate of new contraceptive developments.

The management of FHI believes that it can make its biggest contribution under the Cooperative Agreement first by being responsive to the stated priorities of AID's Population Office, second by using the funds which we have been able to generate from the private donor community and through commercial contracts in such a way as to complement the programs funded by AID and third by continually enlarging the capabilities of our organization to manage all of the elements of a population program.

To our knowledge, none of AID's cooperating agencies in the family planning field has been able to move from almost total AID support to achieve a significant degree of additional funding to support its goals. FHI seeks to be the first. In 1987 we expect to take a small step in that direction by activating a for-profit subsidiary to handle commercial contracts. We hope that a larger volume of for-profit activity will generate funds for our family planning work.

With respect to our current AID programs, long-acting steroids, more particularly the preparation of materials for USFDA marketing approval of NET microcapsules, will again be the main focus of

clinical trials activity in 1987. The NORPLANT® program will also continue to receive the heavy emphasis in 1987 that it had in 1986.

We see a systems approach as being the way that future contraceptive developments will be handled, in a world becoming more sophisticated with respect to contraception and family planning, but still needing the extra push that only large donors such as AID can provide.

FHI's NORPLANT® package, for example, includes training, evaluation and the introduction of postmarketing surveillance and represents a much more systematic approach to the bringing of a new technology to the Third World than has been attempted previously.

Although a large part of the funds available to us from the AID program will be used in the long-acting steroids, we will also be advancing the studies on new spermicides, the Filshie Clip and other contraceptives. Building on our experience with the Latin American Advisory Committee, FHI will actively support efforts to shorten the time span required for the introduction of new contraceptives in the Third World, particularly in Latin America. This work has the promise of materially affecting the length of time which is now required to get new drugs introduced in the Third World and we are enthusiastic about its possibilities.

1987 and future years will see FHI placing more emphasis on the dissemination of information about FHI's research. We have seen that government officials and other people of influence who receive information on maternal mortality, for example, are influenced by

the information and do make better decisions with respect to the allocations of health monies when they are informed.

Although a portion of our work is developed in-house, we are dependent on other organizations for new ideas and new product flow. We are particularly interested in the successful initiation of the CONRAD project and look forward to conducting the clinical trials, systems management and FDA related activities on the new contraceptives and devices generated by the project.

Finally, we see an important need in 1987 and the years thereafter for greater collaboration between the managers of AID's cooperating agencies in a period when funds will not be as plentiful as they have been in the recent past. We wish to be part of a strong effort to obtain as much as possible out of every dollar that AID can invest in Family Planning.

Appendix A

Publications List

FAMILY HEALTH INTERNATIONAL
ANNUAL PUBLICATIONS LIST
October 1, 1985 - September 30, 1986

Published

LP Cole, DM Potts, C Aranda, B Behlilovic, E-S Etman, J Moreno, L Randic, R Apelo, M Thomas. Comparative Copper IUD Trials. In: Intrauterine Contraception: Advances and Future Prospects. GI Zatuchni, A Goldsmith, JJ Sciarra, eds. (Philadelphia: Harper & Row, 1985), p. 95. (85-29)

RG Wheeler, LP Cole, R Santiso. IUDs With or Without Strings. In: Intrauterine Contraception: Advances and Future Prospects. GI Zatuchni, A Goldsmith, JJ Sciarra, eds. (Philadelphia: Harper & Row, 1985), p. 420. (85-30)

LP Cole, A Goldsmith. Contraceptive Services for the Postpartum and Postabortion Woman. In: Gynecology and Obstetrics, JJ Sciarra, ed. (Philadelphia: Harper & Row), 1985, Vol 6, Chapter 15, p. 1. (85-31)

RN Shain, M Potts. Need for and Acceptability of Long-acting Steroidal Contraception. In: Long-acting Contraceptive Delivery Systems. GI Zatuchni, JS Shelton, A Goldsmith, JJ Sciarra, eds. (Philadelphia: Harper & Row), 1985, p. 1. (85-32)

JH Lewis, B Janowitz, M Potts. Methodological Issues in Collecting Data from Traditional Birth Attendants. Int J Gynaecol Obstet 23(4):291, 1985. (85-33)

S Beltran, C Waszak. Estudio comparativo de dos dispositivos intrauterinos, la espiral delta y la espiral de Lippes D colocados a pacientes postparto. Rev Colombiana Obstet Ginecol 26(1):43, 1985. (85-34)

JE Higgins, LR Wilkens, I Chi, RA Hatcher. Hospitalizations Among Black Women Using Contraceptives. Am J Obstet Gynecol 153(3):280, 1985. (85-35)

D Nichols, S Ndiaye, N Burton, B Janowitz, L Gueye, M Gueye. Vanguard Family Planning Acceptors in Senegal. Stud Fam Plann 16(5):271, 1985. (85-36)

R Bhatt, CS Waszak. Four-Year Follow-Up of Insertion of Quinacrine Hydrochloride Pellets as Means of Nonsurgical Female Sterilization. Fertil Steril 44(3):303, 1985. (85-37)

I Chi. IUD Use in Diabetic or Lactating Women or Women After Cesarean Delivery - An Epidemiologic Perspective. Adv Contracept Deliv Syst, Monograph II, p. 287, 1985. (85-38)

I Chi, LR Wilkens, CS Waszak. Difficulty in Removal--A Neglected IUD-related Rare Event. Adv Contracept Deliv Syst, Monograph II, p. 265, 1985. (85-39)

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- P Lamptey, C Klufio, SC Smith, PJ Feldblum. A Comparative Study of Neo Sampoo, Ortho Vaginal Tablets and Emko Vaginal Tablets in Accra, Ghana. *Contraception* 32(5):445, 1985. (85-54)
- S Onay-Basaran, JL Olsen, RG Wheeler. Dissolution Profiles of Long-acting Quinacrine Hydrochloride Pellets II. *Drug Dev Ind Pharm* 11(12):2155, 1985. (85-55)
- I Chi, M Potts, L Wilkens. Rare Events Associated with Tubal Sterilizations: An International Experience. *Obstet Gynecol Surv* 41(1):7, 1986. (86-01)
- JA Fortney, I Susanti, S Gadalla, S Saleh, SM Rogers, M Potts. Reproductive Mortality in Two Developing Countries. *Am J Pub Health* 76(2):134, 1986. (86-02)
- D Nichols, OA Ladipo, JM Paxman, EO Otolorin. Sexual Behavior, Contraceptive Practice, and Reproductive Health Among Nigerian Adolescents. *Stud Fam Plann* 17(2):100, 1986. (86-03)
- I Chi, LR Wilkens, AJ Siemens, J Lippes. Syncope and Other Vasovagal Reactions at Interval Insertion of Lippes Loop D - Who is Most Vulnerable? *Contraception* 33(2):179, 1986. (86-04)
- GS Grubb. Human Papillomavirus and Cervical Neoplasia: Epidemiological Considerations. *Int J Epid* 15(1):1, 1986. (86-05)
- M Potts, AJ Siemens, N Burton. Developpement des produits contraceptifs la situation aux U.S.A. au milieu des annees 1980. *Contraception-fertilite-sexualite* 14(3):247, 1986. (86-06)
- S Saleh, S Gadalla, JA Fortney, SM Rogers, DM Potts. Accidental burn deaths to Egyptian women of reproductive age. *Burns* 12:241, 1986. (86-07)
- JA Fortney, MJ Harper, M Potts. Oral Contraceptives and Life Expectancy. *Stud Fam Plann* 17(3):117, 1986. (86-08)
- M Potts. Doctors and Torture. Letter. *JAMA* 225(20):2760, 1986. (86-09)
- JA Fortney, M Bonhomme, GS Grubb, M Potts. Letter, not titled. (Oral contraceptives and hepatocellular carcinoma). *Br Med J* 292:1392. (86-10)
- I Chi, A Whatley, LR Wilkens, M Potts. In-hospital maternal mortality risk by cesarean and vaginal deliveries in two less developed countries - A descriptive study. *Int J Gynaecol Obstet* 24(2):121, 1986. (86-11)
- MJ Rosenberg, KF Schultz, NN Burton. Sexually Transmitted Diseases in Sub-Saharan Africa. *Lancet* 2:152, 1986 (letter). (86-12)
- B Janowitz, TT Kane, JM Arruda, DL Covington, L Morris. Side Effects and Discontinuation of Oral Contraceptive Use in Southern Brazil. *J Biosoc Sci* 18:261, 1986. (86-13)

L Andolsek, RA Teeter, M Kozuh-Novak, RG Wheeler, JA Fortney, MJ Rosenberg. Time to Conception After IUD Removal: Importance of Duration of Use, IUD Type, Pelvic Inflammatory Disease and Age. Int J Gynaecol Obstet 24(3):217, 1986. (86-14)

JB Smith, NN Burton, G Nelson, JA Fortney, S Duale. Hospital Deaths in a High Risk Obstetric Population: Karwa, Zaire. Int J Gynaecol Obstet 24(3):225, 1986. (86-15)

JA Fortney, JE Higgins, KI Kennedy, LE Laufe, LR Wilkens. Delivery Type and Neonatal Mortality Among 10,749 Breeches. Am J Pub Health 76(8):980, 1986. (86-16)

ET Robinson. The Deathtrap Down Tobacco Road. South, March 1986, p. 96. (86-17)

ET Robinson. Smoke Signals. West Africa 3573:410, 1986. (86-18)

KJ Lassner B Janowitz, CBM Rodrigues. Sterilization Approval and Follow-Through in Brazil. Stud Fam Plann 17(4):188, 1986. (86-19)

DL Covington, EO Otolorin, B Janowitz, DS Gates, PJ Lamptey, OA Ladipo. Physician Attitudes and Family Planning in Nigeria. Stud Fam Plann 17(4):173, 1986. (86-20)

RW Rochat, PP Bhiwandiwalla, PJ Feldblum, HB Peterson. Mortality Associated with Sterilization: Preliminary Results of an International Collaborative Observational Study. Int J Gynaecol Obstet 24(4):275, 1986. (86-21)

B Janowitz, DL Covington, M Suazo, M Potts. Conocimientos y Practicas de las Distribuidoras Comunitarias de Anticonceptivos en Honduras. Bol Of Sanit Panam 101(1):48, 1986. (86-22)

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Appendix B

Consultant Reports

Completed Consultant Reports (CRs)

30 September 1985 - 30 September 1986

<u>Title</u>	<u>Prepared for</u>	<u>Center</u>	<u>Study</u>
A Comparative Clinical Trial of Emko and Ortho Vaginal Tablets in Cairo, Egypt	N. Younis	314	793
Minilaparotomy with vs. without Antibiotics in Rangpur, Bangladesh	M. Ismail Huq	786	6960
A Comparative Study of Norinyl 1/35 vs. Lo-Ovral in Guatemala City, Guatemala	R. Santiso Galvez	841	8825
Surveillance of Female Sterilization in Petit Goave, Haiti	F. Lolagne	8011	6900
Surveillance Study of Female Sterilization in Saint Marc, Haiti	R. Vincent	8013	6900
A Comparative Study of Vasectomy Performed with vs. without Prophylactic Antibiotics	S. N. Bhuiyan	720	7030
A Retrospective Study of Depo Provera Users vs. Oral Contraceptive Uses in Colombo, Sri Lanka	S. Basnayake	703	8880
Norinyl 1/35 vs. Norinyl 1/50 in Yugoslavia	B. Behlilovic	024	8850
Norinyl 1/35 vs. Norinyl 1/50 in Costa Rica	Aranda	831	8850
Surveillance Study of Female Sterilization at Six Centers in Haiti	Division de l'Hygiene Familiale et de la Nutrition	Multi	6900
Surveillance of Female Sterilization in Cap Haitien	G. Lubin	8010	6900
A Comparative Study of Female Sterilization via Minilaparotomy Using the Secu Clip or the Tubal Ring	J. Thow	739	6256
Evaluation of Prophylactic Antibiotics in Male Sterilization, Dhaka Medical College Hospital, Dhaka, Bangladesh	M. A. Begum	714	730

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<u>Title</u>	<u>Prepared for</u>	<u>Center</u>	<u>Study</u>
A Comparative Study of Norinyl 1/35 vs. Norinyl 1/50	S. Basnayake	703	8850
Hysteroscopic Delivery of an Intra-tubal Device for Female Sterilization in Paris, France	J. Hamou	279	6101
Long term Follow-up of Female Sterilization in Bangkok, Thailand	S. Koetsawang	075	Multi
Percutaneous Occlusion of the Vas vs. Standard Incision and Diathermy in London, England	T. Black	295	7120
A Comparative Study of Progestogen-Only Oral Contraceptives vs. Non-Hormonal Methods in Lactating Women in Kuala Lumpur, Malaysia	S. Yuliawiratman	792	875
Surveillance Study of Female Sterilization in Cayes, Haiti	S. Louisaint	8009	6900
Wingsound II	G. Serani	850	594
Wingsound II	Topozada	340	594
Wingsound II	Zighelboim	100	594

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Appendix C

Study Status Lists

STUDY STATUS LIST
FEMALE STERILIZATION

OCTOBER 1986

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Description of Study: Evaluation of Femtest - Pre and Post Sterilization

Study Number: 6102

Total Number of Cases: 110

Total Number of Studies: 1

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed		Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADM	FOLLOW-UP			
850	Guzman-Serani/ Chile	85/003	5/85	7/85	2/87	110	111	88	09/19/86	8/86 CEC	Active pilot study

Description of Study: Evaluation of Femtest - Pre Sterilization

Study Number: 6103

Total Number of Cases: 50

Total Number of Studies: 2

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed		Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADM				
739	Tnouw/ Indonesia	FS 86/010	9/86		1/87	25				10/86 MK	Training 9/86
759	Moeluek/ Indonesia	FS 86/012	9/86		1/87	25				10/86 MK	Training 9/86

STUDY STATUS LIST
FEMALE STERILIZATION

OCTOBER 1986

122

Description of Study: Evaluation of Femtest - Post Sterilization

Study Number: 6104

Total Number of Cases: 50

Total Number of Studies: 2

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed		Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADH				
739	Thouw/ Indonesia	FS 86/011	9/86		1/87	25				10/86 MK	Training 9/86
759	Moeloek/ Indonesia	FS 86/013	9/86		1/87	25				10/86 MR	Training 9/86

**STUDY STATUS LIST
FEMALE STERILIZATION STUDY**

OCTOBER 1986

26

Description of Study: Retrospective Filshie Clip

Study Number: 6240

Total Number of Cases: 800

Total Number of Studies: 1

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed			Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADM	1mo FU	12mo FU			
747	Arshat/ Malaysia	FS 86/009	9/86		9/87	800					9/86 SK	Pretests rec'd

STUDY STATUS LIST
FEMALE STERILIZATION

OCTOBER 1986

Description of Study: Laparoscopy - Filshie Clip

Study Number: 6249

Total Number of Cases: 1900

Total Number of Studies: 9

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed				Date Last Shipment	Date Last Site Visit	Status/ Comments	
							ADH	1mo FU	6mo FU	12mo FU				24mo FU
234	Yuzpe/Canada	FS 85/007	6/85	7/85	4/87	200	94	72	32	11	X	09/08/86	5/86 JB	Active
285	O'Brien/ England	FS 85/020	10/85	1/86	11/87	100	26	23	3		X	09/16/86	8/86 JB	Active
224	Condie/ England	FS 85/021	10/85		11/87	200							8/86 JB	Awaiting 1st forms.
286	Newton/ England	FS 85/021	10/85	4/86	11/87	300	43	37	9			08/05/86	8/86 JB	Active
293	Pogmore/ England	FS 85/021	10/85		11/87	200							8/86 JB	Awaiting 1st forms.
201	Campbell/ England	FS 86/006	04/86	8/86	06/88	300	17				X	09/16/86	8/86 JB	Active
200	Baird/ Scotland	FS 86/007	04/86	7/86	06/88	200	13	6			X	09/17/86	8/86 JB	Active
283	Gomel/Canada	FS 85/009	2/86	7/86	06/88	200	3	2			X	07/29/86	2/86 JB	Active
274	Milne/Canada	FS 86/005	5/86		4/88	200					X		5/86 JB	Awaiting 1st forms.

**STUDY STATUS LIST
FEMALE STERILIZATION**

OCTOBER 1986

12/27

Description of Study: Minilaparotomy - Filshie Clip vs. Secuclip (Admissions closed)

Study Number: 6258

Total Number of Cases: 175

Total Number of Studies: 2

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed				Date Last Shipment	Date Last Site Visit	Status/ Comments	
							ADM	1mo FU	6mo FU	12mo FU				24mo FU
836	Nagahata/ Peru	FS 84/005	2/84	7/84	2/87	75	75	75	74	73	69	08/28/86	7/86 CEC EGW	FU only
865	Bossemeyer/ Brazil	FS 84/004	6/84	8/84	2/87	100	83	69	78	69		09/23/86	4/86 DB	FU only

STUDY STATUS LIST
FEMALE STERILIZATION

OCTOBER 1986

Description of Study: Minilaparotomy - Filshie Clip vs Pomeroy

Study Number: 6260

Total Number of Cases: 1400

Total Number of Studies: 4

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed				Date Last Shipment	Date Last Site Visit	Status/ Comments	
							ADM	1mo FU	6mo FU	12mo FU				24mo FU
075	Suporn/ Thailand	FS 85/017	9/85	12/85	9/87	300	224	237	35		X	09/25/86	10/86 HR	Active
600	Apelo/ Philippines	FS 83/009	4/84	4/84	3/87	300	300	214	140	148	54	10/02/86	9/86 SK	FU only
781	Yan/ Taiwan	FS 84/003	4/84	4/84	2/87	200	200	167	142	102	18	09/17/86	9/86 SK	FU only
832	Lasso de- la Vega/Panama	FS 84/007	2/84	2/84	8/89	600	300	297	291	289	217	09/17/86	7/86 CEC	Active

STUDY STATUS LIST
FEMALE STERILIZATION

OCTOBER 1986

27/2

Description of Study: Minilaparotomy - Filshie Clip vs. Tubal Ring

Study Number: 6264

Total Number of Cases: 1200

Total Number of Studies: 4

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADM	1mo FU	6mo FU	12mo FU	24mo FU			
083	Contreras/ Panama	FS 84/019	7/84	10/84	7/87	300	297	284	283	194	9	09/17/86	7/86 CEC	FU ONLY
451	Githiari/ Kenya	FS 86/004	2/86	10/86	7/88	400	28				X	10/02/86	9/86 PL	Active
836	Nagahata/ Peru	FS 84/011	12/84	3/85	9/87	200	200	186	152	69		08/28/86	7/86 CEC EGW	Active
665	Bossemeyer/ Brazil	FS 84/022	9/85	11/85	9/87	300	54	41	23			08/23/86	4/86 DB	Active

STUDY STATUS LIST
FEMALE STERILIZATION

OCTOBER 1986

Description of Study: Laparoscopy - Filshie Clip vs. Tubal Ring

Study Number: 6265

Total Number of Cases: 1800

Total Number of Studies: 7

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed				Date Last Shipment	Date Last Site Visit	Status/ Comments	
							ADH	1mo FU	6mo FU	12mo FU				24mo FU
081	Moreno/ Panama	FS 85/002	2/85	3/85	10/87	300	300	223	405	227	2	08/28/86	7/86 CEC	FU Only
739	Thouw/ Indonesia	FS 85/018	11/85	6/86	9/87	150	12	6			X	07/25/86	10/86 MR	Active
759	Hoeloeck/ Indonesia	FS 85/019	11/85	7/86	9/87	150	40	37			X	07/25/86	10/86 MR	Active
892	Ortiz- Mariscal/Mexico	FS 85/012	7/85	5/86	3/87	300	44	44				09/08/86	9/86 CEC	Active
8044	Cordero/ Dominican Republic	FS 85/011	8/85	-	4/87	300							6/86 CEC	EGI 10/86

STUDY STATUS LIST
FEMALE STERILIZATION

OCTOBER 1986

212

Description of Study: Nihilaparotomy - Filshie Clip vs. Wolf Clip

Study Number: 6266

Total Number of Cases: 1200

Total Number of Studies: 4

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed				Date Last Shipment	Date Last Site Visit	Status/ Comments	
							ADM	1mo FU	6mo FU	12mo FU				24mo FU
832	Lasso de- la Vega/Panama	FS 85/013	8/85	9/85	4/87	300	300	288	227	22	X	09/17/86	7/86 CEC EGW	FU Only
8044	Cordero/ Dominican Republic	FS 85/014	8/85	10/85	5/87	300	187	166	65		X	09/29/86	6/86 CEC	Active
684	Thambu/ Malaysia	FS 85/024	9/86			200					X		9/86 SK	EDI 9/86
685	Vettivelu/ Malaysia	FS 85/024	9/86			100					X		9/86 SK	EDI 9/86

FEMALE STERILIZATION

OCTOBER 1986

617

Description of Study: Laparoscopy - Filshie Clip vs. Wolf Clip

Study Number: 6267

Total Number of Cases: 1200

Total Number of Studies: 4

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADH	1mo FU	6mo FU	12mo FU	24mo FU			
841	Santiso/ Guatemala	FS 85/010	2/86	2/86	3/87	300	254	207	38		X	09/03/86	7/86 CEC	Active
8009	Louissaint/ Haiti	FS 85/016	8/85	9/85	5/87	300	213	189	57		X	08/11/86	5/86 KJ	Active
864	Uribe/Mexico	FS 85/022	11/85	1/86	9/87	300	123	122			X	09/03/86	9/86 CEC	Active
100	Zigelboim/ Venezuela	FS 86/001	12/85	1/86	12/88	300	105	94	9			09/05/86	6/86 CEC	Active

STUDY STATUS LIST
FEMALE STERILIZATION STUDY

OCTOBER 1986

82

Description of Study: Bipolar Electrocautery vs. Filshie Clip

Study Number: 6269

Total Number of Cases: 1200

Total Number of Studies: 4

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADH	1mo FU	3mo FU	12mo FU	24mo FU			
798	Ratnam/Singapore					150								Under Development
750	Kwak/Korea					300								Under Development
781	Tsai/Taiwan	FS 86/015	9/86		11/88	150						9/86 SK		EDI 9/86
231	Leodolter/ Austria	FS 86/014	9/86		11/88	300						9/86 JE		EDI 9/86
260	Wagenbichler/ Austria	FS 87/001				200						9/86 JB		Under development

STUDY STATUS LIST
FEMALE STERILIZATION STUDY

OCTOBER 1986

10

Description of Study: Minilaparotomy and Laparoscopy - Filshie Clip

Study Number: 6700

Total Number of Cases: 200

Total Number of Studies: 1

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed			Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADM	1mo FU	6mo FU			
b063	Abdala/ Brazil	FS 85/015	6/85	7/85	3/87	200	198	197	197	08/28/86	4/86	FU Only

FEMALE STERILIZATION STUDY

OCTOBER 1986

287

Description of Study: Longterm Follow-up of Female Sterilization

Study Number: Multi

Total Number of Cases: 700

Total Number of Studies: 2

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed				Date Last Shipment	Date Last Site Visit	Status/ Comments	
							ADH	1mo FU	6mo FU	12mo FU				24mo FU
723	Ahmed/ Bangladesh	FS 84/002	8/84	11/84	10/86	200	X	X	X	X	60	7/18/85	3/86	Active

487

STUDY STATUS LIST
NORPLANT® Implant Studies

Description of Study: NORPLANT® IMPLANTS - FCO 3132

DATE: OCTOBER 1986

Study Number: 866

Total Number of Cases: 2500

Total Number of Studies: 20

Center Number	Investigator/ Country	Index Number	Date Initiated	Expiration Date	Proposed No. of Cases	Forms Processed						Date Last Shipment	Date Last Site Visit
						ADM	FU Slot						
040	O. LADIPO NIGERIA	NOR 85/014	10/11/85	8/87	70	68	57	38	20			9/16/86	6/26/86
041	A. COLLISON GHANA	NOR 85/012	10/16/85	8/87	100							7/02/86	6/19/86
042	C. EKWEMPU NIGERIA	NOR 85/013	10/10/85	8/87	50	51	53	44	19			9/29/86	6/19/86
100	I. ZIGHELBOIM VENEZUELA	NOR 86/006		12/87	100								
435	O. FAKEYE NIGERIA	NOR 86/004	1/13/86	12/87	50	49	46	42	10			8/11/86	6/25/86
437	M. DIEJOMAH NIGERIA	NOR 85/015	10/09/85	8/87	50	54	51	50	40			7/30/86	6/25/86
453	J. OTUBU NIGERIA	NOR 86/005	11/08/85	8/87	50	36	26	6				9/25/86	6/20/86
600	R. APELO PHILIPPINES	NOR 86/007	2/14/86	10/87	100	61	44	34	12	1		8/05/86	6/16/86
602	I. BENITEZ PHILIPPINES	NOR 86/008	6/15/86	1/87	100	12	4					9/05/86	6/17/86
703	S. BASNAYAKE SRI LANKA	NOR 85/010	5/14/85	4/87	200	200	218	210	204	148		9/17/86	8/05/86
704	S. BEGUM BANGLADESH	NOR 85/001	2/17/85	2/87	200	200	191	176	139	41		8/06/86	7/20/86
718	T. CHOWDHURY BANGLADESH	NOR 85/002	2/20/85	2/87	200	200	190	190	154			9/05/86	7/17/86

for

Center Number	Investigator/ Country	Index Number	Date Initiated	Expiration Date	Proposed No. of Cases	Forms Processed						Date Last Shipment	Date Last Site Visit
						ADM	FU Slot 1	FU Slot 3	FU Slot 6	FU Slot 12	FU Slot 18		
721	S. RAHMAN BANGLADESH	NOR 85/003	2/19/85	2/87	200	200	196	192	136	54		9/05/86	7/19/86
729	M. CHHETRI NEPAL	NOR 85/004	2/14/85	3/87	300	307	304	263	277	198	7	8/19/86	8/13/86
731	S. RAJBHANDARI NEPAL	NOR 85/008	5/09/85	4/87	100	100	71	67	44	18		8/19/86	8/12/86
749	S. CHINNATAMBY SRI LANKA	NOR 85/009	5/16/85	4/87	200	200	153	139	119	55		9/08/86	7/31/86
758	I. VINITHARATNE SRI LANKA	NOR 85/011	5/17/85	4/87	200	200	200	198	193	19		9/17/86	7/29/86
8017	R. BOULOS HAITI	NOR 86/001	11/11/85	10/87	100	98	87	71	39			9/29/86	11/11/85
8331	G. THEODORE HAITI	NOR 86/003	11/14/85	10/87	100	100	92	65	25			9/29/86	11/14/85
8332	F. LOLAGNE HAITI	NOR 86/002	11/16/85	10/87	50	50	50	36	15			8/11/86	11/16/85

STUDY STATUS LIST
VAGINAL CONTRACEPTION
3172

OCTOBER 1986

5/2

Description of Study: DIAPHRAGM WITH SPERMICIDE VS. DIAPHRAGM WITHOUT SPERMICIDE VS. SPERMICIDE ONLY(DELFEN FOAM)

Study Number: 7788

Total Number of Cases: 432

Total Number of Studies: 1

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	Forms Processed				Date Last Shipment	Date Last Site Visit	Status/ Comments	
						ADM	1 mo FU	3 mo FU	6 mo FU				12+ mo FU
298	Guillebaud/England	85/004	9/84 / 9/85	7/88	432	53	53	44	7	0	09/23/86	8/86	Active

STUDY STATUS LIST
VAGINAL CONTRACEPTION
3171

OCTOBER 1986

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Description of Study: OVT (60 MG. MEFEGOL) VS. OVT (100 MG. NONOXYNOL-9)

Study Number: 7798

Total Number of Cases: 600

Total Number of Studies: 4

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
						ADM	1 mo FU	3 mo FU	6 mo FU	12+ mo FU			
44	Klufio/Ghana	84/008	9/84 / 12/84	12/86	150	150	123	124	120	63	08/19/86	6/86	Active
4500	Ghunney/Ghana	84/007	9/84 / 1/85	2/87	150	27	27	27	25	21	08/19/86	6/86	Active
773	Sumana/Thailand	85/005	9/85 / 7/86	1/88	100	33	8	0	0	0	09/10/86	3/86	Active
Possible Open												Planned	

STUDY STATUS LIST
VAGINAL CONTRACEPTION
3171

OCTOBER 1986

Description of Study: OVT (60 MG. MEFEGOL) VS. OVT (100 MG. NONOXYNOL-9)

Study Number: 7799

Total Number of Cases: 300

Total Number of Studies: 5

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
						ADM	1 mo FU	3 mo FU	6 mo FU	12+ mo FU			
220	Kuoff/Michigan USA	84/003	7/84 / 8/84	5/86	50	16	16	11	7	5	02/20/86	2/85	Closed
930	Pharmaco D./Texas	84/006	8/84 / 10/84	6/86	50	31	19	16	11	4	07/16/86	9/85	Closed
909	Halki/Ohio	85/002	7/85 / 1/86	11/86	50	11	8	5	0	0	08/18/86	2/86	Active

STUDY STATUS LIST
VAGINAL CONTRACEPTION
3170

OCTOBER 1986

Description of Study: EFFECTIVENESS OF TIOCGNAZOLE VS. PLACEBO IN PREVENTING VAGINAL INFECTION

Study Number: 7800

Total Number of Cases: 100

Total Number of Studies: 1

Center	Investigator/ Country	Index Number	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed						Date Last Shipment	Date Last Site Visit	Status/ Comments	
						ADM	2 wk FU	4 wk FU	6 wk FU	8 wk FU	10 wk FU				12 wk FU
8062	Jaramillo/Costa Rica	86/001	7/86	4/87	100	6	0	0	0	0	0	0	08/27/86	9/86	Active

STUDY STATUS LIST
IUD

2

OCTOBER 1986

Description of Study: TCu 200 Strings vs No Strings

Study Number: 530

Total Number of Cases: 1300

Total Number of Studies: 5

FCO: 3152

CENTER NUMBER	INVESTIGATOR/ COUNTRY	INDEX NUMBER	DATE INITIATED	EXPIRATION DATE	PROPOSED NO. OF CASES	FORMS PROCESSED					DATE LAST SHIPMENT	DATE LAST SITE VISIT	STATUS/ COMMENTS
						ADM	1MO FU	3MO FU	6MO FU	12MO+ FU			
020	ANDOLSEK/YUGOSLAVIA	80/002	3/83	6/87	500	499	435	421	420	368	8/19/86	4/86 JB	ACTIVE
086	TACLA/CHILE	81/013	8/81	8/81	100	68	66	60	63	56	2/22/85	3/83 HW	CLOSED
299	COHEN/FRANCE	81/003	7/81	6/85	100	100	90	84	81	77	11/22/85	5/84 CW	CLOSED
841	GALICH/GUATEMALA	80/009	9/80	1/82	300	299	163	113	149	243	5/21/84	3/86 CEC	CLOSED
853	ALVAREZ/DOMINICAN REP	85/010	12/85	8/87	300	244	141	73	17		9/18/86	6/86 CEC	ACTIVE

STUDY STATUS LIST
IUD

6

OCTOBER 1986

BR

Description of study: TCu200 vs Adapted T

Study Number: 534

Total Number of Cases: 200

Total Number of Studies: 1

FCU: 3153

CENTER NUMBER	INVESTIGATOR/ COUNTRY	INDEX NUMBER	DATE INITIATED	EXPIRATION DATE	PROPOSED NO. OF CASES	FORMS PROCESSED					DATE LAST SHIPMENT	DATE LAST SITE VISIT	STATUS/ COMMENTS
						ADM	FU 1MO	FU 3MO	FU 6MO	FU 12MO+			
696	APICHART/THAILAND	85/007	5/85	7/87	200	122	87	49	39	3	7/14/86	3/86 AS	ACTIVE

STUDY STATUS LIST
IUD

3

OCTOBER 1986

Description of Study: Evaluation of TCU 380 A

Study Numbers: 532, 536, 550, 552, 553

Total Number of Cases: 10,400

Total Number of Studies: 22

FCO: 3151

CENTER NUMBER	INVESTIGATOR/COUNTRY	INDEX NUMBER	DATE INITIATED	EXPIRATION DATE	PROPOSED NO. OF CASES	FORMS PROCESSED					DATE LAST SHIPMENT	DATE LAST SITE VISIT	STATUS/COMMENTS
						ADD	1MO	3MO	6MO	12MO+			
342	EKWEMPU/NIGERIA	86/013	6/86	7/88	300	10					9/29/86	9/86 RD	ACTIVE
060	DAVID/PHILIPPINES	86/004	11/86 EDI	1/88	200							9/86 SK	PLANNED
061	ALFORSO/PHILIPPINES	86/006	11/86 EDI	5/88	200							9/86 SK	PLANNED
066	DACALOS/PHILIPPINES	86/007	11/86 EDI	5/88	200							9/86 SK	PLANNED
084	DELGADO/MEXICO	85/008	7/85	6/87	300	266	203	171	130	19	9/16/86	9/86 CEC	ACTIVE
100	ZIGHELBOIM/VENEZUELA	85/006	6/85	1/87	300	299	131	130	103	11	9/ 5/86	6/86 CEC	ACTIVE
101	ACOSTA/PERU	85/16	12/85	11/87	300	56	41	27	4		9/17/86	7/86 EG	ACTIVE
304	KISMISCI/TURKEY	85/002	6/85	6/87	300							7/86 PG	ACTIVE
342	EFCIS/EGYPT	86/008 SUB 3151-4	7/86	2/87	1000	NO IN-HOUSE DATA					N/A	7/86 PG	ACTIVE
363	TCPOZADA/EGYPT	85/005	6/85	6/87	200	111	37	10	9	3	6/3/86	7/86 PG	ACTIVE
401	SUKTAR/SUDAN	85/14	10/85	2/86	300	26	18	14	3		3/27/86	3/86 PG	ACTIVE
452	DOB/CAMEROON	86/012	6/86	6/88	300	11	3				8/26/86	6/86 ED	ACTIVE

STUDY STATUS LIST
IUD

SEPTEMBER 1986

292

Description of Study: Evaluation of TCe 380 A

Study Numbers: 532, 536, 550, 552, 553

Total Number of Cases: 10,400

Total Number of Studies: 22

FCO: 3151

CENTER NUMBER	INVESTIGATOR/COUNTRY	INDEX NUMBER	DATE INITIATED	EXPIRATION DATE	PROPOSED NO. OF CASES	FORMS PROCESSED					DATE LAST SHIPMENT	DATE LAST SITE VISIT	STATUS/ COMMENTS
						ADM	FU 1MO	FU 3MO	FU 6MO	FU 12MO+			
680	AFROZE/PAKISTAN	85/15	3/86	11/87	300	15					7/23/86	3/86 SK	ACTIVE
703	BANDARAGODA SRI LANKA	86/002	2/86	1/88	300	173	139	77			9/17/86	8/86 JM	ACTIVE
741	DAMRONG/THAILAND	85/009 SUB 3151-1	5/85	5/87	1400	1337	1169	906	459		6/23/86	3/86 AS	ACTIVE
779	GUNASEKERA SRI LANKA	86/003	2/86	1/88	300	46	22				8/13/86	8/86 JM	ACTIVE
780	CHOONG MALAYSIA	86/001	1/86	2/88	300	40	37	17			9/29/86	1/86 SK	ACTIVE
821	HENRIQUE EL SALVADOR	85/17	1/86	11/87	300	147	88	36	1		8/ 1/86	6/86 SK	ACTIVE
825	RIVERA/MEXICO	85/12	8/85	9/87	300	264	160	101			8/1/86	9/86 CEC	ACTIVE
854	BELTRAN/CHILE	86/009	6/86	1/88	300	132	55				9/29/86	8/86 CEC	ACTIVE
8020	AQUINAGA/BRAZIL	85/011	10/85	1/87	300	280	84	67	48		8/26/86	4/86 DB	ACTIVE
8052	INSS/HONDURAS	86/010	6/86	6/88	300	96	40	7			9/16/86		ACTIVE

STUDY STATUS LIST
IUD

5

SEPTEMBER 1986

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Description of Study: Evaluation of TCu 380 A

Study Numbers: 532, 536, 550, 552, 553

Total Number of Cases: 10,400

Total Number of Studies: 22

FCO: 3151

CENTER NUMBER	INVESTIGATOR/COUNTRY	INDEX NUMBER	DATE INITIATED	EXPIRATION DATE	PROPOSED NO. OF CASES	FORMS PROCESSED					DATE LAST SHIPMENT	DATE LAST SITE VISIT	STATUS/COMMENTS		
						ADM	1MO	3MO	6MO	12MO+					
8065	FERNANDEZ/ COSTA RICA	86/011	10/86	ED1	5/86	200						9/86	CEC	PLANNED	
BKS PENFIN	INDONESIA	85/18 SUB 3151-3	5/86		9/87	3000	NO IN-HOUSE DATA					R/A	5/86	CW	ACTIVE

STUDY STATUS LIST
 INVESTIGATOR NETWORK NEEDS
 FCO 3114

OCTOBER 1986

Description of Study: NONCOMPARATIVE STUDY OF LIPPES LOOP

Study Number: 5507

Total Number of Cases: 150

Total Number of Studies: 1

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
						ADM	1 mo FU	3 mo FU	6 mo FU	12 mo FU			
42	Ekvempu/Nigeria	IUD 85/001	3/85 / 3/85	4/86	150	150	139	113	89		1/86	6/86 ^{ED}	Closed CR Planned

Description of Study: COPPER T 200 VS. LIPPES LOOP D

Study Number: 5538

Total Number of Cases: 450

Total Number of Studies: 2

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
						ADM	1 mo FU	3 mo FU	6 mo FU	12 mo FU			
33	El-Essaily/Egypt	IUD 83/006	10/83 / 10/83	5/85	300	300	211	210	192	158	5/85	2/85 ^{NB}	Closed CR planned
4000	Akuse/Nigeria	IUD 83/013	9/84 / 9/84	8/85	150	148	129	110	53	31	11/85	10/85 ^{PL}	Closed CR Planned

STUDY STATUS LIST
 INVESTIGATOR NETWORK NEEDS
 FCO 3114

OCTOBER 1986

Description of Study: ML 250 VS. COPPER T 200B

Study Number: 5544

Total Number of Cases: 300

Total Number of Studies: 1

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
						ADH	1 mo FU	3 mo FU	6 mo FU	12 mo FU			
741	Damrong/Thailand	IUD 83/001	3/84 / 3/84	3/86	300	300	271	206	180	1	8/86	3/86AS	Active

STUDY STATUS LIST
INVESTIGATOR NETWORK NEEDS
FCO 3114

OCTOBER 1986

Description of Study: FS SURVEILLANCE

Study Number: 6900

Total Number of Cases: 1700

Total Number of Studies: 2

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	Forms Processed				Date Last Shipment	Date Last Site Visit	Status/ Comments	
						ADH	1 mo FU	3 mo FU	6 mo FU				12 mo FU
451	Githiari/Kenya	FS 84/020	3/84 / 3/85	11/85	300	499	497	493	X	X	3/86	9/86 PL	Closed CR planned
040	Otolorin/Nigeria	FS 86/003	6/86 9/86	2/88	300	28		X		X		9/86 PL	Active

STUDY STATUS LIST
INVESTIGATOR NETWORK NEEDS
FCO 3114

OCTOBER 1986

Description of Study: DMPA (25 MG. PER MONTH) VS. DMPA (150 MG. PER THREE MONTHS)

Study Number: 8819

Total Number of Cases: 100

Total Number of Studies: 1

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	Forms Processed				Date Last Shipment	Date Last Site Visit	Status/ Comments	
						ADH	1 mo FU	3 mo FU	6 mo FU				12 mo FU
893	Czeresnia/Brazil	SYS 83/001	4/84 / 4/84	7/86	100	93	74	50	44	46	2/86	4/86DB	Closed 6/86 CR planned

Description of Study: STANDARD DOSE VS TRIPHASIC

Study Number: 8830

Total Number of Cases: 600

Total Number of Studies: 3

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	Forms Processed				Date Last Shipment	Date Last Site Visit	Status/ Comments	
						ADH	1 mo FU	4 mo FU	8 mo FU				12 mo FU
613	Cruz/Phillipines											9/86 SK	Waiting for PopCom approval.
6000	Villamar/Phillipines											9/86 SK	Waiting for PopCom approval.
7000	Ismail/Malaysia	SYS 86/001	1/86	11/87	200	128	86	23			8/86	9/86 SK	Active

STUDY STATUS LIST
 INVESTIGATOR NETWORK NEEDS
 FCO 3114

OCTOBER 1986

Description of Study: NORIDAY VS. LO-FEMENAL

Study Number: 8850

Total Number of Cases: 200

Total Number of Studies: 1

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
						ADH	1 mo FU	4 mo FU	8 mo FU	12 mo FU			
440	Traore/Mali	SYS 83/032	9/84 / 9/84	6/86	200	200	164	125	55	33	8/86	8/86 KI	FU Only

Description of Study: OVRETTE VS. MICRONOVLEM

Study Number: 8877

Total Number of Cases: 1400

Total Number of Studies: 2

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	Forms Processed			Date Last Shipment	Date Last Site Visit	Status/ Comments	
						ADH	1 mo FU	3 mo FU				6 mo FU
Multi	Hoohene/Zimbabwe	PGC 85/006	10/85/10/85	4/87	400	323	91	68	18	8/86	7/86RE	Active

STUDY STATUS LIST
INVESTIGATOR NETWORK NEEDS
FCO 3114

OCTOBER 1986

162

Description of Study: DEPO VS PILL

Study Number: 8880

Total Number of Cases: 400

Total Number of Studies: 1

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	Forms Processed		Date Last Shipment	Date Last Site Visit	Status/ Comments
						ADH	> 24 Mo FU			
4010	Adama Dabo/Gambia	SYS 84/017	7/84 / 7/84	2/86	400	399	352	4/86	4/86RD	Closed 6/86 CR planned

Description of Study: LOW DOSE VS STANDARD DOSE

Study Number: 8890

Total Number of Cases: 200

Total Number of Studies: 1

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	Forms Processed				Date Last Shipment	Date Last Site Visit	Status/ Comments
						ADH	1 mo FU	3 mo FU	6 mo FU			
463	Maidouka/Niger	SYS 86/013	9/86	6/88	200						9/86 KJ	Awaiting forms approval.

STUDY STATUS LIST
SYSTEMICS

OCTOBER 1986

Description of Study: OC's With vs Without Iron

Study Number: 8856 FCO: 3136

Total Number of Cases: 1280

Total Number of Studies: 6

Center	Investigator/ Country	Index Number	Date Init	Date Actv	Expiration Date	Proposed No. of Cases	Forms Processed			Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADM/ LAB	6 wks FU	14 wks FU			
85*	Bassol/Torreón, Mexico	86/007	7/86	8/86	11/87	320	21/26			9/25/86		Active
603	Ago/POPCOM Legaspi City, Phillipines		9/86									SA to AID
616	Mongkol/Thailand											SA to AID and Investigator
621	BKS PENFIN/ Soeprapti, Indonesia	86/008	11/85									EDI 9/86
704	Barua/BFRP Dhaka, Bangladesh	86/020										SA to AID and investigator
917	Marangoni/Guayaquil, Ecuador	86/017	9/86		3/88	320					9/86 DB	EDI 10/86

*forms received, not loaded

STUDY STATUS LIST
SYSTEMICS

OCTOBER 1986

Description of Study: Crossover - Noriday 1/50 to Lo-Femenal; Lo-Femenal to Noriday 1/50

Study Number: 8845 FCO: 3139

Total Number of Cases: 1200

Total Number of Studies: 4

Center	Investigator/ Country	Index Number	Date Init	Date Actv	Expiration Date	Proposed No. of Cases	Forms Processed				Date Last Shipment	Date Last Site Visit	Status/ Comments	
							ADM	1 mo FU	3 mo FU	4 mo FU				6 mo FU
23	Breznik/Maribor, Yugoslavia	85/008	6/85	11/85	12/86	300	259	229	165	113	104	9/23/86	4/86JB	Active (Adm. closed)
602	Puertollano/ Metro Manila, Philippines	85/009	9/85	2/86	2/87	300	159	125	45	26	30	9/8/86	8/86SK	Active
840	Ramos/Ciudad Juarez, Mexico	85/010	10/85	3/86	5/87	300	11	5	3	1		6/26/86 queried	12/85CC	Follow-up only
843*	Bomfim/Fortaleza, Brazil	86/006	2/86		10/87	300	6	1				9/29/86	4/86DB	Active
8593	Remes/Veracruz, Mexico	86/019												SA to investigator. Being supplied.

*forms received, not loaded

TOTALS ON THIS LIST REPRESENT THE NUMBER OF FORMS LOADED INTO THE COMPUTER.

STUDY STATUS LIST
SYSTEMICS

OCTOBER 1986

Description of Study: Triquilar vs Lo-Femenal

Study Number: 8840 FCO: 3138

Total Number of Cases: 1500

Total Number of Studies: 5

Center	Investigator/ Country	Index Number	Date Init	Date Actv	Expiration Date	Proposed No. of Cases	Forms Processed				Date Last Shipment	Date Last Site Visit	Status/ Comments	
							ADM	1 mo FU	4 mo FU	8 mo FU				12 mo FU
400*	Gerais/Khartoum, Sudan	86/002	2/86		3/88	300	100					2/86PG	Active	
703	Basnayake/Colombo, Sri Lanka	86/004	2/86	4/86	3/88	300	82	60	12			9/17/86	Active	
850	Guzman-Serani/ Valdivia, Chile	86/005	3/86	4/86	3/88	300	189	162	80			8/29/86	8/86CC	Active
8057	Calventi/ Santo Domingo, Dominican Republic	86/003	6/86		3/88	300							6/86CC	Pretests rec'd
8058	Andrade/Curitiba, Brazil	86/018	9/86			300							9/86DB	Being Supplied

*forms received, not loaded

TOTALS ON THIS LIST REPRESENT THE NUMBER OF FORMS LOADED INTO THE COMPUTER.

STUDY STATUS LIST
SYSTEMICS

OCTOBER 1986

Description of Study: Locstrin vs Lo-Femenal

Study Number: 8820 FCG: 3134

Total Number of Cases: 1500

Total Number of Studies: 5

Center	Investigator/ Country	Index Number	Date Init	Date Actv	Expiration Date	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADM	1 mo FU	4 mo FU	8 mo FU	12 mo FU			
314	Saleh/Cairo, Egypt	86/014	7/86		6/88	300						7/86PC	Began admissions 9/15/86	
683	Lubis/Jakarta, Indonesia	86/016	9/86		8/88	300							Being supplied	
8590	Rueda/Bogota, Colombia	86/015	9/86		5/88	300	4				8/19/86	7/86DB	Active	
8594	Perez Palacios/ Mexico City, Mexico	86/011	5/86	6/86	5/88	300	10	4			9/25/86	9/86CC	Active	
	Mukherjee/ Malaysia					300							SA to AID and investigator	

TOTALS ON THIS LIST REPRESENT THE NUMBER OF FORMS LOADED INTO THE COMPUTER

STUDY STATUS LIST
PROGESTOGEN-ONLY ORAL CONTRACEPTIVES

OCTOBER 1986

Description of Study: Progestogen-only Oral Contraceptives in Lactating Women

Study Number: 8875 FCO: 3142

Total Number of Cases: 4000

Total Number of Studies: 20

Center	Investigator/ Country	Index Number	Date Init./	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed				Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADM	2 mo FU	6 mo FU	12 mo FU			
084	Delgado/Mexico Villahermosa	84/034		11/84	12/86	200	164	148	96	59	9/16/86	9/86 CC	Active
102	Guzman/Peru Lima	84/018		7/84	11/87	200	192	102	63	34	9/16/86	12/85 EW	Active
110	Nagahata/Peru Lima	84/014		3/84	9/87	200	193	188	121	117	6/16/86 queried	12/85 EW	Active (Adm. closed)
400	Gerais/Sudan Khartoum	85/002		2/85	2/87	200	200	199	186	174	5/21/86 queried	2/86 PG	Active (Adm. closed)
422	Broquet/Rwanda Gisenyi	84/004		6/85	3/87	200	18	10	1		5/20/86	5/86 RD	Closed
452	Doh/Cameroon Yaounde	84/030		12/84	1/87	200	227	128	96	75	8/26/86	6/86 RD	Active (Adm. closed)
453	Wright/Nigeria Jos	84/035		3/86	1/87	100	40	15			7/1/86 queried	6/86 RD	Active
463	Ndiaye/Senegal Dakar	84/004		11/84	1/87	200	92	68	40	10	8/15/86	4/86 Nb	Active
831	Aranda/Costa Rica San Jose	84/019		9/84	9/86	200	169	115	71	53	2/19/86	1/86 CC	Closed CR in progress
840	FEMAP/Mexico Ciudad Juarez	84/029		10/84	9/86	200	200	164	134	56	5/7/86	12/85 CC	Closed
841	Santiso/Guatemala Guatemala City	84/031		12/84	10/86	200	199	192	160	108	9/3/86	7/86 CC	Active (Adm. closed)
843	Bomfim/Brazil Fortaleza	84/036		12/84	4/87	200	194	157	101	28	9/10/86	8/86 DB	Active

Center	Investigator/ Country	Index Number	Date Init./	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed				Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADM	2 mo FU	6 mo FU	12 mo FU			
865	Barbosa/Brazil Santa Maria	84/038		2/85	4/87	200	139	80	34	10	8/26/86	8/86 DB	Active
869	Cetina/Mexico Merida	84/015		7/84	6/86	200	200	185	141	88	6/11/86	12/85 CC	Closed
871	Moggia/Argentina Buenos Aires	84/020		8/84	9/86	200	200	162	1	129	4/21/86	4/86 CC	Closed
893	Czeresnia/Brazil Sao Paulo	84/037		2/85	4/87	200	127	91	30	14	7/21/86 queried	8/86 DB	Active
8014	Lecoin/Haiti Port-au-Prince	84/016		8/84	6/86	200	199	170	109	79	2/28/86	9/85 KJ	Closed CK in progress
8056	Oliveira/Brazil Londrina	84/039		2/85	4/87	200	195	137	87	15	9/10/86	8/86 DB	Active (Adm. closed)
8058	Andrade/Brazil Curitiba	84/041		5/85	4/87	200	203	150	76	19	8/26/86	8/86 DB	Active (Adm. closed)
8059	Nunes/Brazil Porto Alegre	84/040		2/85	4/87	200	200	169	148	110	7/21/86	8/86 DB	Will Close once status is confirmed

The totals on this list represent the total number of forms loaded to date.

STUDY STATUS LIST
EXPANDED PROGESTOGEN-ONLY OC

OCTOBER 1986

Description of Study: Expanded Strategy for Progestogen-only pills (either several centers per country or through CBD programs)

Study Number: 8876 FCO: 3142

Total Number of Cases: 10,000

Total Number of Studies:

Center	Investigator/ Country	Index Number	Date Init.	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed			Date Last Shipment	Date Last Site Visit	Status/ Comments	
							ADM	2 mo FU	6 mo FU				12 mo FU
043	Gardiner/Ghana Accra	85/001	10/85		11/86	200	194	150	1	8/26/86	6/86 PL	Active	
044	Klufio/Ghana Accra	84/003	10/85		11/86	200	198	172	96	8/19/86	6/86 PL	Active	
440	Doucoure/Traore Bamako/Mali	83/031	1/85		1/87	100	99	78	54	15	9/16/86	8/86 KJ	Active
457	Toure/Traore Kayes/Mali	84/002	9/85		4/87	200	39	4		9/16/86	8/86 KJ	Active	
460	Samake/Traore Bamako/Mali	85/003	9/85		4/87	200	84	38	3	9/16/86	8/86 KJ	Active	
8050	Russowsky/Brazil Porto Alegre	84/001	3/85		12/86	300	149	92	44	20	7/22/86 queried	8/86 DB	Active

The totals on this list represent the total number of forms loaded to date.

STUDY STATUS LIST
 PROGESTOGEN-ONLY OC VERSUS NON-HORMONAL METHODS

OCTOBER 1986

Description of Study: Progestogen-only Oral Contraceptive versus Non-Hormonal Methods in Lactating Women (Repeated Studies)

Study Number: 877, 878 FCU: 3133

Total Number of Cases: 800

Total Number of Studies: 3

Center	Investigator/ Country	Index Number	Date Init./Active	Expiration Date	Proposed		Forms Processed							Date Last Shipment	Date Last Site Visit	Status/ Comments
					No. of Cases	ADM	1mo FU	2mo FU	3mo FU	4mo FU	5mo FU	6mo FU	7mo FU			
340	Etman/Mehalla- Kubra, Egypt	85/005	6/86	4/87	300	34								8/13/86 queried	7/86PG	Active
871	Moggia/Buenos Aires, Argentina	85/004	10/85 10/85	4/87	300	294	220	165	162	126	112	75	18	9/8/86	4/86CC	Active (Adm. closed)
871	Moggia/Buenos Aires, Argentina	86/001			200											Being supplied.

THE TOTALS ON THIS LIST REPRESENTS THE TOTAL NUMBER OF FORMS LOADED INTO THE COMPUTER.

STUDY STATUS LIST
SYSTEMICS

October 1986

20/10

Description of Study: Norinyl 1/35 vs Brevicon

Study Number: 8825 FCO: 3134

Total Number of Cases: 1500

Total Number of Studies: 5

Center	Investigator/ Country	Index Number	Date Init	Date Actv	Expiration Date	Proposed No. of Cases	Forms Processed				Date Last Shipment	Date Last Site Visit	Status// Comments	
							ADM	1 mo FU	4 mo FU	8 mo FU				12 mo FU
81	Moreno/Panama	82/013		2/83	6/86	300	300	268	247	221	222	4/86	1/86	CR in progress
356	Rahman/Egypt	83/015		8/83	12/86	300	220	220	201	149	109	9/86	7/86	Active (Admissions closed)
890	Nunez/Honduras	82/010		11/82	6/86	300	174	120	75	46	46	5/86	9/85	Closed
8003	Albuquerque/Brazil	82/014		10/82	6/86	300	302	284	246	157	95	5/86	4/86	Closed

Totals reflect number of forms loaded.

STUDY STATUS LIST
SYSTEMICS

October 1986

Description of Study: Norinyl 1/35 vs Lo-Ovral

Study Number: 8825, 8850 FCO: 3134

Total Number of Cases: 1500

Total Number of Studies: 5

Center	Investigator/ Country	Index Number	Date Init	Date Actv	Expiration Date	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADM	1 mo FU	4 mo FU	8 mo FU	12 mo FU			
40	Ocolorin/Nigeria	83/027		7/84	3/86	100	95	78	74	56	33	3/86	6/85	Closed
370	Nada/Egypt	83/016		6/84	10/85	300	298	296	291	292	265	1/86	7/86	CR in progress
436	Ayangade/Nigeria	83/028		8/84	3/86	100	96	80	72	70	33	3/86	6/85	Closed
821	Argueta/El Salvador	83/013		6/83	12/85	300	215	202	161	118	95	7/85	6/85	CR in progress
841	Santiso/Guatemala	82/011		11/82	12/85	300	300	116	151	121	156	12/84	6/85	CR 550
871	Moggia/Argentina	82/015		10/82	8/84	300	300	284	239	199	161	8/84	10/84	CR 534
919	Stumpf/USA	83/022		7/83	3/85	300	292	268	264	292	83	12/84	9/84	*

Totals reflect number of forms loaded.

* Data not to be analyzed.

STUDY STATUS LIST
SYSTEMICS

October 1986

2/16

Description of Study: Norinyl 1/35 vs Norinyl 1/50

Study Number: 8850 FCO: 3134

Total Number of Cases: 1500

Total Number of Studies: 5

Center	Investigator/ Country	Index Number	Date Init	Date Actv	Expiration Date	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADM	1 mo FU	4 mo FU	8 mo FU	12 mo FU			
24	Behlilovic/Yugoslavia	83/004		4/83	3/85	300	299	278	282	273	252	11/84	10/83	CR 555
358	Shabaan/Egypt	83/002		7/83	12/85	300	300	194	139	91	96	4/85	7/86	CR in progress
703	Basnayake/Sri Lanka	83/014		9/84	10/85	500	500	454	450	380	316	10/85	7/86	CR in progress
831	Aranda/Costa Rica	82/009		11/82	3/85	300	299	297	296	291	290	4/85	9/85	CR 534
869	Cetina/Mexico	82/012		11/82	12/85	300	300	262	245	202	164	2/86	12/85	CR in progress

Totals reflect number of forms loaded.