

**SEMIANNUAL REPORT**

1 October 1986 – 31 March 1987

Cooperative Agreement  
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## I. INTRODUCTION

The current reporting interval has been a uniquely busy one in the history of FHI. After two decades of stagnation in the introduction of new methods of contraception, FHI believes the 1990s will see a surge in the availability of methods. The organization is proud to be playing a major role in nearly all of the foreseeable new methods likely to reach human use in the first half of the 1990s, and the lead role in developing new injectables, spermicides and methods of female sterilization.

Based on Phase II data, FHI was granted USFDA approval to proceed with expansion into Phase III clinical trials of the NET 90-day injectable on May 11, 1987. Work on propranolol as a spermicide, the Filshie clip for tubal occlusion, and quinacrine as a method of nonsurgical sterilization are all proceeding on schedule.

During the current reporting interval the AID funded CONRAD project was launched and FHI is happy to be coordinating its activities with this important new entity, as well as maintaining long established liaison with the work of the Population Council and the Human Reproduction Program of WHO.

FHI is committed to a businesslike and practical approach to contraceptive development and introduction that plans many years ahead and takes into account long-term financial constraints as well as opportunities. An arbitrary, but realistic, indicator of

widespread contraceptive use could be the date when a new method accumulates its first one million users, and FHI is now reviewing the time and cost of introducing new methods, the manufacture and training of relevant providers, for the mid-1990s. In forecasting future trends, FHI is taking into account possible costs to USAID of supplying large volumes of contraceptives and alternative sources of supply.

All the individuals who will be using family planning in the 1990s are already alive and it is hoped contraceptive prevalence will continue to rise. Therefore, while believing additional fertility regulation choices will prove important in saving deaths from child birth and abortion and in helping couples achieve their fertility goals, FHI also recognizes that current methods must continue to increase in use. Hence, FHI continues to emphasize its large program of testing and improving the use of oral contraceptives, IUDs and voluntary sterilization. Work on progesterone-only pills is providing an important choice for lactating women. FHI's contribution to the introduction of NORPLANT<sup>®</sup> worldwide continues to grow, with a total of about 2500 insertions in 9 countries. As part of its global strategy, FHI also continually extends and upgrades its network of collaborative investigators.

Program Evaluation has continued its important work linking the way contraceptive acceptance and continuation are influenced by provider attitudes, the logistics of services and consumer knowledge and background. Work shows, for example, that in some

parts of the world couples still do not have open access to voluntary sterilization. FHI has also provided the only objective information available to assess the impact of cash reimbursements for male and female sterilization made by some Third World governments. New methodologies have been developed to look at NORPLANT® acceptability and pill compliance. With the spread of AIDS, the work on condom acceptability and use which Program Evaluation has pioneered, is likely to become increasingly significant.

FHI's patient effort to review oral contraceptive risks and benefits promises to yield new fruit in India, where the data is likely to be used more and more in policy setting and in the education of users and providers of contraception.

FHI is deeply committed to the principle of informed choice in family planning and is proud of the success of its recent initiatives in disseminating information to the consumers of family planning services.

A recurrent theme in FHI's work over the past few years has been the beneficial impact of family planning on maternal and infant health. This work received a happy accolade of approval in the current reporting interval when the World Bank hosted an international conference, Safe Motherhood Initiative in Nairobi, on maternal mortality which, to a considerable extent, was driven by the data coming out of FHI's RAMOS and other studies.

FHI has continued its work to make NFP more effective and to increase knowledge about the contraceptive effects of breast-feeding. FHI is the only USAID-supported organization working with new and improved methods of Natural Family Planning: work continues on Dr. Schumacher's device for measuring the amount of fluid that can be aspirated from the vagina on different days of the menstrual cycle, and Professor Brown's low cost device for measuring urinary hormones.

FHI is completing its long-term study of the logistics of making NFP services available in a poor, urban area of the Third World. In Bangladesh, FHI-supported research has demonstrated that non-Catholics as well as Catholics find NFP a useful, additional family planning choice.

Research is now underway to determine whether, when women are instructed to breast-feed their babies in different ways, it is possible to extend the duration of anovulation associated with lactation. If this work is successful, it will be the first intervention of its kind in the world and has a potential to further increase the demographic usefulness of breast-feeding.

Since the 1970s, FHI has been studying the potential of barrier methods of contraception to slow the spread of sexually transmitted diseases. During the current reporting period, one part of this work came to fruition with the completion of an important study on the effect of nonoxynol-9 in slowing the spread

of chlamydia and gonorrhea in sexually active young women in Bangkok.

In January 1987 FHI, using non-USAID funds, sent Dr. Peter Lamptey to Ghana, Cameroon, Kenya and Zimbabwe to assess and report on the AIDS epidemic in Africa and the role, if any, that FHI might play in containing the disease. It was apparent that the AIDS epidemic is moving more rapidly in Africa, and in some other parts of the world, than the international bureaucracies can respond. In order to set up a quick acting, flexible response mechanism, FHI created an AIDS Task Force, headed by Dr. Peter Lamptey and Dr. Barbara Janowitz. After consultation with USAID, approximately \$100,000 of funds from the Cooperative Agreement was assigned to this work and supplemented by \$150,000 voted by the FHI Board.

FHI is now assembling a coherent program of prevention aimed at documenting the effectiveness of new (and improved) barrier methods in clinical situations and applying such knowledge in intervention programs, especially in heterosexual groups at high risk of contracting the disease.

FHI believes its international contacts, track record in clinical research and epidemiology, flexible management structure and Board leadership place it in a powerful position to contribute to slowing the spread of this lethal new disease.

As the response of the Board of the AIDS crisis testifies, FHI is committed to self-help and supplementing Cooperative Agreement

funds from non-federal sources. FHI continues to receive useful support from U.S. philanthropic foundations and in January 1987 FHI established a partly owned, for-profit company (Clinical Research International) that builds on FHI's skills and track record in clinical trials. Seventy-nine percent of the profit of CRI will be available to supplement FHI's world wide programs.

Selected members of FHI helped launch CRI and Dr. Albert Siemens will continue to divide his time between the two organizations. Dr. Siemens has become Vice-President for Research and FHI is in the process of appointing a new Director of Clinical Trials.

Mr. John Ganley, who had been the Executive Vice-President of FHI since 1980, retired from his post during the current reporting interval. During his tenure, he brought about major improvements in the administration of FHI and helped set important new policy directions and the organization has benefited immeasurably from his experience and imaginative leadership.

Dr. Thomas Petrick was appointed to the position of Director of Medical Affairs and Dr. Roberto Rivera was appointed a Special Assistant to the President. Mr. Alfredo Perez is assisting FHI as Senior Advisor to the President in long-term planning and management issues.

In April the Board was happy to approve the appointment of Mr. William Schellstede as Senior Vice-President of FHI. Mr.

Schellstede brings with him a wide experience in family planning, technical assistance overseas and long managerial experience in USAID-supported organizations.

## II. CONTRACEPTIVE DEVELOPMENT

Although FHI continues to focus on the clinical aspects of contraceptive evaluation and development, the exploration of new product leads in selected areas remains important. In addition, preclinical toxicity studies have been required by the FDA to support clinical product development.

NICHD awarded to FHI a contract for the formal full-scale development of D-propranolol as a potential new advance in vaginal contraception. Development and partial funding is being coordinated with AID. 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 Synthron Corporation, proved difficult but the difficulties appear to have been overcome for the present needs. In November 1986, Synthron Corporation delivered 190 grams of D(+)-propranolol hydrochloride. Analysis through the kind cooperation of Dr. H.K. Kim at NICHD revealed that the sample was at least 99.5% pure. In an effort to identify an alternate supplier, several chemical companies were contacted. One, Chemical Dynamics Corporation, South Plainfield, New Jersey, reviewed our requests in detail and concluded that they could produce 99.5%+ D-propranolol by resolution of the racemic mixtures. The estimated cost would be \$17.50/gram. FHI responded to their proposal by indicating that our need for compound was adequately met

at present but that, should problems arise or demand increase in the future, they will be contacted. EB Associates Laboratories, Inc., Buffalo, New York, was requested by FHI to provide a cost and time estimate for complete analysis of D-propranolol samples with particular emphasis on the trace contaminant putatively identified as L-propranolol. An estimate of \$14,500.00 was given and the time of completion estimated to be two months. Based in part on this cost, FHI has postponed this analysis until the contraceptive efficacy of D-propranolol in humans is confirmed. Additional estimates also will be solicited at a later time.

In the development of D-propranolol formulations, efforts focused in three main areas: (a) development of assay methods for preservative and propranolol concentrations in formulation samples, (b) a study of discoloration in stability samples, and (c) a study of diffusion rates from high concentration gels. Extraction of propranolol from the gels was accomplished with C<sub>18</sub> HPLC columns after mixing the sample with a mobile phase solvent. The content of the gels was found to be within expected limits. Assay of propranolol in the creams, however, proved difficult. Liquid-solid phase extraction was found to be unsuitable. Thus, solid phase extraction with Octadecyl (C<sub>18</sub>) disposable columns was used and methodology continues to be refined. These studies continue. To study the discoloration, various antioxidants were included in the gels and creams under different ambient conditions. Elevated temperatures and light were found to increase discoloration. Among the antioxidants used, BHA was most effective but found not to be entirely satisfactory. Gel formulations containing 7% and 10% propranolol hydrochloride were

studied for their in vitro release profiles. The release profile of the two gels was nearly identical for the first 30 minutes. Thereafter, release from the 7% gel began to plateau while that from the 10% gel continued to increase up to 60 minutes, the final time point at which measurements were taken. Experiments presently underway are focusing upon the possible causes of discoloration and further additives and minor alterations to the formulation are being tested as possible means for preventing the problem.

In efficacy tests, both cream and gel formulations exerted potent spermicidal activity in in vitro tests where the semen samples were layered over the formulations without mixing. A dose-response effect was observed with both formulations. The gel, however, appeared to be more potent than the cream. In the former, all or nearly all sperm were immobilized at one minute after exposure to the 3% or 5% gel. The cream required four or five minutes to achieve this effect. Given the variability from semen sample to sample, however, these differences should be viewed with caution. Similar results were obtained with in vitro sperm penetration in the Penetrak Bovine Cervical Mucus Assay. In addition to these "classic" tests, semen samples treated with D-propranolol or nonoxynol-9 were evaluated objectively for motility and velocity analysis by a "Sperm Motion Analysis System". Data generated by this system showed that mean swimming velocity of sperm cells was found to be reduced with increasing concentrations of drug. Finally, in side-by-side comparison to nonoxynol-9, D-propranolol was found to be slightly less potent than nonoxynol-9, although both agents were capable of achieving complete immobilization of all sperm. Results of in vivo

experiments paralleled those of the in vitro studies. Earlier studies in stump-tailed macaques demonstrated a consistent spermicidal efficacy of a gel formulation containing 5% propranolol. A dose-response study was therefore conducted with gels containing 1, 2, 3, 4 or 5% D-propranolol. Again, 5% D-propranolol gel applied intravaginally before mating was found to consistently immobilize all spermatozoa in vaginal washings recovered postcoitally. The doses of 2-4% yielded variable results while the 1% gel clearly was ineffective. Earlier studies with the 5% propranolol cream formulation yielded variable results. Thus, studies of a 7% and 10% D-propranolol cream formulation presently are underway. Dr. L. Zaneveld also tested 5% D-propranolol gel in his in vitro no-mix assay in which human semen is layered on top of the spermicidal gel. The results indicated that D-propranolol moves quickly from the gel into semen as all sperm were immobilized within five minutes.

To test for irritation of the propranolol formulations, the initial screening of up to three possible formulations will be conducted by Dr. D. Waller. This will begin in May 1987. Based upon those results and those of Dr. Zaneveld's, it is planned that three doses of one formulation will undergo an extensive evaluation in the rabbit vaginal irritation assay under Good Laboratory Practices in mid-1987.

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 Phase I clinical investigations. A draft of the IND has been prepared and a pre-IND meeting with the FDA will be scheduled in the near future. The initial clinical 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 women not exposed to the risk of pregnancy will be initiated at two clinics.

The two-year carcinogenicity test of the Filshie Clip and Falope Ring was initiated in February 1986. This study involves 300 female rats and 300 female mice in which the reduced sized Filshie Clips and Falope rings are surgically placed on the fallopian tubes of the animals. The study is being carried out at the University of Nottingham, Nottingham, England, under the direction of Graham Robinson, PhD, Department of Pathology. Quality assurance and Good Laboratory Practice inspections are being regularly carried out and reported by Topical Laboratories, Ltd. This study actually consists of four studies designed to investigate any tumorigenic effects of the implantation of these sterilization devices in mice or rats. The study, sponsored by FHI jointly with Femcare, Ltd. and Cabot Medical Corporation, progresses well and the standards being maintained are exemplary.

In response to FDA requests for a preclinical carcinogenicity safety study of microencapsulated norethindrone, FHI has collaborated with Ortho Pharmaceutical Corporation to develop a protocol for a 2-year study in rats. In addition, the pharmacokinetics will be evaluated simultaneously in additional groups treated the same as those in the safety study. This protocol was sent to several contract laboratories from which cost estimates have since been obtained.

Stolle Research and Development Corporation has been contacted for drug supply and the estimated start date for the study is May 1.

### III. CLINICAL TRIALS

The Clinical Trials Division of FHI emphasizes the development and evaluation of new contraceptive products with the goal of large scale human use of proven products. USFDA marketing approval is one key element in planning global programs of new and established products. As of March 1987, the Division was conducting 153 studies of contraceptive products in collaboration with about 125 investigators in 42 countries.

Long-acting contraceptive steroid delivery systems continue to be a primary focus. FHI holds the IND for 90-day PolyNET microspheres. FHI has taken a leading role in conducting two multicenter Phase II studies of a 90-day norethindrone microspheres formulation and an interim analysis and report of all Phase II data submitted to the FDA in January 1987 formed a basis for the FDA's approval to proceed with a Phase III clinical evaluation of the product. The Phase III program began in April 1987. In collaboration with the Program for Applied Research on Fertility Regulation (PARFR), Stolle Research and Development and Ortho Pharmaceutical, FHI has also completed the data analysis of the Phase I evaluation of a 30-day norethindrone (NET) microencapsulated injectable formulation.

In addition, FHI has continued negotiations with Endocon, Inc. to obtain a satisfactory supply of NET biodegradable subdermal implants. Preclinical studies to assure product quality are scheduled for the summer of 1987 with a confirmatory Phase I trial planned for the fall.

Pre-introductory clinical trials of the NORPLANT<sup>™</sup> implant system continue in 9 countries at 24 sites. The demand for the product exceeds available funding for clinical trials. The profile of contraceptive efficacy and safety of the product are fully consistent with the earlier clinical studies. The primary disadvantage of the method is disruption of regular bleeding patterns with up to 80% of women reporting changes. Amenorrhea, which occurs frequently, seems to be an acceptable phenomenon for most users. Current research activities are designed to assist investigators to become fully comfortable with the method and to obtain data for in-country product approval. FHI's policy will be to try to continue to supply current study sites with implants and to maintain local skills and interest until FDA marketing approval is granted.

The Filshie Clip is being evaluated for the purpose of regulatory approval in the U.S. and other countries. Clinical trials are comparing the clip with other devices and approaches such as the Wolf clip, the tubal ring and electrocautery in a total of 29 studies in 18 countries by 24 investigators. Studies in Canada and Europe are pivotal for submission to the FDA whereas the other studies will be supportive in this application. 526 patients are enrolled in pivotal studies and 4,693 are enrolled in comparative studies. An application for marketing approval will be submitted to the FDA in late 1988. In parallel with these clinical studies, FHI, Cabot Medical Corporation, 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.

In a continuing effort to simplify female sterilization methods, non-surgical approaches are in evaluation. FHI is working on general methods of nonsurgical female sterilization including quinacrine, tetracycline and iodine formulations. A Phase I study of the intrauterine placement of slow-releasing quinacrine is nearing completion in Los Angeles. Phase I studies of tetracycline and quinacrine have been initiated at two other centers in the U.S. but volunteer recruitment has been slow. All Phase I studies are expected to be completed in 1987 and should lead to Phase II efficacy trials early in 1988.

Intrauterine devices (IUDs) continued to be in demand in many countries, and FHI is supporting their evaluation. Primary emphasis has been placed on studies of the FDA-approved TCU 380A. FHI is assisting investigators in 18 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 TCU 380A IUD into family planning programs throughout the world, particularly where inferior products are now being used.

Over the past 3-4 years, FHI has provided assistance to clinicians to become familiar with low-estrogen-dose products. These studies include comparisons of a variety of formulations of the low-estrogen-dose oral contraceptives (OCs) as well as comparisons of low-dose and

standard-dose products. These studies will provide an insight into the clinical safety, efficacy and acceptability of these products not only in individual countries, but will provide an unprecedented, broad international objective evaluation and introduction. These studies have been completed 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. Only one triphasic is being studied, Triquilar from Schering; some 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 three weeks of steroid therapy with an emphasis being placed on product safety and hematology.

The evaluation of menfegol foaming tablets in comparison to comparable nonoxynol-9 products continues as a major strategy for FHI. Overall, the two products are yielding similar pregnancy and continuation rates although significant variations are occurring from country to country. Good results were obtained in Ghana and Yugoslavia and a study recently begun in Thailand indicates these products may have some appeal in this region, even though earlier studies were not successful. In the U.S., however, the studies were discontinued because of poor follow-up resulting from product

complaints. The study of the efficacy of the diaphragm with spermicide compared to its efficacy without spermicide remains in the early stages due to slow recruitment. It is being monitored closely. The effectiveness of Tioconazole, the antifungal agent, as a prophylaxis for sexually transmitted diseases (STDs) and a possible spermicide also remains under investigation.

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. A Phase I study will begin in April 1987.

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, as well as developing new and improved products to supplement 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. Phase II testing of the 90-day injectable biodegradable formulation of norethindrone (NET) that permits the continuous low-dose administration of the progestin is almost complete. In a joint project with PARFR, a comparison of 100 mg and 65 mg of NET was initiated at eight centers in Spring 1986. FHI will provide continued funding for these studies after March 1987. FHI continues to provide regular monitoring of the studies, and processing and analysis of the data, and to work 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. 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 February 1987, a meeting was held at the FDA to review an interim report prepared by FHI on the ongoing Phase II 90-day NET trials and obtain permission to begin Phase III testing. The report covered the clinical experience available to FHI as of December 21, 1986. Over 100 women have been enrolled in the Phase II research program. No disturbing side effects have been observed. One pregnancy has been reported in the 65 mg group. 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. NET blood levels are well-controlled after each dose and the serum concentrations of NET are apparently proportional to dose. Phase III clinical trials of the 65 mg dose are expected to begin in May 1987.

The 30-day NET injectable Phase I study that started in May 1986 is complete. Twenty-one women have been enrolled in this 15 mg and 30 mg once-a-month injectable study. Analysis of data is planned for April 1987.

FHI, Stolle R&D, Ortho, NICHD and AID representatives have reviewed 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).

b) NORPLANT<sup>®</sup> Implants

FHI has undertaken a number of pre-introductory, Phase III clinical trials of the NORPLANT<sup>®</sup> contraceptive subdermal implant system. The objective of these studies is to introduce the NORPLANT<sup>®</sup> 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 are used to evaluate safety, efficacy and acceptability.

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 14 investigators from West Africa, Haiti and Venezuela have been trained in Santo Domingo, Dominican Republic. Investigators from El Salvador and Pakistan are expected to be trained later in 1987.

In countries where the initial pre-introductory clinical trial caseload has already been enrolled, expanded trials will be initiated to attempt to meet the seemingly universal demand for the NORPLANT<sup>®</sup> system while at the same time bridging the gap until local regulatory approval of the method is obtained, which would permit wider distribution. The objective of these studies 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. The Program for the Introduction and Adaptation of Contraceptive Technology (PIACT) has prepared prototype versions of various counseling materials, brochures and handouts, and will provide technical assistance in their adaptation for local use. A

prototype standardized training curriculum has also 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). Many of the expanded clinical trials projects (e.g. Bangladesh, Haiti, Nigeria) and new pre-introductory trials efforts (El Salvador, Pakistan, Senegal) are being supported directly by the local USAID Missions.

The total number of centers currently participating in NORPLANT<sup>®</sup> pre-introductory clinical trials is 24 sites in 9 countries. A summary of admissions is presented in Table 1.

Insertions have been performed in 2,460 women to date. There have been a total of 204 removals, 8 due to accidental pregnancy, 75 for menstrual problems, 47 for medical reasons, 30 for planned pregnancies and 44 for personal reasons. All eight pregnancies were intrauterine. Only one is a possible method failure; in the others, the women were likely pregnant at admission. Six pregnancies resulted in live births, one ended in stillbirth and one was an induced abortion. Three of the six live births ended in neonatal death within six weeks of delivery. Additional information on exact cause of death and precipitating events are being gathered in these cases. Additional data are also being sought to more accurately estimate dates of conception in relation to dates of NORPLANT<sup>®</sup> insertion.

Of the 75 removals for menstrual-related problems, 54 (72.0%) were due to menorrhagia/prolonged bleeding. The remaining menstrual-related removals occurred in women who discontinued because of spotting/intermenstrual bleeding (11 cases), amenorrhea (7 cases) and polymenorrhea (3 cases). Infection at the implant site led to discontinuation in 9 (19.1%) of the 47 removals due to other medical reasons. Hypertension was the second most frequent other medical reason given, accounting for 6 cases. It should be noted that of these six cases, five involved women who were hypertensive at admission and one who had borderline hypertension. Other common removal reasons in this category were changes in weight, depression and combined side effects (3 cases each), weakness/numbness in arm/hand, skin problems, tuberculosis and jaundice (2 cases 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, 99.2, 97.0 and 92.7, respectively, after 1, 3, 6 and 12 months of use. The corresponding follow-up rates are 97.0, 92.6, 83.6 and 53.7.

TABLE 1  
Status of Ongoing NORPLANT® Clinical Trials

	Initiation Date	Planned Caseload	Insertions Performed
<b>Bangladesh</b>			
Center 704	Feb. 1985	200	200
Center 718	Feb. 1985	200	200
Center 721	Feb. 1985	200	200
<b>Ghana</b>			
Center 041	Oct. 1985	100*	4
<b>Haiti</b>			
Center 8017	Nov. 1985	150	100
Center 8331	Nov. 1985	150	100
Center 8332	Nov. 1985	100	50
<b>Nepal</b>			
Center 729	Feb. 1985	500	307
Center 731	May 1985	100	100
Center 735	Feb. 1987	200	0
Center 736	Feb. 1987	200	0
Center 742	Feb. 1987	200	0
<b>Nigeria</b>			
Center 040	Oct. 1985	120	68
Center 042	Oct. 1985	105	51
Center 435	Jan. 1986	105	50
Center 437	Oct. 1985	105	54
Center 453	Nov. 1985	100	50
<b>Philippines</b>			
Center 600	Feb. 1986	100	89
Center 602	Jun. 1986	100	82
<b>Senegal</b>			
Center 482	Dec. 1986	50	8
<b>Singapore</b>			
Center 798	Feb. 1985	100	100
<b>Sri Lanka</b>			
Center 703	May 1985	290	247
Center 749	May 1985	200	200
Center 758	May 1985	200	200
<b>Total</b>		<b>3780</b>	<b>2460</b>

\*Study has been cancelled.

TABLE 2  
 NORPLANT<sup>®</sup> Clinical Trials  
 Cumulative Life-table Event Rates

Event	Rate per 100 users
Accidental pregnancy	
1 month	0.0
3 months	0.1
6 months	0.4
12 months	0.4
Removal for menstrual problems	
1 month	0.0
3 months	0.1
6 months	0.2
12 months	0.4
Removal for medical problems	
1 month	0.0
3 months	0.2
6 months	0.3
12 months	0.5
Continuation	
1 month	100.0
3 months	99.2
6 months	97.0
12 months	92.7
Follow-up*	
1 month	97.0
3 months	92.6
6 months	83.6
12 months	53.7

\*Follow-up rates are based on the number of women who have not previously terminated use of the method and who return for their regularly scheduled follow-up visits.

### Future Plans

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 Investigational New Drug (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 a New Drug Application (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 less developed countries (LDCs).

During 1987, pre-introductory clinical trials of NORPLANT<sup>®</sup> subdermal implants are expected to begin in El Salvador and Pakistan.

In the long-term, building skills and experience using NORPLANT<sup>®</sup> is expected to lay a secure foundation for the wider use of this method if and when it receives FDA approval. If it can be made available in larger quantities, it should also 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 has been 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 was measured by continuation rates at one year. Final 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 had significantly higher discontinuation rates for menstrual problems and side effects, resulting in a significantly lower 12-month continuation rate, 36.7, compared with 50.1 for Norinyl 1/35 users. The most frequently reported side effect causing pill discontinuation for Brevicon users was headaches; breakthrough bleeding was the most commonly reported menstrual problem causing pill discontinuation in the Brevicon group.

A Norinyl 1/35 versus Lo-Ovral comparison was conducted at six centers. Norinyl 1/35 had a significantly higher 12-month termination rate for menstrual problems (Table 4). Breakthrough bleeding was the most frequently reported menstrual problem for Norinyl 1/35 users. However, the two products were similar for all other events. Cumulative life-table continuation rates at 12 months were 78.0 in the Norinyl 1/35 group and 81.1 in the Lo-Ovral group.

Five centers participated in the Norinyl 1/35 versus Norinyl 1/50 trial. There were no differences between the two pill groups with respect to event or continuation rates (Table 5). Continuation rates at 12 months were 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=498)	Brevicon (N=498)
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	1.9	4.4
4 months**	8.5	16.7
8 months**	14.1	28.3
12 months**	20.2	36.0
Side Effects		
1 month*	1.5	4.2
4 months**	2.6	8.6
8 months**	6.1	11.6
12 months**	6.8	12.5
Other Medical Reasons		
1 month	0.9	2.4
4 months	4.3	4.5
8 months	5.9	8.0
12 months	5.9	8.0
Planned Pregnancy		
1 month	0.7	0.7
4 months	2.5	2.8
8 months	5.5	8.1
12 months	7.3	8.5
Other Personal Reasons		
1 month	2.4	2.0
4 months	6.4	7.8
8 months	10.9	11.5
12 months	13.7	15.6
Continuation		
1 month*	89.7	84.9
4 months**	72.6	60.9
8 months**	58.8	43.8
12 months**	50.1	36.7
Follow-Ups		
1 month	96.0	95.2
4 months	92.6	91.4
8 months	89.4	86.9
12 months	81.3	78.1

\*p&lt;0.05

\*\*p&lt;0.01

TABLE 4

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

	Norinyl 1/35 (N=657)	Lo-Ovral (N=653)
<b>Accidental Pregnancy</b>		
1 month	0.0	0.0
4 months	0.6	0.0
8 months	0.6	0.0
12 months	0.9	0.9
<b>Menstrual Problems</b>		
1 month	1.1	0.5
4 months	2.8	1.2
8 months*	3.7	1.2
12 months**	4.2	1.2
<b>Side Effects</b>		
1 month	0.5	0.6
4 months	2.0	1.5
8 months	2.9	2.6
12 months	3.7	3.1
<b>Other Medical Reasons</b>		
1 month	0.3	0.3
4 months	0.5	1.4
8 months	1.4	1.6
12 months	1.4	2.5
<b>Planned Pregnancy</b>		
1 month	0.0	0.6
4 months*	0.0	1.8
8 months	1.1	2.4
12 months	2.1	2.8
<b>Other Personal Reasons</b>		
1 month	1.8	1.0
4 months**	3.8	3.7
8 months	6.9	5.0
12 months	8.1	5.2
<b>Continuation</b>		
1 month	95.8	96.5
4 months	88.3	87.8
8 months	81.6	83.9
12 months	78.0	81.1
<b>Follow-Ups</b>		
1 month	91.6	95.1
4 months	84.3	87.8
8 months	76.7	79.6
12 months	68.7	69.0

\*p&lt;0.05

\*\*p&lt;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=761)
<b>Accidental Pregnancy</b>		
1 month	0.0	0.0
4 months	0.2	0.0
8 months	0.3	0.2
12 months	0.3	0.2
<b>Menstrual Problems</b>		
1 month	1.1	0.8
4 months	2.6	3.5
8 months	4.2	4.7
12 months	4.9	5.5
<b>Side effects</b>		
1 month	0.8	1.3
4 months	2.2	2.8
8 months	3.0	3.7
12 months	3.5	4.3
<b>Other Medical Reasons</b>		
1 month	0.0	0.4
4 months	0.5	1.1
8 months	1.0	2.0
12 months	1.8	2.2
<b>Planned Pregnancy</b>		
1 month	0.3	0.1
4 months	0.9	0.5
8 months	2.5	1.0
12 months	3.8	2.0
<b>Other Personal Reasons</b>		
1 month	0.8	0.6
4 months	3.6	3.0
8 months	6.0	4.4
12 months	7.6	5.7
<b>Continuation</b>		
1 month	96.5	95.7
4 months	88.2	87.5
8 months	80.2	81.6
12 months	75.0	77.1
<b>Follow-ups</b>		
1 month	94.0	93.7
4 months	87.9	87.8
8 months	83.7	84.1
12 months	80.0	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 is being conducted at five centers located in Mexico, Egypt, Indonesia, Malaysia and Colombia. Four of the studies are active with a total of 160 admissions.

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 is being conducted at four centers located in Yugoslavia, the Philippines, Mexico and Brazil. All centers are active and 599 women have been admitted. Continuation rates at 6 months are 85.3 for the Norinyl 1/50 to Lo-Femenal group and 82.0 for the 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 3,337 women from 20 centers in Latin America and Africa show a 6-month continuation rate of 75.2 and a 12-month continuation rate of 62.9. Most discontinuations were for "other personal reasons", such as the women desired a change, forgetfulness, or the pill was no longer needed. Two-thirds of the women have returned for the 6-month visit and half have returned for the 12-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 811 women show a 6-month continuation rate of 79.2. The majority of discontinuations were for the same "other personal reasons" as described above; 50.1 percent of the women have returned for the 6-month visit. In Thailand, an 850-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. A total of 823 admissions have been completed.

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 breastfeeding women, the differences over time in the weight of breastfed infants for both groups will be compared. To date, 450 women have been admitted to the study, and 288 women have completed 3 months of use.

A small study designed to assess the effect of a progestogen-only pill (MICROLUT) on milk yield and composition is underway in Australia. As of December 31, 1986, five of the 32 women had been recruited; there has been one dropout. The Principal Investigator indicated that recruitment would improve after the holidays. A research assistant has been hired to analyze the milk samples.

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 comparative trial will be conducted at centers located in the Philippines, Ecuador, Bangladesh, Indonesia and Mexico. Two centers are active with a total of 26 admissions.

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), is being conducted at five centers in Brazil, the Dominican Republic, Chile, Sri Lanka and the Sudan. Three centers are active and 673 women have been admitted. The four-month cumulative life-table continuation rates are similar, 91.8 for the Triquilar group and 88.9 for the Lo-Femenal group.

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**

### **1. Barriers and Spermicides**

FHI continued its evaluation over the last six months of a number of vaginal contraceptives including: the diaphragm without spermicide (Ortho All-Flex™); the diaphragm with spermicide (Gynol-II<sup>®</sup> 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); Emko<sup>®</sup> and Delfen<sup>®</sup> spermicidal foam, both containing nonoxynol-9; and Tioconazole vaginal cream. There are four strategies for comparative trials of these products ongoing at eight sites. Patient recruitment has continued at two sites for this reporting period.

Table 6 summarizes the active comparative trials evaluating foaming tablets. The incidence of observed pregnancies continues to be high in most studies, although nearly half have been reported by the physician as user failure. Results, as in previous studies, continue to be country-specific. In Yugoslavia (Study 785), the most common reasons for discontinuation of Neo Sampoo and Emko<sup>®</sup> users are accidental pregnancy and itching. Product-related complaints reported most often included itching, product troublesomeness and inconvenience. Tablets are more acceptable in Ghana (Study 7798) where more OVT-nonoxynol users than OVT-menfegol users reported a burning sensation as the most frequently mentioned use-related complaint. In Thailand (Study 7798), patients also are frequently

reporting a warm sensation and/or burning as the most common use-related complaint. Admissions have been halted at U.S. sites (Study 7799) because of difficulties with recruitment. Lost-to-follow-up rates continue in excess of 40% at these sites, and many women have reported some type of method-related complaint; common complaints have been burning, product messiness, difficulty with proper placement and retention of foam.

A study conducted by FHI at the Margaret Pyke Center in London (Study 7788) is comparing the fitted diaphragm with spermicide, the fitted diaphragm without spermicide and spermicide alone (foam). Enrollment has been slow to date, with 66 cases having been recruited thus far. Eight pregnancies have been reported in the diaphragm without spermicide group (6 due to method failure, 2 due to user failure), three in the diaphragm with spermicide group (2 due to user failure, 1 due to a combination of method and user failure), and three in the spermicide-only group (1 due to method failure, 2 due to user failure).

FHI continues to evaluate the bacteriocide/fungicide Tioconazole for its potential effect against Sexually Transmitted Diseases (STDs), such as chlamydia and gonorrhea, in a group of sexually-active, high-risk women in Costa Rica (Study 7800). To date, 47 cases have been enrolled in this study. Over 71 women have been screened, but admission is slow because a larger number of women than expected had chlamydia at the time of their screening. As a result, Tioconazole will receive a stronger test of efficacy. In addition, a majority of women also were diagnosed as having herpes at admission. Tioconazole

is expected to have spermicidal activity and will be studied as a potential vaginal contraceptive pending successful completion of this study.

Table 7 summarizes the 12-month (6 months for Study 7799) gross cumulative life table rates per 100 women for selected comparative vaginal contraceptive studies. In Study 785 conducted in Yugoslavia, the 12-month accidental pregnancy rates (11.7 for Neo Sampoo; 19.2 for foam) and the 12-month continuation rates (48.4 for Neo Sampoo; 39.7 for foam) remain stable since the last reporting period. For all sites in Study 7798, the 12-month accidental pregnancy rates (12.4 for OVT-nonoxynol; 14.7 for OVT-menfegol) and the 12-month continuation rates (74.3 for OVT-nonoxynol; 70.5 for OVT-menfegol) underwent some slight changes with the addition of more study subjects. A similar pattern exists in the 6-month accidental pregnancy rates (11.4 for OVT-nonoxynol; 14.7 for OVT-menfegol) and the 6-month continuation rates (49.5 for OVT-nonoxynol; 63.9 for OVT-menfegol) for the U.S. sites in Study 7799. Follow-up rates, however, have decreased for both groups in Study 7798, while a slight increase occurred for Studies 785 and 7799.

TABLE 6

Reasons for Discontinuation and Primary Method-Related Complaints  
for FHI Comparative Vaginal Contraceptive Studies of Foaming Tablets

	Study 785 Yugoslavia		Study 7798 Ghana, Thailand		Study 7799 U.S.	
	Foam (N=131)	Neo Sampoo (N=135)	OVT-n* (N=141)	OVT-m* (N=137)	OVT-n* (N=29)	OVT-m* (N=218)
<b>Reasons for Discontinuation</b>						
Accidental pregnancy	17	14	12	9	2	5
Planned pregnancy	7	5	2	1	1	0
Medical	0	0	0	6	1	0
Discomfort						
Burning	1	0	6	2	0	0
Itching	15	11	0	0	0	0
Penile irritation	2	1	0	1	1	2
Other	18	18	1	0	0	1
Product-related						
Messy, inconvenient	1	1	0	0	1	1
Failure to dissolve	0	0	1	0	0	0
Other personal	21	22	7	5	4	3
<b>Primary Method-Related Complaints**</b>						
Itching	35	49	1	0	1	0
Messy, inconvenient	6	6	12	2	3	2
Burning	2	1	14	24	3	8
Difficulty with placement	0	0	0	1	1	4
Foam runs out	0	0	3	1	4	4
Woman Months of Use	926	1040	901	817	98	131

\*OVT-n = OVT with nonoxynol-9

OVT-m = OVT with menfegol

\*\*Ever reported during product use

TABLE 7

Twelve-Month Gross Cumulative Life Table Rates per 100 Women  
for Selected FHI Comparative Vaginal Contraceptive Studies

	Study 785		Study 7798		Study 7799*	
	NeoSampoon (n=135)	Foam (n=131)	OVT-n** (n=141)	OVT-m** (n=137)	OVT-n** (n=29)	OVT-m** (n=28)
Accidental pregnancy	11.7	19.2	12.4	14.7	11.4	14.7
Planned pregnancy	5.6	6.4	2.0	1.0	10.5	0.0
Allergic reaction	0.0	0.0	0.0	0.0	0.0	0.0
Other medical	0.0	0.0	0.0	9.7	0.0	0.0
Discomfort	24.6	32.1	6.0	2.6	14.3	16.0
Product-related	1.4	2.1	0.8	0.0	7.4	6.9
Other personal	21.7	20.8	7.3	5.2	21.3	4.3
Continuation rate	48.4	39.7	74.3	70.5	49.5	63.9
Follow-up rate	86.8	92.9	44.7	39.8	30.0	55.0
Women months of use	1040	926	901	817	98	131

\*Only 6-month life table rates available for this study

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

## 2. Development of D-propranolol as a Spermicide

Preclinical studies on propranolol efficacy and safety are in progress and are described in detail in Section II, Contraceptive Development. A draft of the Investigational New Drug (IND) has been prepared. A pre-IND meeting with the FDA will be scheduled in the near future with the intent of beginning early Phase I trials later in 1987.

### 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 or 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, a device which destroys a shorter length of the Fallopian tube than older, more established methods of tubal occlusion. New efficacy and safety 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 40 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 560 interval procedures have been performed. There have been no technical failures; however, in two cases only one tube was occluded. The following table (Table 8) details the surgical difficulties. Eight women, one from the Filshie group and 7 from the Wolf group, were reported as having surgical injuries or major complications. These are also detailed in Table 8.

Early follow-up (<30 days post-sterilization) visits have occurred for more than 75% of the cases. Thirty Wolf Clip cases (11.9%) and 37 Filshie Clip cases (14.7%) reported one or more complications at early follow-up. One luteal phase pregnancy was reported in the Filshie group. One woman in each group was readmitted to the hospital and one woman in the Wolf group had additional pelvic/abdominal surgery. Long-term (>30 days post-sterilization) follow-up visits are underway. Over 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, 23 Filshie Clip cases and 17 Wolf Clip cases reported one or more complications.

The two clips are also being compared in laparoscopic procedures. Four sites (Haiti, Mexico, Guatemala and Venezuela) are now active. Interval sterilizations have been performed on 1,030 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 Table 9. Surgical difficulties were reported in 9.3% of the Wolf Clip cases and in 5.1% of the Filshie Clip cases. Surgical injuries were due to cervical lacerations, uterine perforation, or tubal bleeding. Over 85% of the women in both groups have returned for early follow-up visits (<30 days post-sterilization). Thirty Filshie Clip cases (5.8%) and 50 Wolf Clip cases (9.7%) 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=278)		Wolf Clip (N=282)	
	No.	%	No.	%
<b>A. Events at Surgery</b>				
<u>Surgical difficulties</u>				
With equipment	0	-	1	0.4
Entering the peritoneum	1	0.4	4	1.4
Visualizing/grasping tubes	5	1.8	4	1.4
Occluding tubes	0	-	1	0.4
<u>Surgical Injuries</u>				
Tubal injury without bleeding	0	-	1	0.4
Tubal bleeding	0	-	2	0.7
Uterine tear	1	0.4	1	0.4
Apnea	0	-	1	0.4
Uterine perforation	0	-	2	0.7
Total women with 1+ surgical injuries/ complications	1	0.4	7	2.5
<b>B. Events Reported at Early Follow-up*</b>				
Women returning	252	90.6	252	89.4
Readmissions	1	0.4	1	0.4
Pregnancy	1**	0.4	0	-
<u>Complications</u>				
Serous discharge	10	4.0	13	5.2
Hematoma	6	2.4	2	0.8
Inflammation at incision	11	4.4	8	3.2
Abscess	6	2.4	2	0.8
Perineo-plastic surgery	0	-	1	0.4
Bleeding	1	0.4	4	1.6
Other infection	3	1.2	-	11.9
Women with 1+ complications	37	14.7	30	11.9

TABLE 8 (Continued)

	Filshie Clip (N=278)		Wolf Clip (N=282)	
	No.	%	No.	%
<b>C. Events Reported at Long-term follow-up*</b>				
Women returning for 6-month follow-up	214	76.9	219	77.7
Readmissions	1	0.5	2	1.0
Total women with 1+ complications	23	10.7	17	7.8

\*Eleven non-interval cases are excluded from analysis.

\*\*Luteal phase

TABLE 9  
 Filshie Clip versus Wolf Clip  
 via Laparoscopy

	Filshie Clip (N=513)		Wolf Clip (N=517)	
	No.	%	No.	%
<b>A. Events at Surgery</b>				
<u>Surgical difficulties</u>				
With equipment	0	-	1	0.2
Entering peritoneum	5	1.0	11	2.1
Visualizing/grasping tubes	8	1.5	14	2.7
Occluding the tubes	7	1.4	14	2.7
Occlusive technique to wrong structure	3	0.6	6	1.2
<u>Surgical injuries</u>				
Cervical laceration	0	-	2	0.4
Tubal bleeding	3	0.6	0	-
Clip left in pelvis	0	-	1	0.3
Soft tissue emphysema	2	0.4	5	1.0
Apnea	1	0.3	0	-
Uterine perforation	0	-	1	0.2
Two incisions necessary	0	-	1	0.2
Total women with 1+ surgical injuries or complications	6	1.2	10	1.9
<b>B. Events Reported at Early Follow-up*</b>				
Women returning	459	88.8	465	90.6
Readmissions	1	0.2	0	-
<u>Complications</u>				
Serous discharge	7	1.5	8	1.7
Hematoma	0	-	3	0.7
Inflammation at incision	7	1.5	15	3.3
Bleeding at incision	0	-	4	0.9
Ecchymona	0	-	2	0.7
Vaginal bleeding	4	1.3	7	2.4
Abscess	1	0.2	2	0.4
Other	2	0.4	4	0.9
Total women with 1+ complications at follow-up	30	6.5	50	10.9

TABLE 9 (continued)

	Filshie Clip (N=513)		Wolf Clip (N=517)	
	No.	%	No.	%
<b>C. Events Reported at 6-Month Follow-up*</b>				
Women returning	258	50.3	277	53.6
Readmission	2	0.8	0	-
Total women with 1+ complications at follow-up	26	9.5	26	8.9
Pregnancy	1	0.4	1	0.4

\*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, Mexico and the Dominican Republic. To date 483 procedures have been performed. There have been seven technical failures. Surgical injuries and complications were reported in 12 (5.0%) of the clip patients and 18 (7.5%) of the ring patients and surgical difficulties were reported for sixteen procedures in each group (Table 10).

About 70% of the women in each group have returned for early follow-up (<30 days post-sterilization). Among those women in both groups the most frequently reported complication/complaint was serous discharge. One readmission in each group was reported due to hematoma and vaginal bleeding. Over one-third (34.5% of the ring patients and 42.3% of the clip patients) have returned for 12-month follow-up visits. One pregnancy was reported in the Filshie Clip group. Further pelvic/abdominal surgery was required for two Filshie Clip patients and one Tubal Ring patient. The center in Panama has begun 24-month visits.

TABLE 10

Filshie Clip versus Tubal Ring  
Via Laparoscopy

	Filshie Clip (N=238)		Tubal Ring (N=241)	
	No.	%	No.	%
<b>A. Events at Surgery</b>				
<u>Technical Failures</u>				
Change in approach	2	0.8	0	-
Change in technique	0	-	2	0.8
Two techniques used	0	-	3	1.2
Total	2	0.8	5	2.1
<u>Surgical Difficulties</u>				
Entering the peritoneum	6	2.5	2	0.8
Visualizing/grasping the tubes	5	2.1	11	4.6
Occluding tubes	1	0.4	3	1.2
With equipment	2	0.8	0	-
Occluding wrong structure	2	0.8	0	-
<u>Surgical injuries/complications</u>				
Cervical laceration	5	2.1	3	1.2
Uterine perforation	1	0.4	1	0.4
Tubal bleeding	1	0.4	11	4.6
Bladder injury	1	0.4	0	-
Lesions	0	-	1	0.4
Soft tissue emphysema	5	2.1	2	0.8
Blood loss > 100 ml	0	-	1	0.4
Tubal injury without bleeding	0	-	1	0.4
Total women with 1+ injuries/complications	12	5.0	18	7.5

TABLE 10 (continued)

	Filshie Clip (N=238)		Tubal Ring (N=241)	
	No.	%	No.	%
<b>B. Events Reported at Early Follow-up*</b>				
Women returning	174	73.1	182	75.5
Readmissions	1	0.6	1	0.6
<u>Complications</u>				
Serous discharge	9	5.2	5	2.8
Hematoma	0	-	2	1.1
Incomplete dehiscence	2	1.2	3	1.7
Inflammation/infection	3	1.8	2	1.1
Eczema	1	0.6	0	-
Vaginal bleeding	3	1.7	1	0.6
Total women with 1+ complications at early follow-up	18	10.4	14	7.9
<b>C. Events Reported at Long-Term Follow-up</b>				
Women reporting for 6-month follow-up*	161	67.6	152	63.1
Women reporting for 12-month follow-up*	112	47.1	113	46.9
Pregnancy	1	0.6	1***	0.7
Total women with 1+ complications at long-term follow-up**	13	8.1	8	5.4
Readmissions**	2	1.3	3	2.1

\*excludes technical failures and non-interval women.

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

\*\*\*luteal phase

Three centers in Latin America have been equipped to undertake the comparative study of the Filshie Clip and Tubal Ring via minilaparotomy. One study in Mexico is under development; another center is needed to complete the strategy. One center in Kenya began the study but, due to the transfer of the principal investigator, the study will be suspended after completion of the first 100 admissions. Of the 613 interval procedures performed thus far (Table 11), ten have resulted in technical failures: four in Filshie Clip procedures and six in Tubal Ring procedures. The majority of the problems visualizing or grasping the tubes were found at one center.

Over half 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 19.4% in the clip group and 15.6% in the ring 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. Two centers have begun 12-month follow-up visits.

TABLE 11

## Filshie Clip versus Tubal Ring Via Minilaparotomy

	Filshie Clip (N=282)		Tubal Ring (N=292)	
	No.	%	No.	%
<b>A. Events at Surgery</b>				
<u>Technical Failures</u>				
Change in approach	2	0.7	2	0.6
Two techniques used	2	0.7	3	1.0
Change in technique	0	-	1	0.3
Total	4	1.4	6	2.1
<u>Surgical Difficulties</u>				
With equipment	0	-	2	0.7
Visualizing and/or grasping tubes	18	6.4	26	8.9
Occluding tubes	1	0.4	7	2.4
Entering peritoneum	2	0.7	3	1.0
Closing incision	0	-	1	0.3
Ovarian cyst	1	0.4	0	-
<u>Surgical Injuries/Complications</u>				
Tubal injury without bleeding	7	2.5	9	3.1
Tubal injury with bleeding	5	1.8	10	3.4
Uterine perforation	4	1.4	1	0.3
Cervical laceration	0	-	3	1.0
Spasm of larynx	0	-	1	0.3
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	-
Cardiorespiratory arrest	1	0.4	0	-
Bowel injury	1	0.4	0	-
Total women with surgical injuries/complications	21	7.4	27	9.2
Total women reporting major complications during recovery	15	5.4	13	4.5

TABLE 11 (continued)

	Filshie Clip (N=282)		Tubal Ring (N=292)	
	No.	%	No.	%
<b>B. Events Reported at Early Follow-up*</b>				
Women returning for early follow-up	252	89.4	263	90.1
Readmissions	1	0.4	2	0.8
Pregnancy (luteal phase)	1	0.4	1	0.4
<u>Complications/Complaints</u>				
Serous discharge/abscess	6	2.4	4	1.5
Inflammation	14	5.6	7	2.7
Hematoma	9	3.6	4	1.6
Incomplete dehiscence	6	2.4	12	4.7
Complete dehiscence	2	0.8	0	-
Infections	3	1.4	3	1.3
Vaginal bleeding	2	0.9	3	1.3
Bleeding	0	-	1	0.4
Other complications	5	0.9	6	2.3
Total women reporting 1+ complications at early follow-up visit	48	19.4	40	15.6
<b>C. Events Reported at Long Term Follow-up</b>				
Women returning for 6-month follow-up*	219	77.7	230	78.8
Readmissions	0	-	3	1.8
Women returning for 12-month follow-up*	156	55.3	178	61.0
Total women reporting 1+ complications at long term follow-up**	33	14.9	41	17.6

\*excludes technical failures and non-interval women.  
\*\*includes 6- and 12-month follow-up visits.

### c) Filshie Clip versus Pomeroy Method

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 1,137 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. Surgical difficulties were reported for 28 Filshie Clip procedures (4.9%) and for 31 Pomeroy procedures (5.5%). Tubal bleeding was the most frequently reported surgical injury in both groups. 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 (10.2%) Filshie Clip patients and 55 (11.5%) Pomeroy patients.

Approximately 60% of the women in each group have also returned for their six-month follow-up visit. 62 women in the Filshie Clip group (16.3%) and 66 women in the Pomeroy group (16.8%) experienced one or more complications. During long-term follow-up, 12 women, nine 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.

Half of the women in both groups have returned for their one-year follow-up visit. Although almost 20% of the women 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=569)		Modified Pomeroy (N=568)	
	No.	%	No.	%
<b>A. Events at Surgery</b>				
<u>Technical Failures</u>				
Change in approach	0	-	1	0.2
Two techniques used	2	0.4	2	0.4
Total	2	0.4	3	0.6
<u>Surgical Difficulties</u>				
Entering peritoneum	3	0.5	0	-
Visualizing/grasping tubes	18	3.1	28	4.9
Occluding tubes	5	0.9	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 injury without bleeding	1	0.2	1	0.2
Tubal injury with bleeding	5	0.9	6	1.1
Soft tissue emphysema	0	-	1	0.2
Total women with 1+ injuries/complications	6	1.1	8	1.4

TABLE 12 (continued)

	Filshie Clip (N=569)		Modified Pomeroy (N=568)	
	No.	%	No.	%
<b>B. Events Reported at Early Follow-up*</b>				
Women returning for follow-up*	502	88.2	483	85.0
Readmissions	1	0.2	1	0.2
<u>Incision Complications</u>				
Serous discharge	26	5.2	23	4.8
Inflammation	14	2.8	16	3.3
Abscess	5	1.0	6	1.3
Bleeding	1	0.2	1	0.2
Incomplete dehiscence	3	0.6	8	1.7
Other	1	0.2	0	-
Total women with 1+ complications*	51	10.2	55	11.5
<b>C. Events Reported at Long Term Follow-up**</b>				
Women returning for 6-month follow-up visit*	335	58.9	347	61.1
Women returning for 12-month follow-up visit*	289	50.8	307	54.0
Women returning for 24-month follow-up visit	201	35.3	192	33.8
Total women with 1+ complications	62	16.3	66	16.8
Readmission to the hospital	3	0.8	8	2.7
Pregnancy	3	0.8	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 one active center in Brazil. A second center in Latin America has completed follow-up. Details on the surgical injuries and difficulties have been detailed in past reports. A total of 158 procedures were performed at the two centers prior to 1985.

Six-month follow-up data were collected for 80 (93.0%) of the Filshie Clip group and 68 (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, 15 Secuclip patients (21.4%) and 17 Filshie Clip patients (20.0%) reported complications. Most of these were tender or enlarged adnexa. About 40% of the Filshie Clip patients and 54.2% of the Secuclip patients have returned for two-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 six sites. Studies located in Finland, Austria, Holland, Taiwan and Korea have been initiated. The site in Finland has enrolled 15 women; a site in Austria has also enrolled 15 women. To date no major complications have been reported.

#### f) Non-Comparative Filshie Clip Studies

One investigator in Brazil is undertaking a comparison of the minilaparotomy and laparoscopic techniques using the Filshie Clip. Admissions have been completed and one-year follow-up visits are taking place. Data on surgical and early follow-up events were reported in the previous report. No complications or complaints have been reported at the long-term follow-up visits. This study should be completed in September 1987.

A non-comparative trial of the Filshie Clip applied via laparoscopy is underway in three Canadian centers and four centers in England. One additional center in Canada and one center in England are expected to start in the spring. Sterilization procedures have been completed on 374 interval patients. Table 13 details events at surgery and at follow-up. Surgical difficulties have included eleven cases of difficulty with the equipment, six cases of difficulty entering the peritoneum, six cases of difficulty visualizing/grasping the tubes, and eleven cases of difficulty occluding the tubes. The rate of surgical injuries/complications is 2.4%; there were three cases of tubal or mesosalpingeal bleeding, one case of a ruptured ovarian cyst, one case of vasovagal reaction, and one case of perforating the pouch of Douglas. Four incision complications were reported. At the early follow-up visit, 14.1% of the 256 women returning reported one or more complications. There was one readmission for suture removal. Two luteal phase pregnancies and one readmission for pelvic pain and yeast infection were reported

among the 114 women (30.5%) who returned more than 31 days post-sterilization. Thirteen women (11.4%) reported complications at this long-term visit. The majority of these were menstrual problems.

TABLE 13

Non-comparative Filshie Clip  
Trials

	Filshie Clip (N=374)	
	No.	%
<b>A. Events at Surgery</b>		
<u>Surgical Difficulties</u>		
With equipment	11	2.9
Entering peritoneum	6	1.6
Visualizing/grasping tubes	6	1.6
Occluding tubes	11	2.9
Occluding wrong structure	1	0.3
<u>Surgical Injuries</u>		
Cervical laceration	1	0.3
Uterine perforation	2	0.5
Tubal bleeding	3	0.8
Ruptured ovarian cyst	1	0.3
Vasovagal reaction	1	0.3
Other perforation	1	0.3
Total women with 1+ surgical injuries/complications	9	2.4
<b>B. Events Reported at Early Follow-up</b>		
Women returning for early follow-up	256	68.4
Readmissions	1	0.4
<u>Complications</u>		
Serous discharge	8	3.1
Inflammation	6	2.3
Bleeding	5	2.0
Incomplete dehiscence	3	1.2
Other	2	0.8
Women reporting 1+ complications at early follow-up	36	14.1

#### 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. The details of the Thailand project were reported in the last annual report. A final report was prepared; a paper is in progress.

The long-term follow-up study in Bangladesh has also been completed. Sixty women returned for a long-term follow-up visit. No pregnancies, surgeries or complications were reported.

#### 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 5,000 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 training of interviewers for this phase of the survey took place in October. The first 4,000 sterilization cases were followed up at 1- to 3- months and 12-months post-sterilization. Data analysis will be done in Thailand by the Thailand Fertility Research Association (TFRA). Admission data was 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. Pattakā 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 has been completed in Chile. The Femtest device was tested in 109 women before sterilization and was compared with results from a hysterosalpingography (HSG); 108 of these women had both procedures repeated after sterilization. There was agreement in 97.2% of the cases before sterilization and in 100% of the cases after sterilization. One case of equipment problems (Femtest) was reported. There were three cases with complications. A report is being prepared.

This study has been expanded to two additional sites in Indonesia. At each center 25 women are tested before sterilization and another 25 women are tested after sterilization. Each woman will have both the Femtest procedure and an HSG procedure. Those studies began in March 1987.

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. To date, 49 women have been located and forms for these cases are being processed; one pregnancy was reported.

## 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.

A final report has been prepared for the comparative study of percutaneous occlusion of the vas by diathermy and the standard incision with diathermy. 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 hysterectomies.

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**

FHI 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, is conducted yearly in Chile. The 72-month, cumulative life-table pregnancy rates for three studies shown in Table 14 range from 6.4 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	72-mo. rate
<b>Quinacrine Solution</b>							
Santiago, Chile N=124	6.5 (95.2)*	9.9 (88.9)	11.7 (49.6)	- -	- -	- -	- -
<b>Quinacrine Pellets with Sodium Thiopental</b>							
Santiago, Chile N=148	1.4 (97.3)	4.2 (94.4)	6.4 (84.9)	8.9 (79.6)	8.9 (71.3)	8.9 (66.9)	8.9 (66.2)
<b>Quinacrine Pellets with- out Sodium Thiopental</b>							
Santiago, Chile N=123	1.7 (97.5)	3.3 (96.6)	6.7 (96.5)	6.7 (93.9)	6.7 (89.6)	6.7 (56.5)	6.7 (26.1)
<b>Quinacrine Pellets with- out Sodium Thiopental</b>							
Valdivia, Chile N=149	0.7 (100.0)	0.7 (99.3)	3.4 (99.3)	4.1 (94.4)	5.6 (87.1)	5.6 (85.0)	6.4 (64.0)
<b>Quinacrine Pellets with- out Sodium Thiopental</b>							
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 evidence that 100-minute releasing quinacrine pellets, 250 mg, may be as effective as the 10-minute releasing product when given with only two insertions rather than with three. Two insertions in 106 women have resulted in a 24-month pregnancy rate of 3.0 per 100 women. Sixty-eight percent of the women have completed 24-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 has been initiated at the University Hospital of Jacksonville, Florida. FHI has received a report of a serious adverse experience which occurred in the study. After receiving the tetracycline insertion and a vaginal hysterectomy as scheduled, the woman developed a fever of 102° and was diagnosed as having an abdominal abscess.

Exploratory laparotomy showed severe abdominal inflammation and inflammation of the ovarian pedicles, but no abscesses. Cultures taken during the laparotomy were negative but the woman had a poor leukocyte response and a poor response to antibiotics. She recovered within two weeks. FHI has suspended the study until a thorough review of the project has been completed.

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 non-AID funding. All of the 12 planned cases have been completed; three received quinacrine, four tetracycline and five the sham procedure. Equipment difficulties made the insertion of the drug into the tubes difficult and in three cases, insertion was impossible. The earthquake which occurred in Mexico City in August 1985 totally destroyed one of the hospitals where the hysterectomies were being performed and records for five patients were lost. Results from the study were inconclusive.

#### Future plans

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.

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.

FHI has submitted an IND for the use of iodine containing tubal sclerosing mixtures to the FDA. 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 380Ag**

The TCu 380Ag 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 were received at the end of last fiscal year, and during the first half of this fiscal year data analysis was begun. Two papers are in progress: one an evaluation of the TCu 380Ag in comparison with the Multiload Cu 375 and another comparing the TCu 380Ag with the Copper 7. The three-year follow-up rate was

sufficiently high (at least 70.0 for all devices) to allow analysis of three-year event rates. It is anticipated that these papers will be ready for submission to journals by the end of the fiscal year.

## 2. Copper T IUD With or 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 six months. Two of the five sites participating in this 1,300-case study are continuing to collect data. Preliminary analyses of 1,244 women with an overall 12-month follow-up rate of approximately 62%, reveal no difference between the two groups with respect to the incidence of infection and inflammation. The significant difference observed in previous preliminary analyses between the two group removal rates for bleeding and pain continues to be observed. The 12-month rate is 5.9 for the strings group and 1.5 for the without strings 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. Overall continuation rates are significantly higher for the no strings group (89.8) than for the strings group (85.3). Expected completion date for all the studies under this strategy is December 1988.

### 3. Evaluation of the TCU 380A

A multicenter 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. Data on 1,547 cases have been received from Brazil, Cameroon, Chile, Egypt, El Salvador, Honduras, Mexico and Sudan. An additional study comparing these devices was initiated during January in Costa Rica. Negotiations are continuing to initiate studies at three sites in the Philippines. The Egyptian Fertility Care Society (EFCS) is also coordinating a multicenter trial in Egypt of 1,000 cases. The data are being managed and analyzed with the EFCS computer facilities. To date, 361 women have entered the trial at five sites.

Two studies are in progress to evaluate the TCU 380A in comparison with the TCU 220. A total of 393 patients have been admitted in Mexico and Pakistan. With a six-month follow-up rate of approximately 63%, no significant differences have been found between users of the two devices in terms of termination and event rates.

Three studies designed to compare the TCU 380A with the Lippes Loop D (LLD) have begun in Peru, Nigeria and Turkey. Three month follow-up of the 281 women admitted so far indicates a higher continuation rate for the TCU 380A ( $p < 0.05$ ).

Admissions are complete in Venezuela, where the TCU 380A is being compared to the Nova T. With a six-month follow-up rate of 51%, more method-related terminations have been reported for TCU 380A users than for Nova T users ( $p < 0.05$ ). The respective rates are 7.0 and 1.3.

Studies comparing the TCU 380A with the Multiload Cu 250 are underway in Malaysia, Sri Lanka and Thailand. A total of 1,903 women have been admitted to date, with approximately 67% followed-up at six months. An interim analysis of this data revealed that the TCU 380A has performed better than the Multiload Cu 250 in terms of expulsion and total method-related terminations. Data will continue to be collected through 12 months of follow-up.

A 3,000-case multicenter study comparing the TCU 380A with the Multiload Cu 375 and the LLD is being managed by the BKS PENFIN in Indonesia. As with the EFCS study, the data are analyzed in-country with the BKS PENFIN computer facilities. This study is progressing well, with 2,225 women enrolled so far and a one-month follow-up rate of 78%. For both the BKS PENFIN and EFCS studies, data on printouts and disks are made available to FHI periodically.

Twelve-month follow-up will be attempted at all study sites under this strategy; it is expected that all follow-up visits will be complete by November 1989.

#### 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 143 women have been admitted to date. With a six-month follow-up rate of about 56%, 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. The Mexican Institute of Social Security (IMSS) is managing this multicenter trial as well as processing and analyzing the data. Out of a total planned caseload of 1,800 cases, 857 women have been admitted. It is too early in the follow-up period to note any results.

## 6. IUD Insertion With or Without Antibiotics

Under the supervision of the Clinical Trials Division, a site in Nigeria was 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 risk of infection at the time of insertion was lower than expected when the sample size was first calculated. The initial results suggest a trend towards less intrauterine infection with IUD use when prophylactic antibiotics are used, but additional data is needed before setting major new possible health policies in this area. The site in Nigeria was included in order to provide an adequate sample size to detect a difference between the two groups should one exist. A total of 156 women have enrolled in Nigeria to date and approximately 90% have completed one month follow-up. Sufficient data are not yet available to detect any significant differences between the two groups of women.

## 7. IUD String Retriever

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. In January, the U.S. FDA approved FHI's application for an Investigational Device

Exemption (IDE). At present, FHI is exploring manufacturing possibilities.

### Future Plans

As part of FHI's evaluation of the TCu 380A, plans are being developed to conduct long-term follow-up, up to ten years, of patients enrolled in Thailand's multicenter trial. In addition, FHI continues to be interested in conducting clinical trials of the levonorgestrel-releasing IUD.

### **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 caseload and degree of follow-up a new investigator can achieve.

There have been six studies conducted under FHI's Investigator Network Needs Strategy during this fiscal year. 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

During the first half of this fiscal year, a randomized study comparing the Multiload Cu 250 and the TCU 200 inserted immediately postpartum (via forceps) was completed in Thailand. The follow-up rate at six months was 79.3 for Multiload users and 85.0 for TCU users. Expulsion rates were high for both devices: 24.1 for Multiload cases and 29.6 for TCU 200 cases; high expulsion rates are not unusual for postpartum IUD insertion. Because Thailand's national family planning program provides the Multiload Cu 250, it is expected that this study will provide the government with important information concerning its use during the immediate postpartum period. The consultant report for this study is in the final stage of completion.

### 2. Sterilization Studies

A surveillance study of 200 sterilization procedures is progressing slowly in Nigeria. To date, 67 women have been enrolled in the study; no follow-up data are yet available.

### 3. Systemics Studies

A study is in progress in Mali, at the Maternal and Child Health Center associated with the Ministry of Health, to compare Noriday and

Lo-Femenal, two locally available oral contraceptives. Two hundred women have been admitted into this study. With about 50% follow-up at eight months for these women, there appear to be no differences between the pills in terms of reasons for discontinuation or side effects.

Another systemic study designed to compare two types of progestogen-only oral contraceptives, Micronovum and Ovrette, is ongoing in Zimbabwe. Five hundred women have been admitted to this study. The two-month follow-up rate is 33.0 for each group; there are not sufficient follow-up data to detect any group differences at this time.

An additional systemic study was initiated in Malaysia in January 1986. This study is designed to compare the triphasic pill, Triquilar, with the low-dose combination pill, Marvelon. One hundred eighty-four women have been enrolled in the study, and approximately 26% of these patients have completed eight months of follow-up. No significant differences have been demonstrated between the two types of pill users.

In Niger, a surveillance study was initiated recently to collect data on the use of locally available standard- and low-dose oral contraceptives, Minidril and Stediril. A total of 50 patients have been admitted to the trial so far.

## 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.

FHI is continuing to develop plans for two systemic studies to be conducted by Clinical Trials Workshop participants in the Philippines. The investigators plan to compare two locally available oral contraceptive preparations: a low-dose combination pill and a triphasic pill. Another workshop participant in Nepal will participate in a programmatic evaluation of the TCu 380A IUD.

It is also expected that several participants of the Clinical Trials Workshop held in Panama will conduct studies under the INN strategy. Study proposals were developed during the first half of this fiscal year. One investigator in Colombia has been identified to conduct a programmatic study of the TCu 380A IUD. Other study proposals will be finalized during the remainder of this fiscal year.

### **G. Other Studies**

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 and the Egyptian Fertility Care Society (EFCS). 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 1,200-case clinical trial of NORPLANT®-2 rods. Responsibility for implementation of the project has been assigned to the EFCS, which hopes to initiate these activities by mid-1987.

#### **IV. REPRODUCTIVE EPIDEMIOLOGY AND SEXUALLY TRANSMITTED DISEASES**

Contraception has an impact on people's lives beyond its immediate intended effect of avoiding pregnancy. It can alter the risk of contracting certain diseases, exacerbate or ease already existing disease, and influence the possibility of later conception. It is this second-level of impact that is the focus of research in the Division of Reproductive Epidemiology and Sexually Transmitted Diseases.

The Division investigates the long-term consequences of contraceptive use, including sexually transmitted disease, cancer, and cardiovascular disease. A major emphasis over the past year has been integrating the benefits and risks of contraception in order to allow policy makers to compare the impact of contraceptive use with that of its alternative--pregnancy. The major emphasis of the coming year will be the role of mechanical and chemical barrier contraceptives in preventing the heterosexual transmission of human immunodeficiency virus (HIV, the AIDS virus).

##### **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

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.

a. Breast Cancer: No relationship was found between oral contraception and breast cancer when users and nonusers were compared (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. An increased risk (RR = 2.0; 95% CI = 1.0, 4.1) was found among a subgroup of women who had used oral contraception for 3-5 years, but there was no trend with duration of use, and women who had used for more than 5 years had no increased risk, and the relationship is considered a spurious one.

The findings with DMPA are difficult to interpret. 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. 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, which is biologically implausible. 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. It is possible that bias arising from different utilization of medical services by users and nonusers might explain some of the associations which are not consistent with results of other studies. A paper reporting this analysis has been submitted to the Journal of the National Cancer Institute.

- b. 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 (RR = 1.6; 95% CI = 1.2, 2.2). However, a plausible explanation for this is 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 OC's had a Papanicolaou smear, compared with only 72% of controls who had never used OC's. 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 OC's 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 OC's 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 supports 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 has been submitted to the American Journal of Epidemiology.

## 2. 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 on 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.

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. There were 1.9 maternal deaths per 1000 live births or 44.9 per 100,000 married women aged 15-49 in Menoufia, and 2.4 maternal deaths per 1000 live births or 67.2 per 100,000 married women aged 15-49 in Bali. 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).

These studies 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 submitted for publication. Two papers on data from Bali will be written in the next few months. All the papers using data from Egypt will be published in Egypt in monograph form, using non-AID funds.

FHI was represented at the World Bank's, Safe Motherhood International Conference in Nairobi February 9-13, 1987.

### 3. 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.

A paper describing this analysis appeared in the May 1986 issue of Studies in Family Planning and the same analytic technique was used to put findings about a possible association between hepatocellular carcinoma and OC use in perspective. FHI is disseminating up-to-date perspectives on the pill to users and providers working with other AID-funded agencies in this task.

Work is in progress to use the lifetable program to estimate the number of deaths caused or averted by oral contraceptives for each of the 9 broad categories of cause of death. Among women who use the pill before age 30, 2 deaths are averted for each death caused, while, among women taking the pill after age 30, oral contraceptive use caused more deaths than it averted, as a result of the increased risk of cardiovascular disease associated with the pill.

Fertility and its control appears 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 accepted by the American Journal of Public Health.

Although in the total population of most developed countries 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 seven

times more than a year of contraceptive use. 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, more appropriate choice of contraceptive methods, 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. A paper describing a similar analysis for Britain is now in preparation and a paper is also ready for submission, assessing the reproductive mortality rate in several developing countries as a means of summarizing the mortality risk of fertility and its control.

#### 4. Prostatic Cancer and Benign Prostatic Hyperplasia

One animal study has 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.

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.

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. A paper describing this analysis is in press in the Journal of Urology.

5. Contraceptive Use and the Prevalence of Sexually Transmitted Disease (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 shows that users of barrier methods and spermicides have a risk of gonorrhea 0.7 times and of chlamydia 0.4 times that of oral contraceptive users.

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

The possibility of pelvic inflammatory disease (PID) and infertility resulting from IUD use had become increasingly apparent to lay and professional groups by 1985. FHI collaborated with the CDC and Kenyatta National Hospital to conduct a randomized double-blind trial to study whether prophylactic antibiotics given at IUD insertion help prevent post-insertion PID. The clinical work was completed January 1986 and data analysis was completed November 1986. 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 1986, 1813 women were followed, with a PID incidence rate of 1.3% in women receiving the antibiotic, and 1.9% in women receiving the placebo. It therefore appears that the drug did protect against PID, but due to the low number of cases observed this result was not statistically significant. The rates of PID were lower than the rate presumed by the government which had been used to justify their recommendation not to insert IUDs in young women with few children. A paper is presently in the final stages of preparation. A second study has been initiated by Clinical Trials to try and extend knowledge in this important area.

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

Sexually transmitted diseases are a major cause of infertility in many parts of the world. FHI has completed the most comprehensive study to date of the prophylactic effect of the contraceptive sponge on transmission rates of gonorrhea, chlamydia, and monilia. The study was a collaborative effort with the Venereal Disease Division of the Ministry of Public Health of Thailand. Three hundred and twelve women, half of whom received sponges, participated and accumulated 928

woman-weeks of observation. The sponge reduced the incidence of chlamydia by 30%, and of gonorrhea by 70%. The incidence of monilia, the least common and least pathologically important STD studied in the trial, increased almost three-fold, (Monilia is a fungal infection, not a bacterial one, and it is thought that most cases are acquired by means other than sexual transmission.) Women ceased participation in the study after 6 weeks or when they developed an infection. Women who developed an infection were treated. At termination all women were invited to enter the second phase in which they were crossed over to the alternate group, with former non-users starting to use the sponge and vice versa. The results of this second phase were similar to the larger parallel study. A paper describing this appeared in a May issue of the Journal of the American Medical Association.

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 has been published in The African Journal of Sexually Transmitted Diseases.

#### 8. Conference on Smoking and Reproductive Health

A book summarizing FHI's Conference of Smoking and Reproductive Health has been published. This international conference on the effects of smoking on reproductive health took place in San Francisco on 15-17

October 1985 and has been reported previously. 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.

#### 9. The Effect of Condom Use on Mild Cervical Dysplasia

In 1981, two investigators found in a non-random, uncontrolled 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. In an attempt to confirm or refute these interesting findings, FHI first collaborated with Juarez University in Durango, Mexico and attempted to recruit 200 women with mild dysplasia to a condom or control group.

Unfortunately, recruitment to the study, which started in August 1986, has been slow so another site is being sought.

### **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, 127 women have been interviewed (70 cases and 57 controls) and high rates of internal and out migration. No physician has declined to participate, and the response from cases contacted 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. Home visits are being initiated as part of the efforts to follow up nonrespondents. We anticipate that potential respondents will be more motivated to participate by a personal contact than by a letter.

Colleagues in the Viral Disease Division of the CDC will look for evidence of human papillomavirus (HPV) in the tumors of the women in this study. Where HPV is found, the CDC will identify the DNA type. This study is being conducted in collaboration with the Departments of Pathology and Microbiology of the University of the West Indies.

## 2. 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 further insight into this important problem. FHI used 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 has been 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, however, considerable methodological problems still have to be resolved before we can be certain this data can be used.

### 3. 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. A 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, 19 patients have been admitted to the study, 11 have completed the first phase, and 5 have completed the second 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<sup>®</sup> contraceptive system will be initiated during 1987. This will not be a randomized study, but the hematologic parameters of patients will be evaluated for 3 months while using a nonhormonal method of contraception, and these parameters will be compared with the same parameters at various intervals after NORPLANT<sup>®</sup> insertion. As far as possible in Nigeria the same data collection instruments and the same tests are being used in Jamaica to make the two studies comparable.

#### 4. Effects of In Utero Steroid Exposure

Two studies are being conducted. In Thailand, approximately 1200 children have been identified who were exposed to depot medroxyprogesterone acetate (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 have been 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 and is jointly funded with the WHO.

A similar study, that looks at more subtle indices of development, has been conducted in Israel with children exposed to medroxyprogesterone acetate (MPA) used to treat threatened abortion. Data collection was completed in 1986 and is now undergoing analysis. The Hebrew University in Jerusalem is the collaborating institution. Handedness, degree of aggression, psychological factors and masculine-feminine orientation are being evaluated. Preliminary results show no differences between the two groups for these outcomes. A paper describing the complete analysis is in preparation.

#### 5. 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. A leading cause of salpingitis is Chlamydia trachomatis.

To investigate the relationship between chlamydia and ectopic pregnancy, investigators in Boston are performing a hospital-based case-control study. We will study the prevalence of 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 and is ongoing.

#### 6. The Male Influence on Spontaneous Abortion

It is important to establish male exposure to hazardous substances (usually in the workplace) can impair reproduction. A study was started 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 December 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.

#### 7. 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 an attempt to organize 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). The planned 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 the world's knowledge of the health effects of the pill. The new study, also with the RCGP, is designed to include 100,000 women of reproductive age and 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 shows that it is feasible to follow women as they move around the country and change doctors; inclusion of these women could reduce the high loss to follow-up of the first study. However, due to financial limitations, the Medical Research Council of Britian has withdrawn their support and unless alternative funding is found, the study will not proceed.

#### 8. Cardiovascular Disease and Oral Contraception

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 the currently available data relates to pills with relatively high doses of both estrogen and progestin. Today's 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.

Therefore, FHI is contributing to a case-control study of young women with fatal myocardial infarction being conducted by the Department of Community Medicine and General Practice, Radcliffe Infirmary of Oxford, England. This study began in early 1986. To date, 69 cases have been identified for the first three months of 1986 although, for a variety of reasons, not all of these have been included in the study. Information on contraceptive history and presence of other risk factors for myocardial infarction are collected from surviving family members and the deceased's physician.

#### 9. Pregnancy termination and breast cancer

In Sweden the incidence of breast cancer in young women has increased since 1970 concurrent with an increase in the use of pregnancy termination from the mid-1960s to the mid-1970s.

This project links data from Swedish national computer registries of pregnancy termination, cancer, hospitalization, births and deaths and is designed to test whether the association is accidental or causal. Computerized data have been collected for 166,840 pregnancy terminations. The linked analysis file now comprises about 159,000 records. Checking of the remaining records and keypunching continues.

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

In Zacatecas, Mexico, an investigator has successfully managed certain side effects of oral contraceptives with Vitamin B<sub>6</sub>. The purpose of this study, which was begun in February 1987, is to measure the number and severity of side effects associated with oral contraceptive use in women who also take 150 mgs of Vitamin B<sub>6</sub> daily, or a placebo.

#### 11. 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 has begun a study with the Chapel Hill Spine Clinic to determine whether the bone mineral density of premenopausal and perimenopausal women aged 40-54 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 is

measured by dual photon absorptiometry, and at two sites on the radius by the single photon method. Information on other risk factors for osteoporosis and a contraceptive history is collected on a questionnaire. The mean bone density of never-users of oral contraceptives will be compared with that of current and former users.

## C. Planned Projects

### 1. Maternal Mortality

Building on its past experience in studying maternal mortality, FHI is developing new 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 USAID Mission funds. The Haiti study will be done in collaboration with Columbia University.

Among already existing in-house data, FHI's MCM data bank created files of 577 maternal deaths, together with the same number of controls matched for age and parity, and controls randomly selected from the same institution. The first analysis with this newly created data set will be an analysis of the effect of birth interval.

### 2. Oral Contraceptives and Liver Cancer

Two recent studies published in Britain showed an association between hepatocellular carcinoma and oral contraceptive use. In Britain and the United States hepatocellular carcinoma is extremely rare, and appropriately, the association with oral contraceptives had 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 (HBV) 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 exacerbates the risk of development of liver cancer in women exposed to HBV. FHI is seeking a site in which to do a case-control study of liver cancer. Hong Kong and Taiwan are possible sites, since they have a high prevalence of both HBV exposure and oral contraceptive use, and have tumor registries.

3. Spermicides and male-to-female transmission of the AIDS virus

FHI will undertake several studies among women at high risk for sexually transmitted diseases. Two of these studies will be in collaboration with US universities (Univ. of Washington working in Nairobi, Kenya; the Univ. of California at San Francisco working in Kigali, Rwanda). Other studies will be done in Accra, Ghana and Juarez, Mexico.

4. FHI will work with researchers from the Universities of Washington, Manitoba, and Nairobi to design a case-control study which will compare the recent contraceptive history (<5 yrs) of women who are seropositive for HIV with those who are seronegative.

## **V. PROGRAM EVALUATION**

The Program Evaluation Division supports research in three 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 providers have toward the methods they deliver. The broad goal is to understand the various factors associated with contraceptive acceptance and continuation within the general population. The Division is one where the opportunities for needed research exceed the available resources by a wide margin.

## **A. Family Planning Evaluation**

These evaluations are designed to provide information to improve service programs. Understanding the link between service providers and clients is crucial to establishing effective, acceptable family planning programs. 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, family planning needs, attitudes, and family planning knowledge and attitudes of special segments of the population (adolescents, males).

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. Research methods range from in-depth interviews and focus groups to hospital-based studies and large household surveys.

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

Program Evaluation is playing a major part in developing the work of the AIDS Task Force. The work includes or will include (1) studies to determine the acceptability of spermicidally lubricated condoms, (2) the education of those at high risk for AIDS and STDs in safe sex,

distribution of condoms and spermicides, and evaluation of these efforts and, (3) inclusion of a module in general-purpose surveys on AIDS which includes knowledge of transmission of AIDS and whether concern about AIDS has influenced behavior, especially regarding use of condoms and spermicides.

#### 1. Provider/Client Surveys

Throughout much of the developing world, oral contraceptives (OC's) are generally acquired without first making a visit to a physician. Retailers and community-based distributors play an important role in determining what clients know about OC's 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 Oral Contraceptive Purchasers

When a new source of supplies is added, it may gain customers who switch methods or sources or it 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. 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.

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.

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. A final report is being written.

b) Nepal: Contraceptive Retail Sales Study

The Nepal Contraceptive Retail Sales (CRS) Company 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 contraceptives and contraceptive foaming vaginal tablets were interviewed. Since the vast majority of medical shops selling pills and contraceptive vaginal tablets are in urban areas, the study focused on these areas.

Fieldwork was initiated in late February 1986 and as of the end of March, interviews were completed with 763 consumers and 361 retailers. Data analysis took place from June-August 1986 and a preliminary report was prepared in September 1986. A seminar on the survey findings was held in late November 1986. The final report was also printed in November 1986.

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 had not used any method prior to using the CRS pills. Thus, a large share of CRS consumers are first time acceptors suggesting 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 advertising 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.

Results from this study will be presented at the National Council of International Health meeting in Washington, DC in June 1987. A paper is being prepared on consumer perspectives toward contraceptives.

c) Mexico: Promoter's Knowledge of Contraceptives

In Juarez, Mexico, a survey has been completed of community-based distributors involved in promoting family planning among women, men and young adults. 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 was administered to female promoters and the second to young adult promoters.

One goal was 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.

The data was been collected and analysis will be done during the current fiscal year.

#### d) 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. 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 where 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.

### 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 Sul) 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 were disappointing. While the rate of postpartum sterilization rose, the increase was small. New facilities were not being fully utilized. Services to facilitate interval sterilization were 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.

The Final Report has been completed and is under review.

b) 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 versus 3% in the control group. Dr. Alex Omu, the study director, visited FHI in October 1986 to work on data analysis which has now been completed. Results of the study will be presented at the National Conference on International Health in June, 1987 and have been submitted to the APHA for presentation in October. The Final Report will be completed this fiscal year.

c) 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 is the only study of its type to try to determine if such cash payments could be coercive, or if they have no measurable effect on an individual's capacity to give informed

consent, on the decision to accept sterilization, and on long-term satisfaction and regret with the method. It provides 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 and successfully interviewed 817 women. 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.

Of those followed up, 14 percent regretted, to some extent, their decision to be sterilized. However, regret was not associated with the amount of the reimbursement payment. A logistic model suggests that regret is positively associated with several factors that can be identified at the time of sterilization. These include not having a child of each sex, being younger than 25, having a spouse who opposes the sterilization, and feeling that others have had a greater role in making the decision than the woman herself. Women who suffered the death of a child since sterilization were also more likely to regret being sterilized.

It appears that the quality of counseling at the time of operation is more important in relation to the possibility of subsequent regret than the availability or absence of cash reimbursements. Now that factors associated with regret have been identified, the government

of Sri Lanka may want to encourage additional counselling for women at high risk for regretting the operation.

#### d) 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 was developed that records information for all women considered to be potential acceptors of NORPLANT®. The purpose is to investigate 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 has now been completed for some 13 study sites. Tables and a draft report have been prepared. Examples of several results appears in Table on page 114.

The survey identified potential socio-cultural obstacles to NORPLANT® acceptance (concerns about menstrual irregularities; husband's disapproval). Interest in trying NORPLANT® was high, and the positive aspects of the method identified by respondents included

Willingness to Pay for NORPLANT<sup>®</sup> and Amount  
 Respondents Willing to Pay: Nigeria and Haiti

	<u>Nigeria</u>	<u>Haiti</u>
Percent Willing to Pay for NORPLANT <sup>®</sup>	69.30 (540)	69.8 (411)
Mean Amount Willing to Pay for NORPLANT <sup>®</sup>	16.60 (Naira)	6.10 (\$US)
Percent Distribution of Amount Willing to pay for NORPLANT <sup>®</sup>		
<u>Amount</u> <sup>1</sup>	<u>Percent</u>	
(\$US)		
1	1.5	12.2
2	2.3	11.2
3	0.3	12.2
4	0.6	3.6
5	26.7	34.2
6-10	28.8	19.3
11-15	5.0	2.7
16-20	17.0	2.6
21-25	5.6	1.0
26-30	2.6	0.5
More than 30	<u>9.8</u>	<u>1.0</u>
Total	100.0 (341)	100.0 (196) <sup>2</sup>

<sup>1</sup>At the time of the NAS study, 1 Naira was approximately equal to 1 US dollar.

<sup>2</sup>Excludes all women who said they were willing to pay for NORPLANT<sup>®</sup> but did not specify an amount.

effectiveness, reversibility, and convenience of use. Survey findings pointed to the need for thorough counseling to reduce apprehensions and misinformation women and their husbands may have about the method (e.g., fear of side effects; misgivings about insertion and removal procedures). Such actions should lead to increased acceptance, satisfaction and continuation of use. A target group of potential acceptors most likely to want to try the method has also been identified in each country.

e) Bangladesh NORPLANT<sup>®</sup> Acceptability Research

Several studies examining various aspects of NORPLANT<sup>®</sup> acceptability in Bangladesh began in 1987. Stage I examines issues regarding NORPLANT<sup>®</sup> removal (e.g., difficulties in obtaining removals, reasons for removals, advice given at the clinic). In the second stage, an intervention strategy to counsel and motivate husbands as well as wives will be evaluated to determine its impact on NORPLANT<sup>®</sup> acceptance and continuation of use. The Bangladesh Fertility Research Program will coordinate these studies with technical assistance from FHI. Other components include a community based survey and secondary analysis linking clinic records and acceptability questionnaires.

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 and AIDS, 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 is increasing.

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. Results 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.

During the period covered by this report, interviews with current users, former users and those who had never used condoms were

completed in the study area. Information on over 1,100 individuals is available for analysis, which is scheduled for March-May 1987 at the Centre Haitiano-Arabe in Port-au Prince, with technical assistance from FHI. A final report is expected by September 1987.

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

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

The TODAY <sup>TM</sup> sponge is a new barrier contraceptive for which FHI conducted initial clinical trials. FHI is currently conducting a study through the Los Angeles Regional Family Planning Council (LARFPC) that is designed to compare the use of the contraceptive sponge at every intercourse with the use of the sponge only during the fertile phase as identified by Fertility Awareness Method (FAM) of Natural Family Planning. Fifty-three women were admitted to the study, with 25 women randomly assigned to the "Sponge only" group and 28 to the group using the Sponge in conjunction with FAM. These women were followed for a year and responded to questions about their satisfaction with the method.

The data collection phase of the study has just been completed. All data have been received at FHI and were loaded during February 1987. A report of the admission data has been prepared and is available upon request. Analysis of the outcome data will begin in April 1987, following a meeting with the investigator.

#### h) Colombia: Pill Compliance

User dependent methods, such as oral contraceptives (OCs), may have disappointingly low use-effectiveness in the general population, especially if providers give little or no instruction to acceptors. Studies of user compliance, provider knowledge and client-provider interaction can yield practical information on how use-effectiveness can be increased.

There are almost no quantitative data on the compliance patterns among women who accept the pill outside of a clinic setting. In many countries, poor compliance may contribute to method failure as well as 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.

The study in Magdalena, Colombia is the first of a series of oral contraceptive compliance and continuation studies FHI intends to conduct. Magdalena is the only Department (State) in Colombia in which all rural health promoters have been 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.

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; (2) a series of five focus groups 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 750 new acceptors of the pill which began in October 1986, asking 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; and (4) an interview with the 220 rural health promoters in Magdalena in April of 1987 to explore their perceptions and knowledge of the methods. The first two interviews of new acceptors were completed by March of 1987. The third follow-up interview will be completed in May. We will then compare the knowledge, attitudes and service practices of the health promoters with the contraceptive behavior of their clients. All data collection will be completed by June 1987.

i) Africa: Reasons for Discontinuation of Contraception

Efforts have been made in recent years by government and privately funded family planning programs in sub-Saharan Africa to increase acceptance of contraceptive methods. However, the drop-out rate for women initially accepting a temporary method of contraception can be

substantial. In the absence of follow-up studies, program managers are unable to learn the causes of poor compliance and discontinuation.

FHI is currently developing studies of contraceptive users and drop-outs in Senegal and Zaire, with local USAID Mission funding. The investigation seeks to understand the various factors associated with contraceptive acceptance and continuation among family planning clients. Of particular interest are factors that can be influenced by changes in the service delivery program: client costs; screening practices, including lab work information; education and counselling programs; method availability; clinic hours and accessibility; and attitudes of clinic staff.

#### Zaire: Contraceptive Continuation and Reasons for Discontinuation

The Conité Regional de Naissances Desirables in Kinshasa (the regional office of the Zairean PPF affiliate) is very interested in determining who accepts family planning services, the percentage of women who continue using services, and reasons for discontinuation. Service statistics of family planning clinics in Kinshasa indicate that although new acceptors are being enrolled in substantially increasing numbers, many clients do not return for resupply. It is unclear whether these women have discontinued use of contraceptives.

The goal of this investigation is to understand the various factors associated with contraceptive acceptance and continuation among clinic acceptors. Specific objectives are:

- (1) to profile new acceptors of family planning services, comparing characteristics of continuers with drop-outs;
- (2) to assess continuation rates of new acceptors over a seven month period, comparing rates by clinic and by methods;
- (3) to determine reasons clients discontinue use of a specific method or clinic;
- (4) to identify clinic procedures that influence the choice of method for acceptors and may influence satisfaction with the method/services;
- (5) to evaluate clinic practices, including education and counselling, which could affect satisfaction/continuation.

This will be a prospective study of approximately 1400 new female clients coming to five clinics in Kinshasa over a one year period. At the clinic, women will be initially interviewed to assess relevant characteristics. They will get short follow-up interviews at subsequent visits. If a woman discontinues use or fails to return for a scheduled visit, she will be interviewed at home to determine her current contraceptive status, her perceptions of the clinic and the method, and her reasons for discontinuation if she is no longer a user.

As part of a Subagreement between Tulane University and the Project des Services des Naissances Desirables, FHI will be primarily responsible for technical assistance during the study, with travel costs paid by the Kinshasa USAID Mission.

Senegal: Contraceptive Acceptance and Discontinuation: "Les Inactives"

During the past three years, health centers under the Project Sante Familiale (PSF) program in Senegal have made substantial efforts to enroll new acceptors for family planning services. Although these efforts have met with considerable success in increasing contraceptive prevalence among reproductive-age women, service statistics indicate that many clients either do not return to receive a method from the center following an initial consultation visit, or discontinue use in the first few months following acceptance. Such individuals are referred to as "les Inactives" and are the subject of growing concern among service providers in Senegal. USAID/Dakar, a principal source of financial support for PSF activities, is similarly interested in improving the effectiveness of the family planning program, as measured both by the number of new acceptors and continuing users.

Specific objectives of this study are as follows:

- (1) to determine the proportion of clients at sampled PSF centers who do not become acceptors of a modern method of contraception;
- (2) to understand why non-acceptors do not choose to use a contraceptive method;

(3) to ascertain the six-month continuation rate among acceptors;

(4) to understand the factors associated with early discontinuation.

FHI is presently drafting a proposed workplan for this study with participating agencies in Senegal. If accepted for funding by USAID/Dakar under its bilateral program, the study should commence in mid 1987.

j) Multi-country Acceptability of Spermicidally-Lubricated Condoms

Concern about STDs, especially AIDS, continues to grow throughout the world. Although definitive studies are lacking, it appears likely that spermicidally lubricated condoms are more effective than untreated condoms in preventing the transmission of STD's. In order to determine whether USAID should supplement its current procurement policy to include spermicidally lubricated condoms, FHI will test the acceptability of those two new condoms in up to six countries. The Prime is lubricated with a spermicide containing 25 mg of nonoxynol-9; the Double-S is lubricated but with a spermicide containing 100 mg in the tip.

Each country site is recruiting 120-140 current users of condoms. One group of 60-70 current users at one clinic or pharmacy receives the Prime condom and another group of 60-70 at another outlet the Double-S. In some settings, there will be a third comparison group which is switched to a non-spermicidally lubricated condom.

Each man will be asked to use only the study condoms during the next one-month period. At the end of that time, he will be interviewed about his own and his partner's experiences with the condoms. An attempt will be made to interview partners, but we anticipate interviewing only one-half of them. The interview will gather information on the number of study condoms that he used, satisfaction with these condoms, and any discomfort or other problems for user or partner; and finally, what type of condom the user now prefers and why.

During the months of March and April, FHI staff have been visiting the following countries to determine if they are appropriate study sites: Bangladesh, Indonesia, Egypt, Haiti, Ghana, Zaire, Brazil, Honduras, El Salvador, Guatemala, and Sri Lanka, as well as Durham, NC. Efforts will be made to include at least one country in each region of the world. If participants in this pilot study have reservations about the spermicidally lubricated condoms, a more extensive study will be undertaken.

k) Sri Lanka: Compensatory Payments and Vasectomy Acceptance

In Sri Lanka over the past 15 years, voluntary sterilization services have been provided under varying amounts of monetary compensation from none to four different levels of payments. A study in collaboration with the Sri Lanka's Family Planning Association examined the effects of alternative payments on the acceptance of vasectomy. The findings showed that higher levels of payments have

significantly helped enhance the adoption of vasectomy, particularly among the low economic status group. Higher levels of payments led to the acceptance of vasectomy by a special group of low income people who had already achieved a larger family size than those who underwent vasectomy under less or no compensatory payments. Thus, higher monetary payments did not induce men to become sterilized who would otherwise be considered ineligible for sterilization. The results also showed a high level of satisfaction with the decision to have a vasectomy, regardless of payment level. Further, no systematic influence of payment levels on post-operative problems were found.

A second paper focused specifically on the differential impacts of compensatory payments on economically worse-off and better-off acceptors. The results showed that with higher levels of payment, an increasingly larger proportion of economically disadvantaged people accepted vasectomy in urban Sri Lanka. However, the two strata of acceptors had equal numbers of living children. The average age of the youngest child among the poorer acceptors was lower than among the wealthier acceptors. This difference was found to be due to a higher level of contraceptive use among the acceptors in the higher income stratum. There were no significant differences between the two strata regarding post-operative satisfaction and attitudes toward sterilization.

Both the papers have been submitted for publication.

1) Women's Perceptions of Health Risks Associated with Oral

## Contraceptives

Although the birth control pill has been in use for three decades and is the most thoroughly tested contraceptive, remarkably, misinformation about potential risks and lack of information about benefits prevail in both developed and developing countries. In this study, data from 3,253 women of childbearing age in a developing country (Sri Lanka) were analyzed to ascertain their knowledge of potential health risks of pill use. Two out of three women, regardless of their socioeconomic and demographic differences, believed that the pill was harmful to women's health. Further, one out of three women incorrectly believed that taking the pill carried more risk than childbearing. Between 10% and 30% believed that the pill caused cancer, permanent sterility or birth defects. Women who had a higher level of educational attainment or who had used the pill were consistently less concerned about the pill's potential health risks than less educated women and never-users. Risks that do not exist were feared and risks that genuinely do exist were incorrectly understood. This suggested that "knowledge" of actual risks associated with oral contraceptives is the result of a generalized and uniformed fear rather than informed opinion. The findings reinforce the need for information-education-communication programs to provide correct information about the pill to the public and to women considering or continuing pill use.

### 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. 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 described below 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.

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. Reports in both English and Spanish were prepared. A research paper "Contraceptive Use and Fertility" has been written and submitted for publication.

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

AID/Tegucigalpa has asked FHI to provide technical assistance in carrying out the 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 and fertility among women 15-44 and infant mortality. There will be several questions on AIDS. 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 approximately 11,600 households--about double the number in 1984.

The agencies involved in the 1984 survey (Ministry of Public Health, Honduran Association for Family Planning and Management Sciences for Health) are also carrying out the 1987 survey. An FHI consultant constructed a sampling frame based on the updated maps to be used in the 1988 Census as well as older maps when the newer ones were not

available. As before, the survey will be a multi-stage probability sample.

The pre-test for the questionnaire took place in both urban and rural areas of Honduras in March 1987. Field work is scheduled to begin in 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.

Over 3000 women age 15-44 were successfully interviewed from almost 5700 households. The estimated total fertility rate was 4.4 for Saltillo and 5.0 for Leon.

Contraceptive knowledge and use was high among women in both cities. Over 50 percent of the currently married women age 15-22 in both cities were currently contracepting and over 60 percent of women with more than two children were contracepting. The most commonly used method differed between the two cities: in Saltillo 44 percent of the users were sterilized and in Leon 24 percent of the contraceptors were using the IUD. Natural family planning methods, particularly the Ovulation Method, were used by 21 percent of the users in Leon, but only by 5 percent of the users in Saltillo.

Of the women who were not contracepting, about 30 percent were either pregnant, trying to become pregnant, subfecund or not sexually active. About 14 percent of the women in each city had an unmet demand for contraception. Half of this unmet demand was for a spacing method and half for a limiting method.

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 national 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 visited in November and December 1986 to analyze the study results and assist in the writing of the final report which will be completed by the end of March 1987.

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 for adolescents.

a) 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 knowledge on reproductive health.

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 was accepted for publication in Studies in Family Planning (May/June 1987, forthcoming). In addition, the questionnaire used in Monrovia has been adapted for subsequent FHI-supported studies in Zimbabwe and Gambia.

b) 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 probability sample of households 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.

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

Some of the findings include:

- (1) 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;
- (2) 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;
- (3) 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. Condom use reported by 3% of these women and 12% by the men.
- (4) for unmarried men and women, the primary source of contraception is the private sector whereas for the married, the government is the primary source;
- (5) the preferred family size is two for both young men and women;
- (6) 78% of the women and 73% of the men have had a sex education class in school;
- (7) only about a quarter of each sex 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.

Numerous papers have been presented on this work. The Final Report in Spanish and a summary version in English will be completed in April and March of 1987, respectively.

c) Zimbabwe: Reproductive Health Survey of Young Adults

This project supported a survey of young adults in Harare, the capital of Zimbabwe. The survey included both married and unmarried women but only unmarried men. Forty-eight enumeration areas were selected and within each enumeration area, a cluster of 100 households were selected. This yielded a sample of 1420 eligible female and 941 eligible male respondents aged 14-24.

Data collection began in August 1986 and was completed in October 1986. Eighty-five percent of the eligible females and 78 percent of the eligible males were interviewed. Coding was 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.

d) Gambia: Technical Assistance to Survey of Young Adults

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

pregnancies among adolescents. The Gambia Reproductive Health Survey of Young Adults was 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 were interviewed. Information was collected on young people's attitudes and behavior regarding dating, marriage, sexual activity, contraception, childbearing, and problems facing young people in Gambia such as unwanted pregnancy and sexually transmitted diseases.

The goal of the study, partially supported by the Pathfinder Fund, is to provide data to the GFPA to enable it to develop, evaluate, and improve programs 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 of 1986, and work was initiated by November of 1986. Coding of questionnaires is expected to be completed in March 1987, and the forms will then be shipped to FHI for scanning, key punching, editing and analysis in the spring and summer of 1987.

e) Sri Lanka: Young Adults Reproductive Health Survey

A fuller understanding of the perceptions and attitudes of today's unmarried young adults is an effective way in dealing with tomorrow's likely reproductive health issues and family planning needs. In September 1986, FHI initiated a study with Sri Lanka's Family Planning Association to make an assessment of reproductive health problems, perceptions and attitude toward sex, timing of family formation, and contraception behavior. Interviews with 2,400 unmarried, adults (both men and women) aged 16-24 have been completed. Data entry is underway, and data analysis is planned to begin June 1987. The results of the study will be utilized to formulate recommendations for policymaking and program development.

5. Survey of Men

a) Nigeria: Male Attitudes Study

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 focused on women. However, in a male-dominant society such as Nigeria and many other developing countries, the attitudes of men may be as important in fertility control as they are in other areas of health care.

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

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

During the period covered by this report, field interviewing was completed at both urban and rural sites. Information is available on a total of 1978 men. During a February 1987 site visit by FHI's technical monitor, data entry was done at the University of Benin's Institute of Computer Science. Data analysis will follow, both on site and at FHI. A final report is expected by September 1987.

### C. Natural Family Planning

The Program Evaluation Division's main goal in the area of natural family planning and breast-feeding (NFP/BF) has been to support innovative, useful and high quality scientific research that (1) contributes toward making NFP methods more effective and available for those couples who choose these methods and (2) increases our knowledge about the contraceptive efforts of breast-feeding in order to aid women in their choices about how long they are protected by breast-feeding, when to start other methods, and which method to use.

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 regulate 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 regulation. FHI has encouraged 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.

The vaginal aspiration technique developed by Dr. Gebhard Schumacher and supported by FHI initially continues to be tested by other

groups. FHI is continuing to support 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 activities are being coordinated with the AID funded NFP project at Georgetown University, Washington, DC.

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, particularly among women in urban areas of developing countries. Some countries may have to increase contraceptive use just to keep fertility constant, if breastfeeding declines. FHI's work is directed toward measuring the child spacing effects of breastfeeding as well as studying ways to enhance this effect.

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 addressed the temporal relationship between the cervical changes found by self-examination and the mucus and basal body

temperature signs. The findings demonstrated 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.

FHI conducted an extensive review of the medical and popular women's self-help literature and found that studies of the cervix symptom are lacking. This analysis by SERENA appears to be the only one of its kind and represents a valuable contribution to our understanding of the basics of NFP.

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

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 Lobbok at Johns Hopkins University. The findings support the use of full lactational amenorrhea with NFP as a method for avoiding unplanned pregnancy, although it must be noted that few of the findings were statistically significant. Partial lactation does not provide the same efficacy, even during amenorrhea.

c) Study of NFP Use by Breastfeeding Women in Selected

## Countries

FHI is conducting a multi-center study of NFP use among breastfeeding women with SERENA, Canada, Birmingham Maternity Hospital, United Kingdom and Westmead Hospital, Australia; the latter two are being done with field support from the Institute for International Studies in NFP at Georgetown University.

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. Recruitment is on schedule at all three sites. Data collection is scheduled to end in June 1988.

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

FHI has provided core support to Professor James Brown at the University of Melbourne for the purpose of manufacturing and field testing enzyme immunoassay home test kits called "The Ovarian Monitor," for predicting and detecting ovulation.

This system uses a single tube which contains all the constituents required for the test. To this tube is added 50 microlitres of a

suitably prepared timed specimen of urine (overnight or greater than 3 hours) and 350 microlitres of water. The tubes are then mixed in a specified manner and the hormone concentration is measured by the rate of change caused by an enzyme reaction. This reaction is measured in a simple thermostatted photo-electronic rate-meter as a change in transmission (T). The T is a measure of the hormone concentration. A total time of 20 minutes is required for the pregnanediol measurement and 40 minutes for the oestrogen measurement: However, all the timings and the readings are performed automatically by the meter.

I. Tubes are provided for the quantitative measurement of:

- a) urinary oestrogen glucuronides
- b) urinary pregnanediol glucuronide
- c) urinary oestriol in pregnancy

Each tube can be used only once.

II. The system can be used by:

- a) a woman at home
- b) centres and clinics
- c) hormone laboratories

The Ovarian Monitor is intended to improve a couple's confidence while learning and using NFP, as well as to improve the effectiveness of NFP in normally cycling women and in women during breastfeeding or peri-menopause. The FHI Subagreement supported the manufacture of a prototype spectrophotometer adapted for home use, and included designing and creating the die from which the meters were 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 to the following questions: 1) how much effort, in terms of human and financial resources, is required to set up an NFP service program in a developing country; 2) how many people, at what cost, will use such a service; and 3) what would be the program's effectiveness in limiting, spacing and achieving pregnancy. A total of 278 couples were enrolled in NFP instruction through the Asociacion de Trabajo Laico Familiar (ATLF). The couples were trained in the NFP method of choice and followed for one year.

The data collection phase has been completed, and the data will be loaded and ready for analysis in April 1987, pending the final shipment of data. A report of the admission data has been prepared. ATLF is writing the final report of subcontract activities and is scheduled to send it to FHI in April 1987.

Using the cycle information from this study, we are undertaking a further analysis of the timing of intercourse and pregnancy relative to the phases of the cycle. ATLF has agreed to put forth the extra effort required to code the information for every cycle in the study (approx. 1200 cycles) onto a specially designed form. The forms have been pretested and translated by the staff at ATLF. These forms will be printed by FHI and coded by ATLF.

A wealth of information has been produced by the Peru NFP project with ATLF and many papers are planned.

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 living children. 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 more an efficient data recording system.

c) 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 describing the acceptors have been prepared, 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 Lobbok 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.

This study serves to dispel several existing myths about "Natural Family Planning" acceptors and cross-cultural variations. These findings, of interest to family planning service providers, include:

- Acceptors are not necessarily religiously motivated.
- Many acceptors attend along in all programs.
- Acceptors come from a variety of socioeconomic backgrounds and previous family planning experiences.
- OM is acceptable in populations with widely varying fertility goals.
- The percent of couples that have discussed family size is not apparently influenced by prior use of family planning.
- Culture, rather than educational level, is apparently associated with discussions concerning intercourse.

The study suggested that OM has a wide and diverse potential audience and that neither previous family planning use nor level of education has a major influence of levels of communication with the couple.

The ability to verbalize intercourse desires seems to be most influenced by cultural patterns.

Data from India and the US were inadequate to make any assessment of pregnancy rates among NFP users. The data from Bangladesh, Kenya and Korea yielded cumulative lifetable unplanned pregnancy rates of 15, 11, and 13 per 100 women, and Pearl pregnancy rates of 16, 13, and 14 per 100 women at the end of the first year of use. As in previous studies, a significant number of acceptors changed their contraceptive intention during the time of study. "Spacers" tended to have more "planned" pregnancies (i.e. switching contraceptive intention) while limiters tended to have more unplanned pregnancies.

While much work remains to be done in the complete understanding of motivation to accept specific family planning methods, this study has addressed several issues of interest to family planning service providers. Perhaps, the information provided will encourage wider provision or discussion of OM and greater emphasis on communication within the couple by service providers.

#### d) Kenya: Evaluation of Two NFP Programs

Two NFP studies in Kenya were initiated in July 1986. The first project in Nyeri District was designed to: (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. In December 1986, the interviews with nearly 600 respondents were completed. Data analysis will be initiated in April 1987.

The second project is being carried out in Meru district which has a population of nearly one million. The project is sponsored through the Kenya Catholic Secretariat (KCS). The field work for this project was completed in January 1987 and the data are being key punched and verified. A total of about 1250 ever-users of NFP were interviewed. Data analysis will begin in May 1987.

e) Mexico: Prospective Study of Use Effectiveness and Continuation of the Ovulation Method in Metropolitan Mexico City

There has been a lack of objective information on the use effectiveness of natural family planning (NFP) in Mexico. It is likely 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 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 approximately 500 couples in the training phase beginning in May of 1987 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. CEIPLAN has been trying hard to develop its services in order to meet the clientele requirements of the NFP study. It remains to be seen whether their case load will be adequate by the time the study is to begin in May. If not, the study may be cancelled.

f) 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. One form which will 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.

g) Indonesia: Use-Effectiveness of 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 Billings ovulation method, 2) the modified mucus method and 3) a mix of the two methods. The project is being carried out in five locations in Indonesia where there are ongoing NFP programs. The implementing agency is PERDHAKI (Voluntary Health Services Association of Indonesia). As of December 1986, about 800 subjects had been recruited to participate in this project. Key punching and verification have been initiated.

### 3. Surveys to Assess NFP Knowledge and Use

#### a) 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 good deal 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 partly on this work has just been published in 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 April 1987. The report includes seven 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.

b) 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. A project report is being completed and several important methodological and substantive papers are also being

prepared, including one on the demand for NORPLANT® among rural Sri Lankan women.

c) Sri Lanka: Trends and Determinants of 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. A paper based on this project was prepared for publication. The paper showed that the rise in traditional contraceptive use was due to compositional changes (i.e., higher proportion of newly married women in the second survey) in its components as well as measurement differences between surveys.

A second set of analyses examined determinants of natural versus other methods used in the 1982 survey using a multinomial logit model where the probability of using a method is modeled as a function of various background and motivational variables. This paper focused on the factors influencing some women to use traditional as opposed to "modern methods", including the role of birthspacing motives.

This paper will be presented at the annual meeting of the Population Association of America in April 1987.

**b. 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 (Secondary Analysis)

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, presented findings from twelve developing countries at the IFFLP Congress. 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). The findings were published in a special issue on Birth Spacing in International Family Planning Perspectives. Further analysis of the data is underway.

b) Philippines: Infant Feeding Trends (Secondary Analysis)

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 report has been prepared by the Principal Investigator, Dr. Barry Popkin.

c) Multi-Center Longitudinal Study of Breastfeeding and Return to Fertility in Four 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 (Mexico, Egypt, Thailand, and Pakistan) are involved in the Family Health International study. A comparable study in a developed country was completed at the Federal Research Council in Edinburg from 1981-1983. 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 in Egypt have been collected and are being queried at this time. The hormone assay results from Egypt have been examined by an expert consultant for evaluation estimation. Data collection is in progress at the

National Research Institute for Fertility Control in Karachi,  
Pakistan.

The second paper from this data, "Breastfeeding and the Return to Ovulation in Durango, Mexico" is in final preparation for submission to Obstetrics and Gynecology. An analysis of the effects of breastfeeding in infant health, infant growth, and maternal morbidity is in progress.

- d) Philippines: Effect of an Education Program on Breastfeeding Practices and Duration of Postpartum Amenorrhea - Rural Component

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 have been recruited and most have completed followed

up, having experienced two postpartum menses. All data collection will be complete by July, 1987.

e) Philippines: Effect of an Education Program on Breastfeeding Practices and Duration of Postpartum Amenorrhea - Urban Component

An urban study to assess the impact of an educational program promoting intensive breastfeeding on the postpartum amenorrheic period was initiated in Manila on 1 January 1987. The study is being conducted by the staff of the Philippine General Hospital (PGH) with the assistance of a biostatistician from the Institute of Public Health, University of the Philippines. A similar study conducted in a rural area of the Philippines is nearing completion.

The staff at PGH is currently pretesting the data collection forms, and developing recruitment and group assignment strategies. The prenatal and admission forms have been pretested and will be revised and printed at FHI. Admission to the study is scheduled to begin in May 1987.

f) 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 in 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.

Two papers based on the results of the study are being completed for publication.

g) 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 will be ready for production and distribution in 1987.

h) Breastfeeding, Birth Spacing and Infant Survival

Using data from 29 developing countries, a study was undertaken to review and evaluate the impact of changes in breastfeeding practices on fertility and infant survival. It was found that a 25% reduction in breastfeeding duration in Africa can translate into a 12% rise in fertility, while halving the duration of breastfeeding can mean a 25% rise. Similar figures for Asia are 11% and 23%. The contraceptive prevalence required to offset an increase in fertility was found to be large in Africa, more modest in Asia and often small in Central and South America. The reduction in birth spacing as a consequence of the decline in breastfeeding if uncompensated by contraceptive use could lead to an increase in infant mortality. For the 29 countries, the current total of 2-6 million deaths to children under age one year could fall by 20%, or approximately 500,000 lives saved a year, if mothers were to space their pregnancies by two years.

i) Thailand: Initiation of Contraception Postpartum (Secondary Analysis)

A paper entitled "The Initiation of Postpartum Contraception in Thailand: Results from the 1984 Contraceptive Prevalence Survey" was prepared by John Knodel and Peerasit Kamnuansilpa with FHI support. It has been submitted to Studies in Family Planning and is under review.

**Future Plans: Natural Family Planning/Breastfeeding**

1. 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, and condoms. Six affiliates will enroll the first 60 acceptors of each of these four temporary methods. Clients will be followed up for one year. The current plan is for Georgetown University to fund the project, upgrading NFP services, while FHI would provide technical assistance to the evaluation phase. FHI's contribution would start in FY '88.

## 2. Future Work on Development of Home Assays

One area of NFP where FHI plans continued support is in the development of home test kits that predict and detect ovulation. Emphasis will be placed on support of technologies that are practical and easy to use with the potential for low cost and availability. In the near future, support for home kits (e.g. See the "Ovarian Monitor" in section C.1.d.) may be required in evaluating the actual use of this technology.

## 3. Africa: Breastfeeding and Child Spacing

The East Africa Journal of Obstetrics and Gynecology, which is published quarterly by the Department of Obstetrics/Gynecology,

University of Nairobi, has requested FHI for assistance in the publication of a special issue of the Journal on "Breastfeeding, Birth Spacing and Child Survival". The proposed issue would include about eight articles and an editorial with focus on African breastfeeding and child spacing practices. The opportunities for research and methodologies for the evaluation of ongoing programs aimed at promoting and maintaining breastfeeding practices would be discussed.

This will be done, pending availability of funds.

#### 4. Use-effectiveness of Contraceptives in the General Population

There is a dearth of data on use-effectiveness of various family planning methods in the general population. The best data now come from studies in the Philippines by Dr. John Laing. In recognition of the need to gain future insights on use-effectiveness, FHI has been supporting several studies that seek to provide new data through improved methodologies. The data from Sri Lanka and Kenya are now being analyzed. The purpose of the proposed project would be to publish a collection of papers on use-effectiveness. The volume is proposed to review several methodologies and report results based on new, improved studies. FHI could also solicit papers on the subject based on studies carried out by other investigators and organizations. In 1985, FHI published a collection of papers on "Breastfeeding and Fertility" as a special supplement of the Journal of Biosocial Science. The proposed publication might be formulated along the similar line, pending availability of funds.

5. NFP Research Methods Workshop (Hong Kong, Summer 1987)

Fhi plans to contribute one of its staff to serve as an instructor for the IFFLP sponsored research methods workshop.

## 6. AIDS Projects

Given the current absence of an AIDS vaccine, the most effective way to slow the spread of AIDS in Africa is through preventive education. One important group to reach is urban prostitutes. Prostitutes may spread AIDS to their customers and to their partners; they may spread it to rural villages when they go home. A small number of very sexually active individuals spreads the disease more rapidly than a larger number of only moderately promiscuous individuals (Peto J., Lancet, October 25, 1986).

This project tests an approach to slow the introduction and spread of HIV infection. The study will be conducted in Accra, Ghana and continue for six months. Three to five prostitutes who are identified as leaders will be trained to counsel other prostitutes to practice safe sex including the use of condoms and spermicides. They will also distribute condoms and spermicides and encourage their use for all sexual contacts. They will provide information on STDs and referral to an STD clinic or hospital if necessary.

The project's success will be assessed by:

- (1) Surveys conducted with the cohort of participating prostitutes (40) to determine sexual contacts and use of condoms and spermicides during the past two weeks. This will be done at 1, 3, and 6 months.
- (2) ELISA and Western blot tests to measure exposure to the AIDS virus to be conducted at admission and at 6 months.

The project is scheduled to begin in June 1987.

FHI has also surveyed mens' knowledge of and attitudes toward AIDS in four sub-Saharan African countries: Nigeria, Ghana, Cameroon, and Kenya. Convenience samples of approximately 100 sexually active adult males in each site were interviewed; coding is currently underway of questionnaires received at FHI thus far. As a first step in implementing programs to reduce the spread of this disease, the results of these pilot studies will be used to design more detailed and culturally-specific investigations, for which more vigorous sampling techniques will be used.

#### 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 well thought-out 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 analysis continued for projects in Senegal and Ivory Coast in which field work is complete. 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. 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, to 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 has been drafted, translated into French,

and reviewed by the Ivoirien collaborating investigators. 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 TBA's. 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.

The final report for the pregnancy monitoring study is in preparation. A paper entitled "Causes and Circumstances of Death in the First Year of Life: TBA-Attended Deliveries" has been submitted for the APHA annual meeting in October 1987. This paper is based on early data from the infant mortality follow-up of home deliveries.

## 2. Maternity Care Monitoring Studies

### 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 mid 1987 to identify problems and recommend action that will improve obstetric outcomes and reduce morbidity and mortality.

### 3. Pregnancy Wastage Studies

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.

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.

#### 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 Comité 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 FY '87. 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 curettage), and 35% by non-MTP's (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 curettage 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 a lack of knowledge as their reason. 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.

An additional request has been made for hospital-specific information on costs of treatment, hospitalization, and services to further determine the non-personal costs of spontaneous and illegal abortion.

#### 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 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 family planning, the relative risks of contraception compared with pregnancy and childbearing in developing countries are very low.

a) Egypt: Giza Maternal Mortality Study

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 12 months of data collection, approximately 130 maternal deaths were identified and interviews with family members completed.

Data collection for this study was 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. Coding of household symptoms questionnaires is expected to be completed in March 1987 and then shipped to FHI for analysis.

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 (TBA's) and village health workers

(VHW's) 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 TBA's. 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, 1,690 births were reported.

Of the 1,198 women attended by TBA's, 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 were 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 been followed up at least once. When a child died, a physician interviewed the mother to determine the cause of death. Records on 125 infant deaths have been collected. Forty percent of those 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.

The training and use of TBA's 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. A paper on the impact of TBA training in rural Northeast Brazil was submitted to the American Journal of Public Health and is being revised.

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.

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 was being carried out by the Thailand Fertility Research Association (TFRA) and FHI has just received their report.

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 visit once information on the completeness of data is received.

## 6. Other

### a) 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 related studies will be completed under this buy-in. The first will be conducted by the Institute for Population Studies at Chulalongkorn University (field costs to be funded by UNFPA) with the technical assistance of Dr. John Knodel (funded by FHI). Using qualitative and quantitative approaches, it will 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 study will be conducted by the Thailand Development Research Institute (TDRI). 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.

In early 1987, Knodel and IPS staff made site visits in rural Thailand to conduct informal interviews on people's perceptions of

the economic costs and benefits of smaller families. Knodel will return to Thailand in May to start the study. The work with TDRI will begin April, 1987.

b) Nepal: Vasectomy Reversal

In Nepal, the demand for vasectomy reversal is approximately one for every 1,000 vasectomy acceptors. During the period 1980 to 1985, approximately 300 men have undergone recanalization at a referral clinic of the Family Planning Association of Nepal in Kathmandu. A paper is being prepared that analyzes the sociodemographic characteristics of those having reversal operations and their reasons for seeking recanalization.

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

During FY 87, we are 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. Listed below are several new areas the Program Evaluation Division will be pursuing in the coming year.

### 1. Acceptability of Long Acting Steroids

Given the tremendous investment required to develop new methods of contraception, it is very important that efforts to introduce the methods to the general population be handled sensitively. To further this aim, FHI, along with other organizations, has been developing new approaches to assess acceptability of new methods. The first studies have been done with NORPLANT®. They will be applied to other methods (i.e., NET injectables) as they become available.

### 2. Pill Compliance

FHI has initiated one study of pill compliance and continuation in Colombia and is seeking other sites to conduct the 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.

### 3. Honduras: Follow-up Survey of Pregnant Women and Women with Small Children

This survey will measure perinatal and neonatal mortality prospectively. The results can be compared with more obtained retrospectively in the 1987 Maternal and Child Health and Family Planning Survey.

The primary objective of this follow-up survey will be to provide information on infant deaths and fetal loss and compare the prospective data with retrospective findings. (It is generally accepted that retrospective data often fail to include very early infant deaths, resulting in an underestimation of infant mortality.) Also, we will collect information on maternal morbidity and the use of health care services, postpartum adoption of contraceptives and infant feeding practices. Field work is scheduled to begin in March or April of 1988.

Those women who are either pregnant or have an infant less than six months of age at the time of the nationwide 1987 MCH/FP Survey will be contacted nine months after the initial survey. Based on results of the 1984 survey as many as 1800 women are estimated to be eligible for follow-up. Assuming an infant mortality rate of 70 per 1000 deaths, we would expect between 90 and 130 deaths. The number of reported deaths would be between 70 and 100 since the exposure time is less than one year.

## **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 selected collaborating researchers to spend several months at FHI working on a project of their choice. In addition to providing funding and staff support for all 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**

Support to six maturing Family Health Research Centers (FHRC) 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 high quality research to meet a variety of needs in their own countries. FHI believes, along with the USFDA, that ultimately all nations should develop the capacity to develop, introduce and regulate new drugs and devices to meet local needs.

The following section describes each program and the development activities underway with FHI support through core subagreements, as well as summarizing other FHI contract activities being carried out by the FHRCs. In the last analysis, technical assistance in building in-country skills may prove to be FHI's most long term and worthwhile contribution to global health and family planning but it is also probably amongst the most difficult. While most FHRC's have continued to do good work in the reporting interval with one or two outstanding achievements, FHI has also had to make a couple of difficult decisions, planning to stop support to the Sudan and Brazil. Had more funds been available under the Cooperative Agreement, it might well have been both practical and worthwhile to continue this assistance, but with limited resources hard choices must be made.

FHI continues to follow-up in the meeting of the Latin American Advisory Committee held May 19 & 20, 1986 and, as a policy, intends to continue to explore this new model of technical assistance and collaboration.

1. 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 become recognized by the Ministry of Health and Family Planning as the gateway for introduction of new contraceptive methods into the country. It receives funding from several sources, in addition to FHI.

The BFRP was established in 1976 as a quasi-governmental research organization funded by FHI, previously known as the International Fertility Research Programme (IFRP). 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 period, studies were underway at five different centers. Subcontract studies included three 200-case pre-introductory NORPLANT® trials, a non-comparative study of the progestogen-only pill, Exluton, and a comparative study of Triquilar and Marvelon. A new study of oral contraceptives with vs. without iron will begin in April.

Studies funded by earlier subagreements ended during the previous six-month period, including a double-blind three-way oral

contraceptive study which was supported by bilateral funds. This study, which compared a popular standard dose OC versus another standard dose and a low dose pill, provided useful information to policymakers in the country. A final report has been prepared and distributed. The BFRP and FHI intend to publish an article on the findings. The BFRP also plans to write its own consultant reports on recently completed studies such as oral contraceptives supplemented with and without vitamins; a comparison of the IUD's TCu380A and ML 375; a comparison of the CuT 200 IUD with and without vitamin supplements; and a long-term follow-up of female sterilization cases. Considerable work has gone into developing a protocol for a new study of prophylactic antibiotics with female sterilization cases, and initiation of this study is scheduled for June.

During this reporting period, a clinical trials research methods workshop was held in Cox's Bazar and was attended by 25 mid-level physicians, many of whom had participated in FHI studies in the past but who have no formal training in research methods. Two FHI staff led the 5-day session, with assistance from BFRP staff.

Another major event during the period was the Contraceptive Technology Update Conference held in November. This two-day conference convened 150 family planning policymakers and service providers who listened to Bangladeshi and international experts discuss advances in contraception and implications for the national family planning program. The BFRP hosted the conference and two FHI staff participated in the program.

The BFRP also printed its first newsletter, "News and Views", a high quality eight-page production which included information about a variety of family planning research and service topics. The newsletter was published in time to be distributed at the conference.

This period also saw fruition of nine months of work by BFRP staff to obtain clearance for the import of a TI-352 microcomputer purchased by FHI. The computer was shipped to the BFRP in March and an FHI staff member will install the computer and train BFRP staff as soon as it has cleared customs in Dhaka. Once the computer is installed, in-house data analysis will become possible for the first time and the BFRP will be much less dependent on FHI for data processing and analysis.

## 2. 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 Obstetrics/Gynecology 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 support is to develop an independent research institution through training and research assistance. The current Subagreement concentrates on clinical trials, information dissemination, institutional development and individual training and workshops. All projects are designed to expand knowledge of the safe, effective and acceptable use of family planning methods; increase the knowledge and skills of the EFCS staff; expand the research capabilities of the EFCS through the motivation and training of a large network of medical collaborators; and develop the EFCS managerial and financial capabilities to coordinate projects from multiple sources funding.

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<sup>®</sup> project in Egypt (see Section on Transfer of Contraceptive Technology-Egypt-NORPLANT<sup>®</sup> Support). This project strengthens the EFCS and gives it the experience of coordinating a large scale research project. It assists in the development of the EFCS's funding base and increases staff and

computer capabilities, adding to the financial stability of the organization.

During the latter part of Calendar Year 1987 and the first quarter of 1987, the EFCS conducted the following activities:

#### Institutional Development and Training

- A follow-up training for staff using the microcomputer was conducted during October 1986.

- Development of a Five Year Plan of Operations continued.

- The international management firm of Deloitte, Haskins and Sells management. The consultants have developed a new accounting system for the EFCS and are training managerial and accounting staff in its use. An overhead rate has been calculated to negotiate later contracts.

- A MCM meeting was conducted in December 1986.

#### Research Activities

- A comparative study of the TCu versus the ML 250 versus the Lippes Loop C was completed at five university hospitals. Data analysis for this project was initiated, with technical assistance provided by FHI for the analysis process and report preparation.

- A multicenter maternity care monitoring study continued. Recently incorporated centers include Ministry of Health (MOH) hospitals.

- A comparative study of the oral contraceptives Triovular<sup>®</sup> versus Ovral<sup>®</sup> versus Nordette<sup>®</sup> involving 2,400 cases randomly assigned and divided among eight centers continued.

#### Information Dissemination

- Published a "Fertility Care Bulletin".

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<sup>®</sup> research projects. Originally under the administration of the National Population Council, this project will become an EFCS project as soon as contractual negotiations are completed between the EFCS and AID/Cairo. At that time all expenses incurred by EFCS in the execution of this project will be charged directly to the bilateral agreement between AID and EFCS.

During the coming period the following activities are planned:

- Continuation and expansion of the MCM study,

- Conclusion of the ongoing three-way IUD study and data analysis with report preparation,

- Continuation of the Comparative Three-Way Oral Contraceptive Study (Triovular<sup>®</sup> versus Ovral<sup>®</sup> versus Nordette<sup>®</sup>),

- The Data Analyst will receive advanced training at a local university and at FHI during April 1987,

- The Data Collection Coordinator will receive further training at FHI in early 1987,

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

- The analysis of data from an injectable contraceptive study funded by the WHO will continue,

- A comparative study of the TCU 380A versus the Cu 200C will continue,

- Processing and analysis of data will continue 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 progress towards financial independence and institutional autonomy.

3. 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 Micro computer provided in 1982 has been transferred to BKS PENFIN's center in Yogyakarta. They plan to

acquire an IBM-compatible PC in the near future for both administrative/clerical and data analysis applications.

Several FHI contract studies are being conducted 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. They are currently working with the Indonesian Ministry of Health and WHO to develop a major new study on maternal and perinatal mortality. Also, BKS PENFIN makes its data processing facilities available under subcontract or fee for services to other organizations, including PERDHAKI (which is conducting an FHI study of three NFP approaches) and the West Java Provincial Health Department.

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 and FY 87 core support budgets reflect this policy. 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.

These new procedures are now being implemented and a consolidated 1986 financial report is expected. 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 businesslike and independent as an organization, but the process is slow and difficult. A follow-up visit by our DH&S consultant was made in February 1987.

Activities also continue to focus on strengthening research capabilities. Four or five representatives of the BKS PENFIN will participate in a one-week regional workshop on clinical trials research methods, to be presented by FHI in Singapore in May 1987. In addition to mastering the course content in order to strengthen their own research skills, the objective of the BKS PENFIN representatives' participation is to prepare them to serve as trainers in similar workshops in Indonesia, sponsored by BKS PENFIN. The target audiences of these subsequent workshops will be the wider BKS PENFIN research network and, ultimately, investigators from other institutions and research coordinators at BKKBN.

#### 4. 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.

During this reporting period, activity has focused on three areas: clinical trials research, network development, and report writing. Subcontract clinical trials of NORPLANT® involving 565 women (including 75-cases under a research contract with Leiras Pharmaceuticals) and a 90-case expansion 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 IUD's TCU 380A and the Multiload. Training in data collection methods was provided by FPA staff.

Last May a research methods workshop based on the standard curriculum materials developed by FHI was held in Colombo. Because the first was so well received, the workshop will be repeated this May. The workshop will be led by FPA staff, an FHI biostatistician, and three of the Sri Lankan physicians who were trained in the first workshop in Singapore.

Reports written during the period include "The New Contraceptive NORPLANT<sup>®</sup> Implants: One-Year Evaluation of their Safety, Efficacy and Acceptability in Sri Lanka", by Dr. Sriani Basnayake. This has been submitted for publication in Studies in Family Planning. This paper and one entitled "A Comparative Study of Norinyl 1/35 versus Norinyl 1/50", also authored by Dr. Basnayake. were accepted to be read at the Sri Lanka Medical Association annual meeting in March, 1987. Dr. Basnayake has written a paper about clinical management of NORPLANT<sup>®</sup> patients and an article called "Contraception in Ancient Society" was published in the Sri Lankan newspaper Daily News.

In addition to the contract clinical trials studies mentioned above, the FPA/SL has undertaken a survey called the Sri Lankan Young Adults Reproductive Health Survey. This is an expansion of a pilot study of Colombo youth completed last year which yielded results of great interest to the Ministry of Education and the populace at large. The new study has a larger and more nationally representative population and asks reproductive health and family planning questions which will be useful for programmatic purposes. The field work for this study was completed during this reporting period, and data analysis has begun.

FHI is also assisting the FPA/SL to increase its computing capability by the purchase of an IBM PC/AT which can be linked to the existing TI-352 system. Purchase was initiated during this reporting period, and the computer should be shipped to Sri Lanka late in the spring. Once it has arrived, FHI will assist in linking it to the TI system, and training staff in its use.

#### 5. Sudan Fertility Control Association (SFCA)

The SFCA has received assistance from FHI since 1979. Since its inception this FHRC has attempted to establish itself as a national organization for research in family planning and maternal and child health. The membership in the SFCA has grown, and includes mostly obstetrician-gynecologists and other physicians interested in family planning. 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.

The SFCA emphasizes training, workshops and projects that 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 USAID/Khartoum and AVS. USAID is supporting a Model Family Planning Clinic that is utilized by the SFCA as a research center. Although the SFCA has been a slow growth institution over time, it has maintained a sufficient level of progress to justify continued FHI support and carefully monitored technical assistance. During the last year the Sudan has been under economic and political stress. This situation has made it difficult to provide the SFCA with the level of technical assistance it has needed to continue its development. As a result the SFCA has regressed to a level of development reminiscent of its beginning years.

During the report period, the following activities were conducted:

- The Model Family Planning Clinic initiated operations at a new location in Khartoum in August 1986. Average patient intake is 30-40 patients per day. Only a small portion of them are consulting for Family Planning Services.

- A clinical trial workshop was conducted in Kassala in November 1986, originally planned for the Spring of 1986. This workshop was postponed several times due to the political situation in the

country and its final execution was considered weak by FHI evaluators.

- During the same period the SFCA failed to produce satisfactory protocols for the following proposed studies in their current Subagreement workplan:
- 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.

The IUD comparative study (TCu 380A versus TCu 200) initiated in Port Sudan Civil Hospital in 1985 progressed at such a slow pace that discontinuation has been recommended.

Unfortunately the SFCA performance during the reporting period reflects a continuing lack of leadership and shows the strains imposed by many problems experienced by the country. As a result of the poor performance combined with the diminished funding availability and the extreme difficulties of working in Sudan, FHI has decided to reorient its assistance to the family planning program of the Sudan by concentrating on a small number of

individuals who continue to demonstrate interest and motivation to work in research.

The current two-year agreement became effective on 1 March 1986 and will extend until 30 September 1987. At this time no extension of funding for the SFCA beyond September is contemplated. SFCA officers and USAID Khartoum have been notified of this decision.

6. 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 TRFA'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 since October 1983. It has also assumed the direct study costs for the Sukhothai Province MCM program (formerly supported by FHI), and more recently the MOPH has funded a TFRA study to evaluate an IUD campaign in one Thai province. The TFRA has also conducted clinical trials with funding from private pharmaceutical companies and has initiated three major studies under separate contracts with FHI.

The TFRA has made good progress in developing its data processing and analysis skills. Several TFRA staff have visited FHI in the past for data collection coordination and microcomputer training. In the next reporting period, Ms. Pornsinee Amornwichee, will spend about one-week at FHI for follow-up training on the TI system.

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

- Comparative study of mini IUD's: Minigravigard versus Nova T versus ML Short (follow-up stage)
- Comparative interval female sterilization study:  
Filshie clip vs tubal ring via laparoscopy
- Comparative interval female sterilization study:  
Filshie clip vs modified Pomeroy technique via  
minilaparotomy (follow-up stage)

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

- Infant health follow-up in Sukhothai (FHI)
- Postpartum sterilization by nurses (FHI)
- Progestogen-only pills for lactating women (FHI)
- Follow-up study of Uttradit IUD campaign (MOPH/AID)
- Eugynon vs Microgynon 30 (Schering)
- Ovral vs Marvelon (Organon)
- MCM research in Sukhothai (Ministry of Health)

Currently under development is a proposal to study OC pill compliance by Thai women.

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 seek additional core support from the Thai Ministry of Public Health and allocable cost reimbursement as part of their grants and contracts from all sources. 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. This was

reiterated during a brief stop-over visit in November 1986 by one of our DH&S consultants. TFRA will seek local accounting assistance as needed to upgrade their systems and procedures.

Five representatives of the TFRA will participate in a one-week workshop on clinical trials methods, to be conducted by FHI in Singapore, May 1987. The purpose of this participation is to strengthen both organizational and individual research skills within the TFRA. Participants will include both professional staff and clinical investigators.

#### 7. Technical Assistance To The AMPPF/MALI

FHI technical assistance to the Association Malienne pour la Protection et la Promotion de la Famille (AMPPF), began in 1981. It is continuing with the current two-year Subagreement. An analysis of clinic records (1981-84) of the AMPPF and 30 MCH centers shows the increasing demand for family planning services. However, the problem of high early discontinuation levels is evident. The AMPPF has been asked by the USAID mission in Mali to update the clinic record analysis (for 1985-86) for the 15 participating MCH centers in the recently signed bilateral agreement. This analysis will take place in Spring '87.

The research assistant continues to monitor two ongoing clinical trials of Ovrette and a comparison of Noriday versus Lo-Femenal in 3 MCH centers in Bamako. The quality of the data received has

improved since the forms are reviewed and corrected before coming to FHI.

The AMPPF has recently completed a survey of midwives working in the MCH centers throughout the country. The objective of the survey was to determine the midwives who are most in need of continuing education and which aspects of family planning services should be emphasized. With this information, a training program will be developed later this fiscal year.

The President of the Association and the Program Coordinator visited the Family Planning Association of Morocco. They were especially interested in the VDMS community distribution program. They hope to begin a small pilot CBD project in Mali.

The Association is very interested in implementing a program on STD's and money was set aside in the present Subagreement for a consultant to help define a project. The National Public Health Research Institute (INRSP) has also proposed a research project on STD's to another donor. An expert from CIRMF in Galon recently visited Mali to explore the possibility of a collaboration between the INRSP and the AMPPF.

8. 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.

A study of Vanguard Acceptors of Family Planning Services was carried out at the CNSF and completed at the beginning of FY'86. The final report of the Vanguard Study has recently been completed. It provided a profile of the sociodemographic characteristics of new family planning acceptors, their reasons for desiring contraception and preferred methods. Emphasis was given to reviewing clinic procedures and formulating recommendations for improvements in service delivery. The report will be translated into French during the next report period.

The CNSF in collaboration with FHI, is continuing a surveillance study of the two most commonly prescribed pills in Niger, Stediril and Minidril, to determine their side effects and continuation rates. About half of the women in the 200-caseload have been recruited.

#### 9. 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 early 1987.

FHI has concentrated on building a larger institutional understanding of the issues associated with the implementation and coordination of multicenter clinical research. To this end, FHI provided the impetus and financial support during this reporting period 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 proposed to facilitate the strengthening of ABEPF's clinical research program.

Although the investigator network has expressed interest in a Brazilian research coordination agency, ABEPF staff have viewed this as low priority, and there have been problems with the functioning of ABEPF in this capacity.

As a result, FHI financial support for this project was terminated when the Subagreement for core support expired in November. The ABEPF DCRC continues to coordinate the progestogen only pill study and will remain involved in the project throughout the final follow-up of the patients, using funds provided with ABEPF's corporate resources.

#### 10. GIMIESAR, Mexico

As an outgrowth of the FHI supported epidemiologic training program at the Institute de Investigacion Cientifica of the Universidad Juarez, Durango, Mexico, the Mexican Interuniversity Group for Epidemiologic Research in Reproductive Health (GIMIESAR) has been formed. GIMIESAR, based in Durango, is made up of representatives from major Mexican Universities and Medical Schools who were trained in the epidemiologic research method workshop.

FHI is providing some core support to GIMIESAR during this fiscal year. The support seeks to provide the organization with the funds necessary to permit periodic meetings to review ongoing projects, develop new research proposals and to plan for future efforts to obtain funds from the international donor community. Also, FHI has provided technical assistance to GIMIESAR in the field of microcomputer technology. FHI staff have traveled to Durango to conduct a microcomputer needs assessment for the organization.

As the only interuniversity epidemiologic research organization working in Mexico, GIMIESAR has attracted a great deal of attention

from national health authorities. Plans are currently underway to work more closely with the national health ministry in addressing some of the more pressing epidemiologic concerns facing the Mexican maternal child health care program.

#### 11. Mali: Baseline Data Study

The USAID mission in Mali has recently signed a bilateral project to improve Maternal & Child Health Services. FHI has been asked to provide technical assistance in gathering baseline data. These data will be used to set quantifiable goals and to evaluate the impact of the bilateral maternal and child health project.

FHI staff will collaborate with the Sahel Institute and the Malian Family Planning Association to collect the data. The baseline data are needed in target areas: nutritional surveillance; vaccinations, oral rehydration and family planning. Another component of the survey will focus on the organization and management of services in the MCH centers. Two approaches will be used to gather the data; an analysis of family planning clinic records and site visits to the 15 participating MCH centers. Site visits and the clinic record analysis will be carried out during the Spring '87.

#### 12. Microcomputer Training and Development

- A. New Microcomputer Installations
- B. Follow-up Visits to Existing Microcomputer Sites

### C. In-house Microcomputer Related Training

#### A. New Microcomputer Installations.

A new microcomputer installation is being planned for the Bangladesh Fertility Research Programme (BFRP). This installation has been planned for some time, but was held up pending customs approval in Bangladesh. This has been obtained and the installation is now planned for late Spring of 1987. The system to be installed there is 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 were reviewed with Dr. Halida Akhter during her visit to FHI in February 1987, and included electrical current, proper grounding, air conditioning and flooring.

#### B. Follow-up Visits to Existing Microcomputer Sites.

Follow-up visits were made to: Dakar, Senegal and Cairo, Egypt. Additional follow-up visits are planned for Sri Lanka, Indonesia, and Thailand in the summer of 1987.

A follow-up visit was made to the Bureau National du Recensement in Dakar, Senegal, in November 1986. The primary purpose of this trip was to install the Microgate 931 terminal emulation package onto the TI BS352 computer at the BNR. The Bureau now has three IBM machines, one PC and two XT's. The Microgate was successfully installed and tested with one of the XT's. The XT can now be used as an additional terminal into the TI system, with the additional capacity of transferring both data and other files back and forth between the two systems. In addition, the letter quality printer, which is attached to the XT, can now be used as an option with the TI system, specifically as a printer for the TIPE word processing package. The on-line systems diagnostics procedure was installed, as was the DX10 Recover volume Space (RVS) command. Housekeeping techniques were discussed with the new BNR staff, including backups, when to use what copy command and system backup and rebuilding.

A follow-up visit was made to the Egyptian Fertility Care Society (EFCS) in Cairo in October 1986. Several new programs were installed on the TI BS352. These included the FHI developed Oral Contraceptive Patient Summary Clinical Trials package, the DX10 Recover Volume Space (RVS) command, and the Microgate 931 terminal emulation package, although the EFCS does not as yet have an IBM compatible PC to link to their TI BS352. Time was also spent in

assisting the EFCS in reviewing options for the purchase of a new computer system to be used primarily for the NORPLANT<sup>®</sup> activities planned for bilateral support.

A follow-up visit to the Instituto de Investigacion Cientifica, Universidad Juarez del Estado de Durango, Mexico, is planned for March of 1987. Topics to be covered will include housekeeping, advanced operating system use, and more in-depth use of SPSS. The Recover Volume Space (RVS) command and the Microgate 931 communication package will also be installed.

#### C. In-house Microcomputer Related Training.

In-house training was provided for Ms. Susanty of the BKS PENFIN in November 1986. Ms. Susanty's training consisted 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.

In-house training is also planned for Ms. Porsinee Amornwichet and Ms. Pattaka Piyapinyo of the Thai Fertility Research Association, and for Dr. Mervat Rushdi and Ms. Mahinez El Helw of the Egyptian Fertility Care Association in the spring and summer of 1987.

### 13. Financial Management Assistance

Under a subagreement from FHI, Deloitte, Haskins and Sells (DH&S) International is providing technical assistance to FHRCs 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. The second phase, now underway, includes the development of a shell for a generic accounting system, the design of customized manuals for each FHRC, and site visits to train FHRC staff and 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 has been developed and finalized in both English and Bahasa. Full implementation of the new accounting system began in January 1987.

A visit to the Sri Lanka FHRC reviewed the system already in place. As it was found to be similar to the one proposed by DH&S consultants, only recommendations and technical assistance was provided to refine the system.

During the reporting period initial and implementation visits were conducted in Bangladesh and Egypt. In both countries, the accounting system was installed and staff trained in its utilization and maintenance. A manual has been finalized for the BFRP, and one is under development for EFCS. In Egypt, this technical assistance has proved timely and essential in planning for the initiation of the bilaterally funded NORPLANT® program.

Thailand, after receiving one initial visit, preferred to maintain its present accounting system and Sudan could not receive an initial visit due to the political situation in their country.

## 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 Standardized Clinical Trials Research Methods curriculum has been successfully implemented in several workshops since 1985. The curriculum has been translated and utilized in Spanish; French and Portuguese translations are in progress. FHI has been pleased to receive several third party requests to use the material. Programs in Egypt and Sri Lanka are now able to carryout workshops, using these curricula, with minimal technical assistance from AID.

FHI is currently 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 1988.

b. Asia: Regional Workshop on Clinical Trials Methods for  
Contraceptive Research

During the funding period, plans were initiated for a regional clinical trials methods workshop, to be held in Singapore, 4-9 May 1987. The purpose of this workshop will be to strengthen the clinical research skills of organizations and investigators working with FHI on clinical trials in Asia. In particular, the workshop is aimed at strengthening the capacity of the BKS PENFIN (Indonesia) and the Thailand Fertility Research Association to design, plan and implement clinical trials. Each of these FHRCs will be represented by 4-5 investigators and/or research staff. In addition, investigators from Malaysia (3), Pakistan (1), and Taiwan have been invited. The workshop will be held in cooperation with the OB/GYN Department of the National University of Singapore.

c. Brazil: Clinical Trials Workshop

A workshop on Clinical Trials Methods for Contraceptive Research is being developed in Brazil during FY '88. The preparation for this program has already begun with the translation of the standardized training modules to Portuguese. The translation is expected to be completed by August of 1987.

The development of this program in Brazil marks an important step for Family Health International's Latin American program. It is anticipated that the organization and implementation of the Clinical Trials workshop in Brazil will greatly improve FHI's ability to conduct policy relevant clinical research in this Latin American country. The preliminary plans include the coordination of this workshop with the National Brazilian Research Institute, Osvaldo Cruz. This affiliation, and with the participation of other prestigious public and private sector family planning and research organizations, is expected to facilitate the evaluation of new contraceptive technologies through official government channels.

d. Mexico: Epidemiologic Training

FHI has just completed the fourth 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. The third annual three-week workshop was held in November 1986. Eleven physicians from six cities in Mexico were trained. Eight of the participants were proposed by 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.

The 1986 workshop marks the end of the formal training phase of the five-year project. Over the course of the three workshops, thirty-one Mexicans, one Panamanian, and one Guatemalan were trained. During the next year the project will focus on follow-up of the studies that were designed by trainers.

e. Applied Research Methodology Workshop in Reproductive and Family Health in Niger

Interest in research activities focusing on family planning and specific contraceptive methods is increasing in Africa. African health professionals and program planners are no longer satisfied to base program and policy decisions on data from other regions; they desire data which is specific to their region and conditions.

However, interested professionals often have insufficient research skills to conduct studies yielding valid and reliable data. A

number of research methodology workshops focusing on health/family planning have been held for anglophone researchers: few have involved francophone investigators and even fewer have emphasized the practical aspects of developing a research project.

A three-week workshop on applied research methods in reproductive health is planned for September 1987. This workshop will gather a small number of interested professionals (social scientists and health professionals) in Niger. Workshop participants will learn basic research skills and how to develop a research project. Teaching methods will emphasize "learning by doing" with each participant involved in the development of a project to be submitted for funding upon completion of the workshop. Proposals will focus on country research priorities in family planning.

## 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 important target audiences for training in contraceptive technology. In other cases, they serve to bring researchers, service providers and planners up to date on recent developments.

a. Bangladesh: Contraceptive Technology Update Conference

In November, 1986, a cooperative agreement to fund a contraceptive technology update conference was held in Dhaka, Bangladesh. FHI, in collaboration with the Bangladesh Fertility Research Programme (BFRP), invited 4 international experts (including FHI President, Dr. Malcolm Potts) and many local experts to address an audience of 150 leading policymakers and family planning physicians during the two-day conference. The conference included such topics as: Risks and Benefits of Modern Contraception, Oral Contraceptives, Male and Female Sterilization, NORPLANT<sup>®</sup>, Injectables, and Contraception for Breastfeeding Women. The conference was an opportunity to update the audience on contraceptive advances, to dispel misconceptions about the risks of modern contraception, and to discuss incorporation of new contraceptive technologies into the national family planning program. Discussions during the meetings were lively, and the information seemed to be well-received by the invited guests.

b. Egyptian Ultrasound Training Project

As a completion of the ultrasound project initiated in Egypt in 1985, four Egyptian physicians were selected to attend advanced ultrasound training in Europe and America. Two physicians traveled to the United States in February 1987 and two physicians traveled to Germany and England. All four attended university ultrasound OB/GYN departments and viewed different techniques in ultrasound usage.

### **C. SUPPORT FOR CONFERENCES, SEMINARS AND EXPERT MEETINGS**

FHI believes that international meetings, conferences and seminars, if carefully and appropriately chosen, 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.

#### **1. Chile: 3rd Congress on Human Reproduction and Reproductive Risk**

Family Health International provided partial support for the "Third Congress on Human Reproduction and Reproductive Risk: Twenty-One years of Family Planning in Chile." The meeting, which took place on November 23-27 in Santiago, Chile, was a forum for the Chilean scientific community to discuss recent developments in the field of fertility regulation within the context of reproductive risk and human reproduction. Chile's long history of leadership in the field of family planning and human reproduction made this meeting especially significant. Family Health International enjoys a close working relationship with several of the most prominent Chilean scientists. Our support for this meeting permitted Family Health International to participate in the scientific program and to learn first hand from our Chilean colleagues about the current status of their work and future plans for research in the new frontiers of fertility control.

## 2. Panama: OB/GYN Meeting

Family Health International provided partial support to the OB/GYN society of Panama for their National Congress, which took place on January 14-16, 1987. FHI support for this event provided an opportunity for reviewing the most critical issues in the area of reproductive and maternal/child health with the leading Panamanian scientists and policymakers. Over one-hundred health care professionals from Panama City and the provinces attended the meeting. The meeting focused on several specific topics relating to maternal and child health, including the management of high risk pregnancy, new developments in contraceptive technology and social marketing.

Family Health International staff attended the National Congress and the initial reports indicate that the meeting was a great success in terms of achieving its specific goals, which were:

- (a) to present the latest information on contraceptive technology to those who provide family planning within the private and public sector and, present an update on the latest advances in the field of Obstetrics and Gynecology;
- (b) to further integrate into the Panamanian scientific community the nurses and paramedical personnel who provide health and family planning services; and

(b) to further integrate into the Panamanian scientific community the nurses and paramedical personnel who provide health and family planning services; and

(c) to present to the scientific community data from studies carried out by FHI with Panamanian Investigators.

FHI support covered the travel costs for six international participants who had been invited to participate in the program by the organizing committee. In addition, funds provided by FHI covered some of the core expenses for the event. We are currently awaiting the final report from the field on this project and FHI continues to carry out high quality research with our Panamanian colleagues affiliated with the National OB/GYN society.

### 3. Mexico: AIBIR Conference

FHI provided support to the Mexican Academy of Research in Reproductive Biology (AIBIR) for their Twelfth Annual Meeting held 23-25 April 1987. The annual symposium included sessions on "Advances in Non-surgical Female Sterilization", and "Quinacrine, Long-Term Follow-up Outcome". FHI was represented at the meeting by Dr. Malcolm Potts, President of FHI, and a Chilean scientist and long-term collaborator, Dr. Rene Guzman-Serani who will deliver the paper on "Quinacrine". The meeting provided an opportunity for FHI to discuss new research directions in reproductive health and contraceptive technology with our Mexican colleagues, as well as with other international health research organizations.

Specifically, the meeting provided a forum for reviewing the current prospects for non-surgical female sterilization with the Mexican scientists and initiated an important new scientific dialogue in this area.

#### 4. Ivory Coast: Medical Standards Workshop

Interest in family planning is increasing in Francophone, Africa, but medical policies in many countries create unnecessary barriers to providing contraception. These policies are based on fear of the risks of medical complications associated with contraceptive use. AID's regional population office in Abidjan (REDSO) feels that there is a need to bring professionals responsible for family planning and service programs delivery together to discuss the risks and benefits of contraception and the delivery of quality family planning services.

A regional meeting is planned for May in Abidjan. The program will focus on issues of quality service provision. FHI will coordinate the presentation on hormonal contraception including: pills, injectables, and NORPLANT<sup>®</sup>. FHI has also been requested to make the presentation on research needs. The hormonal methods discussions will focus on risks and benefits of systemic contraceptives, the role of screening, and regular follow-up visits for patients and how proper patient management can minimize risk. Provider's training will also be discussed.

## 5. Guatemala FLASOG

FHI will provide partial support for the XII Latin American Congress of Obstetrics and Gynecology (FLASOG). The special position that Latin America enjoys in the field of contraceptive development highlights the importance of this event for FHI. Latin America has provided the world with some of the most important advances in the field of health and contraceptive development. Scientists from Latin America have contributed to the development of the copper bearing IUD, the sustained release of low dose progestens and non surgical alternatives to tubal occlusion. Latin America continues to be involved in much of the most promising work in the field, including the early development and field testing of new long acting injectable products and contraceptive implants. FHI anticipates that the FLASOG meeting will allow for an excellent opportunity to participate, along with our Latin American colleagues, in the scientific discussions scheduled to take place at this bi-annual event.

Several of the official themes of the Congress are of direct relevance to FHI: The Past, Present and Future of Contraception, The Risks and Benefits of Hormonal Contraception and Family Planning in the Developing World. FHI has received approval from AID to provide funds for the support and organization of these sessions. FHI plans to send senior staff and one Latin American expert consultant to assist in aforementioned sessions.

## 6. Peru: Family Planning Meeting (Early Development)

Plans are being developed to provide partial support for a meeting of private family planning entities working in Peru. The organization of this meeting is being discussed on a preliminary basis with IMPPARES, the IPPF affiliate in Peru. The purpose of the meeting would be to bring together organizations and individuals active in the provision of family planning services in Peru. The meeting will provide a forum for discussing both service delivery and research priorities with the international donor community.

#### 7. 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:

- a. To identify the most effective strategies for meeting regulatory requirements of specific Latin American countries for the evaluation and introduction of new contraceptive products.
- b. 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. A follow-up meeting is being developed which would focus on the development of a strategy for local manufacture and evaluation of a specific contraceptive technology during FY 87.

8. Conference Travel (Non-FHI Staff)

FDT provided support for many of our international colleagues to attend and participate in international meetings and conferences. The meetings in this reporting period were attended by the following individuals:

- a. XII World Congress on Fertility and Sterility, Singapore, October 26-31, 1986

Dr. Lasso de la Vega, Panama City, Panama  
Dr. Ang Eng Suan, Kuala Lumpur, Malaysia  
Dr. Debhanam Muangman, Bangkok, Thailand  
Dra. Rebecca Ramos, Manila, Philippines  
Dr. Ariawan Soejoenes, Semarang, Indonesia  
Dr. Suraiya Jabeen, Dhaka, Bangladesh  
Dr. Kanchana Kanchanasinith, Bangkok, Thailand  
Dr. Paiboon Sa-Ngoowarchar, Bangkok, Thailand

- b. International Conference on Voluntary Sterilization and Family Welfare, New Delhi, India, October 18-20, 1986.

Dr. Louella Klein, Atlanta, Georgia, USA  
Dr. Patricia Saling, Durham, North Carolina, USA

- c. First Brazilian Congress on Health Informatics, Campinas, Sao Paulo, Brazil, November 19-23, 1986.

CPAIMC Staff Members:

Dr. Helio Aguinaga, Rio de Janeiro, Brazil  
Ms. Lia Kropsch  
Ms. Karen Johnson Lssner  
Mr. Luiz Claudio de Souza Benguigui  
Mr. Paulo Pecanha

#### **D. TECHNOLOGY TRANSFER**

While all FDT activities (institutional development, training, conferences and information dissemination) enhance the transfer of contraceptive technology to programs in LDC's, 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.

##### **1. 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. To date over 1,200-cases have been collected. All data is currently in-house and is being analyzed.

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 physicians 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.

## 2. 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. The decision to shift this project to the EFCS Offices was made in July 1986. During this reporting

period the EFCS has been negotiating a direct contract with USAID/Cairo to fund the project.

The project has several components: a large scale program of training and introduction designed to assess the performance of NORPLANT<sup>®</sup> 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<sup>®</sup> 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.

This program also supports an FHI staff member, Mr. Peter Miller, to serve as Program Director based in Cairo, Egypt. He currently has an office and support staff at EFCS. Mr. Miller is coordinating and facilitating activities of the various agencies and organizations involved in support of this project.

#### **E. SHARON CAMP FELLOWSHIP**

The Sharon Camp Fellowship Program was established at FHI in 1984, to enable a collaborating researcher 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, was in residence at FHI, for the period July-December 1986, during which time he completed a family planning program project manager's manual for use in Egyptian clinics.

At this time no funds have been allocated for a new Sharon Camp Fellow in 1987.

#### **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. FHI's program of information dissemination includes the publication of three newsletters: network, network en francais and network en espanol; support for journal subscriptions for LDC investigators and programs; and the production and dissemination of country-specific informational materials. These materials are designed to make scientific literature and contraceptive research more accessible and therefore useful to policymakers and health care providers and family planners.

##### **1. International Journal of Gynecology & Obstetrics**

Distributing subsidized subscriptions to the International Journal of Gynaecology and Obstetrics is an important part of Family Health International's information dissemination strategy. FHI continues

to help research collaborators submit papers to the Journal for publication, and edits all developing country manuscripts that appear in the Journal. This year, 400 subscriptions are being provided to research collaborators who depend on the medical information the Journal contains to update their knowledge of the latest contraceptive methods and techniques. A letter of notification was sent to all subsidized subscribers to solicit address corrections and find out how many were interested in continuing to receive the Journal. The response has been very good--readers say they continue to find the Journal useful to their work.

## 2. Network

The fall issue of Network, FHI's quarterly newsletter, focused on the contraceptive needs of breast-feeding women. Family Health International received requests for bulk orders of this issue from NGOs, rural African women's breast-feeding organizations, and primary health care training organizations. The winter issue discussed IUD's and the spring issue focuses on information dissemination by family planning organizations. Circulation of the newsletter has increased by 300 since September 1986 to 3,047, excluding the increasing number of bulk orders received for health personnel training purposes and for informational purposes at medical society conferences in developing countries.

## 3. Network in SPANISH

Many of the individuals and programs in FHI's network are in non-English speaking areas of the world. The first edition of 1,500 copies of Network en espanol, designed to serve investigators in Latin America, quickly "sold out". A questionnaire to readers showed that the new newsletter was much needed and appreciated. Subscriptions have increased to 2,000 and the second annual edition of the Spanish-language newsletter has been published. The second edition includes a special examination of adolescent fertility and contraceptive use in Mexico.

#### 4. Network in FRENCH

Response during this reporting period to the publication and distribution of FHI's 12-page newsletter in French has been tremendous. More than 600 health, family planning and IEC personnel in Africa and Haiti subscribe to the French newsletter, and FHI has received bulk orders from AID/Senegal for use by midwives and rural health trainers, from the Department of Public Health of Zaire for use by practitioners and directors of their public health services, from the African Institute for Economic and Social Development, from rural health agents in Zaire, and from hospitals and clinics in Tunisia and Cameroon.

#### 5. Other Information Dissemination Activities

FHI is a treasure house of information on contraception and reproductive health. FHI's survey of consumer perceptions of oral contraceptives, risks and benefits around the world was a

particularly forceful demonstration of the misunderstandings that exist about contraception in many countries. Family Health International has developed a program to report research findings and accurate information on contraception to the media, policymakers and IEC personnel in family planning organizations in the U.S. and around the world. The formal system established in 1986 to do this has evolved into a system that produces and disseminates appropriate country-specific informational materials to journalists, health policymakers and health organizations.

In this reporting period, FHI received requests for information from the Christian Science Monitor, a radio medical news service, the Washington Post, CBS Morning News, WNET-TV, NY, Savvy Magazine, The Leader, Essence Magazine, Mademoiselle Magazine, Community Nutrition, the Norwegian Broadcasting Company, Good Housekeeping, and the Greensboro News and Record. FHI conducted a mass mailing to more than 225 journalists on Dr. Judith Fortney's piece on "Contraception by American Women 40 and Over" and started work on organizing a press conference on spermicides and STD's. FHI wrote and submitted two articles on breast-feeding and contraceptive use to Al Ahram Newspaper in Cairo, an article on maternal mortality written for a lay audience was accepted by South: A Third World Magazine, and West Africa magazine published an article in February 1987 written by an FHI editor on STD's in Africa. A group of World Press Institute journalists visited FHI Nov. 24 for a briefing on family planning issues.

Country-specific information packets are produced and then distributed to directors and IEC personnel at Family Health Research Centers, clinics and hospitals. These personnel are encouraged by FDT staff through visits and correspondence to use the materials in their own information dissemination efforts. The packets include articles on STD's and spermicides, maternal mortality, contraceptive research, IUD's and the liability crisis in the U.S., risks and benefits of the pill, chlamydia, smoking and reproductive health, and breast-feeding. Our initial distribution in this reporting period has been to Asian and Middle Eastern health decision makers, as few of the materials have been translated into French or Spanish.

A special mailing of this type of materials on sexually transmitted diseases was sent to senior journalists in Africa in March 1987. Packets have also been sent upon request to the Sri Lanka Family Planning Association, the Bangladesh Fertility Research Center, and The Nation newspaper, Kenya. A packet developed to answer a request by USAID/India on oral contraceptives is now under consideration by USAID/India for bulk production and mass distribution within India.

#### **G. MONITORING OF COMPLIANCE WITH AID REGULATIONS**

During this reporting period, FHI finalized a documentation system to monitor compliance with AID regulations for core funding to programs in less developed countries. A consultant made site visits in March,

1987 to FHI programs in Bangladesh to monitor compliance. At the time of this report, he has not yet submitted his report of findings.

Protection of Human Subjects Committee (PHSC)

Three meetings of the Protection of Human Subjects Committee (PHSC) were held at FHI on November 7, 1986; February 13, 1987; and March 6, 1987 to review 23 research proposals, inclusive of amendments and those for expedited review.

One member rotated off at the end of the calendar year: Dr. Dorothy Glenn, an obstetrician/gynecologist, who is retired from civil service and resides in Gastonia, North Carolina.

Reappointed to the committee to serve another three-year term were:

Betty H. Dennis, PharmD, an Assistant Professor of Clinical Pharmacy at the University of North Carolina's School of Pharmacy and as a Contributing Lecturer in several Pharmacy, Nursing, and Medical Allied Health Professional courses. She is also the Director of Continuing Education for the School of Pharmacy at UNC.

John Shelton Reed, Jr., PhD, a Professor of Sociology and an Adjunct Professor of American Studies at the University of North Carolina. He is a scholar and author of a number of publications in the sociology field, including six books, as well as the recipient of several distinguished honors.

One new member was appointed as a consumer representative for a three-year term:

Susan G. Dull, MA (Humanities), a Legislative Aide to Senator Joseph V. Gartland, Jr. (Fairfax, Virginia) and the Virginia Coordinator of the Chesapeake Bay Commission. She currently serves as the President of the Board of Directors of the Virginia League for Planned Parenthood, Inc. and resides in Richmond, Virginia.

Dr. John Shelton Reed, Jr. was appointed as Chairperson, effective January 1, 1987, replacing Dr. Betty Dennis who had chaired the Protection of Human Subjects Committee for four years.

Dr. Betty Dennis represented the Protection of Human Subjects Committee at the First International Conference on Ethical and Moral Problems of Pharmacotherapy, held in Vatican City, October 23 - 25, 1986, and sponsored by the Pontifical Commission for the Apostolate of Health Care Workers for the Catholic Church. The conference focused on various topics related to research in less developed countries and emphasized the medical needs and issues concerning the safety and distribution of medicines. There was a general consensus that a spirit of cooperation rather than confrontation was important to the successful promotion of health around the world.

#### Scientific Meeting

Regulation of male fertility is an area of contraception presently in need of new research strategies for pharmacologic intervention. Noted scientists in the male fertility field were invited by the World Health Organization (WHO) to meet in Oaxtepec, Mexico, March 11 - 13, 1987, to target the needs for male fertility regulation. FHI sponsored the travel of the 12 North American participants. A proceedings of the symposium, "Golgi, Lysosome and Centriole Events in Early Spermiogenesis: Targets for Male Fertility Regulation", will be published.

AID/DPE-0537-A-00-4047-00

Expenditures

1 October 1986 - 31 March 1987

Salaries and Fringe Benefits	\$1,060,472
Service Centers	284,885
Consultant and Professional Fees	33,652
Contracted Labor	18,772
Travel - Domestic	22,348
Travel - Foreign	200,422
Supplies - Office	7,995
Supplies - Medical	32,285
Printing and Reprints	12,649
Office Equipment, Maintenance and Repair	3,194
Freight	8,014
Dues and Registration Fees	3,490
IJGO Subscriptions	21,400
Other Purchased Services	19,767
Keypunching	13,498
Other Expenses and Bank Service Charges	17,140
Data Purchases	155,335
Subcontracts	697,282
General and Administrative Costs	870,823
TOTAL:	\$3,483,423

490

## VIII. FUTURE PLANS

FHI's number one priority remains in keeping the Clinical Trials, particularly of those new methods that will be submitted to the USFDA for marketing approval (long-acting steroids, Filshie Clip and spermicides), on schedule. It is FHI's policy to supplement the funds it receives under Cooperative Agreement AID/DPE-0537-A-00-4047-00 with non-AID funds as necessary and when available.

FHI expects to see the recruitment and follow-up of volunteers in the Phase III NET 90-Day injectable study program continue to be the focus of new investigation in the next fiscal year. Volunteer enrollment should be completed at all 44 clinics which are currently studying the Filshie Clip. The work on spermicides, jointly funded by AID and NIH, should reach Phase I clinical trials.

FHI is unlikely to initiate new studies in NORPLANT<sup>®</sup> but will be carrying an important and heavy load of maintaining the follow-up of those women who have already received NORPLANT<sup>®</sup>.

FHI hopes to continue to explore ways of accelerating the registration of new methods of contraception in Third World countries and in achieving cost-effective, safe and responsible large scale use of new methods. In the coming fiscal year the studies on the relationship between breast-feeding and return of

ovulation should be completed and it is hoped that analysis of this important body of information will lead to specific policy guidelines for family planning programs around the world.

FHI is very aware that the great majority of new and continuing users of family planning in the 1990s will depend on methods that are already in widespread use. Therefore, FHI intends to continue its work in information dissemination, its efforts to educate users and providers about the benefits as well as the risks of oral contraceptives, its documentation of the clinical outcome of USFDA-approved intrauterine devices when used in various countries around the world, and its work on male and female sterilization. The organization continues to believe that the beliefs and attitudes of those who provide family planning options can be as important in determining use as the needs and motivation of the consumers of services and will continue research in this area.

In the long-term, FHI's greatest contribution is likely to be in its continued encouragement to local individuals and institutions and in the careful program of training and support which it is giving to numerous countries, with the goal of creating autonomous, self sufficient skills that can make informed policy choices about various methods of fertility regulation.

The area of activity which is most difficult to predict in the next fiscal year revolves around the AIDS crisis. There is no

doubt that the spread of AIDS is going to have an important impact on various aspects of contraception. It may well prove to be a source of adverse rumors which, unless countered with scientifically based information, could damage ongoing family planning programs. It is certain that AIDS will change some policies, and that barrier methods either by themselves or supplementing other methods of birth control will become more important. FHI's commitment to the field of AIDS research and intervention is strong. How much of the wide range of work that needs to be done in this area will be conducted through the Cooperative Agreement and how much will be funded from other sources remains to be determined.

FHI intends to coordinate its activities with other AID-funded agencies and with the WHO, so that the limited resources which are available for fertility regulation, to combat rapid population growth, to deal with the distressingly common problem of maternal/infant mortality and with the global epidemics of sexually transmitted diseases, can be used to help as many people as possible.

APPENDIX A

PUBLICATIONS LIST

FAMILY HEALTH INTERNATIONAL

PUBLICATIONS LIST

October 1, 1986 - March 31, 1987

- I Chi, G Ji, AJ Siemens, CS Waszak. IUD Insertion at Cesarean Section - the Chinese Experience. *Adv Contracept* 2:145, 1986. (86-23)
- JE Higgins, I Chi, LR Wilkens, RA Hatcher. Patterns of Depo-Provera Use in a Large Family Planning Clinic in the United States. *J Biosoc Sci* 18:379, 1986. (86-24)
- TT Kane. The Fertility and Assimilation of Guestworker Populations in the Federal Republic of Germany: 1961-1981. *Zeitschrift für Bevölkerungswissenschaft* 12(1):99, 1986. (86-25)
- M Potts. Neglected Mothers. *People* 13(2):33, 1986. (86-26)
- PC Chijioke, S Zaman, RM Pearson. Comparison of the Potency of D-Propranolol, Chlorhexidine and Nonoxynol-9 in the Sander-Cramer Test. *Contraception* 34(2):207, 1986. (86-27)
- WJ Wertheimer, MJ Rosenberg. AIDS: Opportunity for Wider Public Education. *The New York Times*, letter, Nov. 22, 1986. (86-28)
- RJ Stillman, MJ Rosenberg, BP Sachs. Smoking and Reproduction. *Fertil Steril* 46(4):545, 1986. (86-29)
- PJ Feldblum, NN Burton, MJ Rosenberg. Pelvic Inflammatory Disease and Oral Contraceptive Use. *African J Sex Trans Diseases* 2(2):36, 1986. (86-30)
- MJ Rosenberg, PJ Feldblum. Do Spermicides Protect Against Sexually Transmitted Diseases? *African J Sex Trans Diseases* 2(2):42, 1986. (86-31)
- AJ Siemens. Clinical Evaluation of Drugs Used in Fertility Regulation. *Human Reprod* 1(6):405, 1986. (86-32)
- MJ Rosenberg, KF Schultz, NN Burton, A Meheus. Sexually Transmitted Diseases: The Common Denominator (editorial). *African J Sex Trans Diseases* 2(2):30, 1986. (86-33)
- SL McIntyre, JE Higgins. Parity and Use-Effectiveness with the Contraceptive Sponge. *Am J Obstet Gynecol* 155(4):796, 1986. (86-34)
- CA Melendez, CS Waszak, CE Colven. Estudio Comparativo del DIU T Delta y la T de Cobre 220 en Costa Rica. *Ginecol Obstet Mexico* 54:164, 1986. (86-35)
- M Potts. Can Family Planning Reduce Maternal Mortality? *J Obst Gyn East Cent Afr* 5:29, 1986. (86-36)
- PJ Feldblum, MJ Rosenberg. Spermicides and Sexually Transmitted Diseases: New Perspectives. *NCMJ* 47(12):569, 1986. (86-37)

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- I Chi, CS Waszak, LR Wilkens. Do Insertion-Related Problems Affect Subsequent IUD Performance? *Contraception* 34(5):497, 1986. (86-38)
- I Chi, LF Galich, PF Tauber, LR Wilkens, CS Waszak, AJ Siemens, J Lippes. Severe Pain at Interval IUD Insertion: A Case-Control Analysis of Patient Risk Factors. *Contraception* 34(5):483, 1986. (86-39)
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- BB Gubhaju, MK Choe, RD Retherford, S Thapa, Infant Mortality Trends and Differentials in Nepal. *Stud Fam Plann* 18(1):22, 1987. (87-03)
- JA Fortney. Contraception for American Women 40 and Over. *Fam Plann Perspect* 19(1):32, 1987. (87-04)
- KW Childers. Fertility Factors. *West Afr*, Feb. 16, 1987, p. 316. (87-05)
- JDO Mariscal, CG Barrera, RG Wheeler, C Waszak. Use of Echsonography to Monitor Uterine Placement of Intrauterine Devices after Immediate Postpartum Insertions. *Int J Gynaecol Obstet* 25(1):53, 1987. (87-06)

APPENDIX B

CONSULTANT REPORTS (CRs)

Completed Consultant Reports (CRs)

October 1986 - March 1987

Title	Prepared for	Center	Study
A Comparative Study of the Lippes Loop D IUD and Copper T 200 IUDs in Cairo, Egypt	Ismail El-Essaily	033	5538
A Comparative Study of the Lippes Loop D IUD and the Copper T 200 IUD in Kaduna, Nigeria	J.J. Akuse	4000	5538
A Comparative Study of Norinyl 1/35 Versus Brevicon	J. Moreno	081	8825
Evaluation of Exluton for Breastfeeding Women in Mwanza, Tanzania	Ambrose Chanji	0492	8875
A Retrospective Study of Depo Provera Users Versus Oral Contraceptive Users in Merida, Yucatan, Mexico	Thelma Canto de Cetina	869	8880
A Comparative Study of Norinyl 1/35 Versus Norinyl 1/50 in Assiut, Egypt	Mamdouh Shaaban	358	8850
A Study of Progestogen-Only Oral Contraceptives for Lactating Women in Port-au-Prince, Haiti	Alfredo Solano	8014	8875
A Comparative Study of Norinyl 1/35 Versus Norinyl 1/50 in Merida, Yucatan, Mexico	Thelma Canto de Cetina	869	8850
Two Comparative Clinical Trials of Ortho Foaming Vaginal Tablets with Nonoxynol-9 Versus Ortho Foaming Vaginal Tablets Containing Menfegol in the U.S.	Gary Ruoff & Nina Niland	0220 0930	7799
A Study of Progestogen-Only Oral Contraceptives for Lactating Women in San Jose, Costa Rica	Alfredo Solano	831	8875
A Study of Progestogen-Only Oral Contraceptives for Lactating Women in Buenos Aires, Argentina	Angel Victor Moggia	871	8875
A Comparative Study of Norinyl 1/35 Versus Lo-Ovral in Ile-Ife, Nigeria	O. Ayangade	436	8825
A Comparative Study of Norinyl 1/35 Versus Lo-Ovral in Cairo, Egypt	Samir Nada	370	8825

<u>Title</u>	<u>Prepared for</u>	<u>Center</u>	<u>Study</u>
A Comparative Study of Norinyl 1/35 Versus Brevicon in Tegucigalpa, Honduras	ASHONPLAFA	890	8825
A Comparative Study of Norinyl 1/35 Versus Lo-Ovral Versus Noriday 1/50 in Ibadan, Nigeria	E.O. Otolorin	040	8825
A Comparative Study of the Multiload Cu 250 IUD and TCu 200B IUD Inserted Immediately Postpartum	Damrong Reinprayoon	0741	5544

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**STUDY STATUS LIST\***  
**FEMALE STERILIZATION**

APRIL 1987

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	120	12/19/86	8/86 CEC	analysis in Progress

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	Follow-Up			
739	Thou/ Indonesia	FS 86/010	9/86		1/87	25				3/87 NR	Awaiting forms
759	Mcloek/ Indonesia	FS 86/012	9/86		1/87	25				3/87 NR	Awaiting forms

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**STUDY STATUS LIST  
FEMALE STERILIZATION**

APRIL 1987

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
							ADM	Follow-Up			
739	Thouw/ Indonesia	FS 86/011	9/86		1/87	25				3/87 MR	Awaiting forms
759	Moeloeck/ Indonesia	FS 86/013	9/86		1/87	25				3/87 MR	Awaiting forms

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STUDY STATUS LIST  
FEMALE STERILIZATION STUDY

APRIL 1987

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	Inc FU	5mo FU	35+mo FU			
747	Arshat/ Malaysia	FS 86/009	9/86		9/87	800	*97	*8	*34	*17	3/26/87	2/87 SR	Active

\*Forms received/not processed

STUDY STATUS LIST  
FEMALE STERILIZATION

APRIL 1987

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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
							ADM	1mo FU	6mo FU	12mo FU	24mo FU			
284	Yuzpe/Canada	FS 85/007	6/85	7/85	6/87	200	*151	*111	*41	*22	X	03/23/87	1/87 SMC	Active
285	O'Brien/ England	FS 85/020	10/85	1/86	11/87	100	44	41	24	14	X	03/16/86	3/87 SMC	Active
224	Condie/ England	Subcontract	10/85		11/87	300							3/87 SMC	Awaiting 1st forms.
236	Newton/ England	Subcontract	10/85	4/86	11/87	300	117	78	50	7		03/05/87	3/87 SMC	Active
293	Pognore/ England	Subcontract	10/85	10/86	11/87	300	29	37				03/05/87	3/87 SMC	Active
201	Campbell/ England	FS 86/006	04/86	8/86	06/88	300	85	53	8		X	03/16/87	3/87 SMC	Active
200	Jaird/ Scotland	FS 85/007	04/86	7/86	05/88	200	*87	*45	*24		X	03/27/87	3/87 SMC	Active
283	Gemel/Canada	FS 85/009	2/86	7/86	06/88	200	25	27			X	03/03/87	2/87 SMC	Active
274	Milne/Canada	FS 86/005	5/86	12/86	4/88	200	5	4			X	02/06/87	1/87 SMC	Active
268	Eugene/Canada	FS 87/005	1/87		4/89	200					X			Awaiting forms

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STUDY STATUS LIST  
FEMALE STERILIZATION

APRIL 1987

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	08/23/86	1/87 CEC	CR in Progress
865	Bossemeyer/ Brazil	FS 84/004	8/84	8/84	2/87	100	83	69	20	70	*26	03/30/87	3/87 DB	FU only

\*Forms received/not processed

STUDY STATUS LIST  
FEMALE STERILIZATION

APRIL 1987

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	
							ADN	1mo FU	6mo FU	12mo FU				24mo FU
075	Suporn/ Thailand	FS 85/017	9/85	12/85	12/88	300	300	293	92	53		03/06/87	10/86 MR	FS Only
600	Apelo/ Philippines	FS 83/009	4/84	4/84	3/87	300	300	214	140	148	82	02/04/87	2/87 SK	FS only
781	Yan/ Taiwan	FS 84/003	4/84	4/84	5/85	200	200	169	176	142	61	03/06/87	9/86 SK	FS only
332	Lasso de- la Vega/Panama	FS 84/007	2/84	2/84	8/89	300	300	297	291	334	267	03/16/87	1/87 ES	Active
				12/86	8/89	300	*105	47				03/16/87		Active

\*Forms received/not processed

052

STUDY STATUS LIST  
FEMALE STERILIZATION

APRIL 1987

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			
433	Contreras/ Panama	FS 84/019	7/84	10/84	7/87	300	300	294	283	299	11	01/20/87	7/86 CEC	FU ONLY
451	Githiari/ Kenya	FS 86/004	2/86	10/86	7.88	100	*68	*55	*35		X	03/17/87	9/86 PL	Active
836	Nagahata/ Peru	FS 84/011	12/84	3/85	9/87	200	200	197	159	72	1	01/19/87	1/87 CEC	FU Only
865	Bossemeyer/ Brazil	FS 84/022	9/85	11/85	1.87	100	69	*44	*37	*11	X	03/30/87	3/87 DE	Active
8594	Garza-Flores/ Mexico					200								Under Development
	Religaswatte/ Sri Lanka					300								Under Development

\*Forms received/not processed

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**STUDY STATUS LIST  
FEMALE STERILIZATION**

APRIL 1987

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
							ADM	1mo FC	6mo FC	12mo FC	24mo FC			
075	Suporn/ Thailand	FS 84/015	10/84 Subgrant	10/84	7/87	300	301	299	239	211	7	03/12/87	10/84 NA	FU Only
081	Moreno/ Panama	FS 85/002	2/85	3/85	10/87	300	300	223	405	227	3	12/08/86	1/87 NA	FU Only
739	Thouw/ Indonesia	FS 85/018	11/85	5/86	9/87	150	*95	17	1		X	02/23/87	3/87 NA	Active
741	Kohchitt/ Thailand	FS 84/023 Subgrant	5/85	3/85	9/87	300	158	123	100	61	X	12/23/86	10/86 NA	Admissions terminated
				4/86	9/87	300	112	35	34		X	12/23/86		Active
759	Noelook/ Indonesia	FS 85/019	11/85	7/86	9/87	150	*53	37			X	02/23/87	3/87 NA	Active
892	Ortiz- Mariscal/Mexico	FS 85/012	7/85	5/86	4/88	300	*119	*107	*45	*2	X	03/26/87	9/86 CEC	Active
894	Cordero/ Dominican Republic	FS 85/011	8/85	3/87	7/88	300	*5					03/06/87	2/87 C.C.	Active

9

**STUDY STATUS LIST  
FEMALE STERILIZATION**

APRIL 1987

Description of Study: Minilaparotomy - 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	
							ADH	1mo FU	6mo FU				12mo FU
832	Lasso de- la Vega/Panama	FS 85/013	8/85	9/85	4/87	300	300	289	286	232	03/16/87	1/87 EW	FU Only
8044	Cordero/ Dominican Republic	FS 85/014	8/85	10/85	5/87	300	302	250	150	80	03/26/87	2/87 CLC	FU Only
684	Thambu/ Malaysia	FS 85/024	9/86	12/86	9/88	200	16	14			02/04/87	2/87 SK	Active
685	Vettivelu/ Malaysia	FS 85/024	9/86	12/86	9/88	100	*5	*6	*4		03/26/87	2/87 SK	Active
8593	Remez/Mexico	FS 87/006				300							Under Development

\*Forms received/Not processed

STUDY STATUS LIST  
FEMALE STERILIZATION

APRIL 1987

Description of Study: Laparoscopy - Filshie Clip vs. Wolf Clip

Study Number: 6257

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
841	Santiso/ Guatemala	FS 85/010	2/86	2/86	3/88	300	283	235	208	*51	X	03/30/87	2/87 CEC	Active
8009	Louissaint/ Haiti	FS 85/016	8/85	9/85	5/87	300	237	208	117	47	X	02/04/87	4/87 SB	Active
864	Uribe/Mexico	FS 85/022	11/85	1/86	9/87	300	300	286	65		X	02/24/87	9/86 CEC	FU Only
100	Zigelboim/ Venezuela	FS 86/001	12/85	1/86	12/88	300	239	185	54			03/02/87	11/86 CEC	Active

\*Forms received/not processed

STUDY STATUS LIST  
FEMALE STERILIZATION STUDY

APRIL 1987

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
							ADM	1mo FU	5mo FU			
029	Kauppinen/ Finland	FS 87/002	12/86	2/87	3/89	200	33	19		03/12/87	4/87 JB	Active
750	Kwak/Korea	FS 87/004	3/87		5/89	300						Awaiting Equipment
731	Tsir/Taiwan	FS 86/015	9/86	3/87	11/88	150	*10			03/23/87	2/86 SK	Active
231	Leodolter/ Austria	FS 86/014	9/86	3/87	11/88	300	15	2		03/09/87	4/87 JB	Active
260	Wagenbichler/ Austria	FS 87/001	12/86		1/89	200					4/87 JB	Awaiting 1st Forms
256	Vaspels/ Holland	FS 87/003	12/86		1/89	200					4/87 JB	Awaiting 1st Forms

\*Forms received/not processed

STUDY STATUS LIST  
FEMALE STERILIZATION STUDY

1987

12

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/ Comment
							ADM	1mo FU	6mo FU			
8903	Abdala/ Brazil	FS 35/015	6/85	7/85	3/87	200	193	197	197	4/21/87	4/36DB	FU Only
						Corrected forms	200	*196	*196			

Forms Received/Ret Processed

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1

**STUDY STATUS LIST  
FEMALE STERILIZATION STUDY**

Description of Study: surveillance - Minilaparotomy

1987

Study Number: 6906

Total Number of Cases: 2450

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	3mo FU			
8591	Quinones/ Mexico	Multi Subgrant	1/85	8/85	11/86	750	766	758	755	10/02/86	8/86 MW	
8592	Quinones/ Mexico	Multi Subgrant	1/85	9/85	11/86	750	101	98	91	05/21/86	8/86 MW	Analysis in Progress
8593	Quinones/ Mexico	Multi Subgrant	1/85	11/85	11/86	750	306	253	246	02/19/87	2/87 dw	

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**STUDY STATUS LIST**  
**NORPLANT® Implant Studies**

Description of Study: NORPLANT® IMPLANTS - FCC 3132, FCO 3180<sup>a</sup> and FCO 0681<sup>b</sup>

DATE: APRIL 1987

Study Number: 866

Total Number of Cases: 3700

Total Number of Studies: 24

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			FU Slot 24
040	O. LADIPO NIGERIA	NOR 85/014	10/11/85	8/87	120	68	57	40	27	39		1/06/87	1/16/87	
041	A. COLLISON GHANA	NOR 85/012	10/16/85	8/87	100	4	5	3				3/10/87	9/22/86	
042	C. EKEMPU NIGERIA	NOR 85/013	10/10/85	8/87	105	51	53	47	50	15		3/20/87	6/19/86	
435	O. FAKYE NIGERIA	NOR 85/004	1/15/86	12/87	105	50	50	49	47	7		1/13/87	6/25/86	
437	M. DEJOMOH NIGERIA	NOR 85/015	10/09/85	8/87	105	54	52	51	47	9		1/06/87	6/25/86	
453	J. OTUBU NIGERIA	NOR 86/005	11/08/85	8/87	100	47	38	40	39			1/30/87	6/20/86	
482 <sup>a</sup>	P. CORREA SENEGAL	NOR 87/002	12/10/86	10/88	50	8	1					3/26/87	2/02/87	
600 <sup>b</sup>	R. APELO PHILIPPINES	NOR 85/005	2/07/85	10/88	50	50	48	45	51	41	9	2	3/26/87	6/16/86
600	R. APELO PHILIPPINES	NOR 86/007	9/27/85	10/87	100	88	64	58	43	10			3/25/87	6/16/86
602 <sup>b</sup>	P. PUERTOLLANO PHILIPPINES	NOR 85/006	2/07/85	10/88	50	50	44	48	59	55	16	1	2/19/87	6/17/86
602	I. BENITEZ PHILIPPINES	NOR 85/008	6/27/86	2/88	100	82	63	34	2				3/26/87	6/17/86
703	S. BASMAYAKE SRI LANKA	NOR 85/010	5/14/85	10/88	275	275	294	286	285	295	196		3/23/87	2/11/87

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 24		
704	S. BEGUM BANGLADESH	NOR 85/001	2/17/85	3/88	200	200	193	192	190	143	24	3/20/87	7/22/86
718	T. CHOWDHURY BANGLADESH	NOR 85/002	2/20/85	8/88	200	200	195	194	182	153	41	2/26/87	7/17/86
721	S. RAHMAN BANGLADESH	NOR 85/003	2/19/85	8/88	200	200	202	201	196	115	37	3/31/87	7/19/86
729	H. LAMA NEPAL	NOR 85/004	2/14/85	3/87	300	307	304	283	279	241	47	3/29/87	2/24/87
731	S. RAJESHWARDARI NEPAL	NOR 85/008	5/09/85	4/87	100	100	71	57	81	37	2	2/20/87	2/24/87
735	S. ACHARYA NEPAL	NOR 87/003	2/18/87	10/92	200								2/18/87
736	H. SHARMA NEPAL	NOR 87/004	2/21/87	10/92	200								2/21/87
742	K.P. YADAV NEPAL	NOR 87/005	2/17/87	10/92	200								2/17/87
749	S. CHINMAYEY SRI LANKA	NOR 85/009	5/16/85	10/88	200	200	153	167	207	121	37	3/14/87	2/10/87
758	I. VIKITHARATNE SRI LANKA	NOR 85/011	5/17/85	10/88	200	200	200	198	193	190	38	3/23/87	7/29/86
798 <sup>b</sup>	S. RATNAM SINGAPORE	NOR 85/007	2/04/85	10/88	100	100	104	100	99	103	4	2/26/87	10/31/86
8017	R. BOULOS HAITI	NOR 86/001	11/11/85	10/87	150	99	95	96	91	33		3/24/87	11/14/86
8331	G. THEODORE HAITI	NOR 86/003	11/14/85	10/87	150	100	94	71	40	63		2/04/87	11/13/86
8332	F. LCLAGNE HAITI	NOR 86/002	11/16/85	10/87	100	50	50	37	27	30		3/02/87	11/15/86



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STUDY STATUS LIST  
VAGINAL CONTRACEPTION  
3171

APRIL 1987

Description of Study: NEO SAMPOON (60 MG. MEFEGOL) VS. ENKO FOAM

Study Number: 785

Total Number of Cases: 1050

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
						ADM	1 mo FU	3 mo FU	6 mo FU	12+ mo FU			
20	Andolsek/Yugoslavia	81/014	6/81 / 4/82	12/85	350	266	203	216	166	132	12/16/86	4/86	Closed
360	Mahran/Egypt	80/012	12/79 / 1/81	12/83	350	330	61	39	15	11	09/19/83	Closed	CR 531
368	Youssef/Egypt	80/013	4/80 / 2/81	10/82	350	349	280	258	273	247	02/02/83	Closed	CR 468

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STUDY STATUS LIST  
VAGINAL CONTRACEPTION  
3172

APRIL 1987

Description of Study: DIAPHRAGM WITH SPERMICIDE VS. DIAPHRAGM WITHOUT SPERMICIDE VS. SPERMICIDE ONLY (DELPHEN 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	66	66	59	41	14	02/06/87	3/87	Active

STUDY STATUS LIST  
VAGINAL CONTRACEPTION  
0674

APRIL 1987

Description of Study: 100 MG. PROPRANOLOL TABLET (DAILY VAGINAL ADMINISTRATION OF TABLET EXCEPT DURING MENSES)

Study Number: 7790

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	1 mo FU	3 mo FU	6 mo FU	12+ mo FU			
88	Zipper/Chile	84/002	12/83 / 2/84	3/85	200	42	56	51	20	4	09/19/86	11/86	Closed

STUDY STATUS LIST  
VAGINAL CONTRACEPTION  
0674

APRIL 1987

Description of Study: 100 MG. PROPRANOLOL OVULE (PRE- AND POST-COITAL VAGINAL ADMINISTRATION OF OVULE ONLY)

Study Number: 7791

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	1 mo FU	3 mo FU	6 mo FU	12+ mo FU			
88	Zipper/Chile	85/001	12/83 / 10/84	3/85	200	52	52	41	24	11	12/22/86	11/86	Closed

012

STUDY STATUS LIST  
VAGINAL CONTRACEPTION  
3171

APRIL 1987

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	125	122	79	03/18/87	6/86	Active
4500	Ghunney/Ghana	84/007	9/84 / 1/85	2/87	150	27	27	28	26	23	10/03/86	6/86	Active
773	Sumana/Thailand	85/005	9/85 / 7/86	1/88	100	101	94	61	1	0	02/10/87	11/86	Active
Possible Open												Planned	

STUDY STATUS LIST  
VAGINAL CONTRACEPTION  
3171

APRIL 1987

Description of Study: OVT (60 MG. MENFEGOL) 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	Roo ff/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	30	19	15	10	4	07/16/86	9/85	Closed
909	Halki/Ohio	85/002	7/85 / 1/86	11/86	50	11	9	6	2	0	03/30/87	2/86	Active

212

STUDY STATUS LIST  
VAGINAL CONTRACEPTION  
3170

APRIL 1987

Description of Study: EFFECTIVENESS OF TIOCONAZOLE VS. PLACEBO IN PREVENTING VAGINAL INFECTION

Study Number: 7800

Total Number of Cases: 200

Total Number of Studies: 1

Center	Investigator/ Country	Index Number	Date Active	Expiration Date	Proposed No. of Cases	ADN	Number of Cases Completing X Number of Weeks of Use						Date Last Shipment	Date Last Site Visit	Status/ Comments
							2	4	6	8	10	12			
8062	Jaramillo/Costa Rica	86/001	7/86	4/87	200	47	37	33	27	20	13	8	02/11/87	9/86	Active

127

STUDY STATUS LIST  
IUD

APRIL 1987

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	424	442	430	3/17/87	4/87 JB	ACTIVE
086	TACLA/CHILE	81/013	8/81	8/81	100	68	66	60	63	56	2/22/85	3/83 MW	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	299	231	227	222	40	3/16/87	2/87 CEC	ACTIVE

Description of Study: Evaluation of TCU 380 A vs. TCU 220

Study Number: 532

Total Number of Cases: 600

Total Number of Studies: 2

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 FU	3MO FU	6MO FU	12MO+ FU			
084	DELGADO/MEXICO	85/008	7/85	6/87	300	300	260	269	234	114	3/19/87	9/86 CEC	ACTIVE
680	AFROZE/PAKISTAN	85/15	3/86	11/87	300	94	68	41	16		2/10/87	3/86 SK	ACTIVE

STUDY STATUS LIST  
IUD

MARCI 1987

6  
pct

Description of study: TCU200 vs AAdapted T

Study Number: 534

Total Number of Cases: 200

Total Number of Studies: 1

FCO: 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+
698	APICHART/THAILAND	85/007	5/85	7/87	200	143	105	72	71	36	4/02/87	10/86 MR	ACTIVE

STUDY STATUS LIST  
IUD

2  
312

Description of Study: Evaluation of TCu 380 A vs. Nova T

APRIL 1987

Study Number: 536

Total Number of Cases: 300

Total Number of Studies: 1

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+			
100	ZIGHELROIM/ VENEZUELA	85/006	6/85	1/87	300	300	172	184	173	72	3/ 2/87	11/86 CEC	ACTIVE

Description of Study: Evaluation of TCu 380 A vs. TCu 200

Study Number: 550

Total Number of Cases: 4100

Total Number of Studies: 13

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+			
060	DAVID/PHILIPPINES	86/004	6/87 EDI	1/88	200							3/87 SK	FULLY APPROVED
061	ALFONSO/PHILIPPINES	86/006	6/87 EDI	5/88	200							3/87 SK	FULLY APPROVED
066	DACALOS/PHILIPPINES	86/007	6/87 EDI	5/88	200							3/87 SK	FULLY APPROVED
342	EFCS/EGYPT	86/008 SUB 3151-4	7/86	2/87	1000	641	227	126	40	5	N/A	11/86 CBC	ACTIVE
363	TOPUZADA/EGYPT	85/005	6/85	6/87	200	139	37	17	18	16	11/19/85	3/87 PG	ACTIVE
401	MUHAMMAD/SUDAN	85/14	10/85	2/89	100	26	20	15	5		9/03/86	3/87 PG	CLOSED

Description of Study: Evaluation of TCu 350 A vs. TCu 200

(cont'd)

Study Number: 550

Total Number of Cases: 4100

Total Number of Studies: 13

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+			
452	DOII/CAMEROON	86/012	6/86	6/88	300	63	56	36	14	5	2/22/87	1/87 RD	ACTIVE
821	HENRIQUE EL SALVADOR	85/17	1/86	11/87	300	284	215	149	109	3	2/12/87	3/87 MW	ACTIVE
825	RIVERA/MEXICO	85/12	8/85	9/87	300	299	248	238	224	55	3/31/87	9/86 CEC	ACTIVE
854	BELTRAN/CHILE	86/009	6/86	1/88	300	297	279	260	74		3/23/87	4/87 CEC	ACTIVE
8020	AGUINAGA/BRAZIL	85/011	10/85	1/87	300	300	206	101	52		9/10/86	3/87 DB	ACTIVE
8052	IHSS/HONDURAS	86/010	6/86	6/88	300	168	115	64	34		2/22/87	11/86 CEC	ACTIVE
8065	FERNANDEZ/ COSTA RICA	86/011	3/87	6/88	200	11					3/20/87	9/86 CEC	ACTIVE

STUDY STATUS LIST  
IUD

APRIL 1987

Description of Study: Evaluation of TCu 380 A vs. LL2

Study Number: 552

Total Number of Cases: 900

Total Number of Studies: 3

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+			
042	EKWEMPU/NIGERIA	86/013	6/86	7/88	300	101	57	24	1		3/20/87	9/86 RD	ACTIVE
101	ACOSTA/PERU	85/16	12/85	11/87	300	178	98	56	33	1	2/04/87	1/87 CEC	ACTIVE
304	KISNISI/TURKEY	85/002	7/86	6/87	300	40					2/23/87	3/87 PG	ACTIVE

Description of Study: Evaluation of TCu 380 A vs. HLCu250

Study Number: 553

Total Number of Cases: 2300

Total Number of Studies: 4

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+			
703	BANDARAGODA SRI LANKA	86/002	2/86	1/88	300	299	296	262	175	14	3/23/87	8/86 JH	ACTIVE
741	DAMRONG/THAILAND	85/009 SUB 3151-1	5/85	5/87	1400	1386	1230	1095	1004	575	1/22/87	11/86 HR	ACTIVE
776	GUNASEKERA SRI LANKA	86/003	2/86	1/88	300	170	115	38			3/31/87	8/86 JM	ACTIVE
787	CHONG MALAYSIA	86/001	1/86	2/88	300	56	48	41	30		3/31/87	3/87 SK	ACTIVE

STUDY STATUS LIST  
IUD

APRIL 1987

Description of Study: Post C-Section IUD Insertion

Study Number: 564

Total Number of Cases: 1800

Total Number of Studies: 1

FCO: 3155

CENTER NUMBER	INVESTIGATOR/COUNTRY	INDEX NUMBER	DATE INITIATED	EXPIRATION DATE	PROPOSED NO. OF CASES	ADM	FORMS PROCESSED				DATE LAST SHIPMENT	DATE LAST SITE VISIT	STATUS/COMMENTS
							1MO FU	3MO FU	6MO FU	12MO+ FU			
868	AZNAR/MEXICO	86/015	8/86	12/87	1800	978	483				N/A	1/87 MW	ACTIVE
							NO FORMS IN-HOUSE						

Description of Study: IUD Insertion with and without Prophylactic Antibiotics

Study Number: 2400

Total Number of Cases: 1800

Total Number of Studies: 1

FCO: 3156

CENTER NUMBER	INVESTIGATOR/COUNTRY	INDEX NUMBER	DATE INITIATED	EXPIRATION DATE	PROPOSED NO. OF CASES	ADM	FORMS PROCESSED				DATE LAST SHIPMENT	DATE LAST SITE VISIT	STATUS/COMMENTS
							1MO FU	3MO FU	6MO FU	12MO+ FU			
040	LADIPO/NIGERIA	86/014 SUB 3156-1	7/86	6/88	1800	158	145	41			2/ 4/87	2/87 NB	ACTIVE

STUDY STATUS LIST  
IUD

APRIL 1987

Description of Study: Evaluation of TCu 380 A vs MLCu 375 vs. LLD

Study Number: 5554

Total Number of Cases: 3000

Total Number of Studies: 1

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+			
BKS PENFIN	INDONESIA	85/18 SUB 3151-3	5/86	9/87	3000	2511	2132	1511	530	8	N/A	3/87 MR, TP ACTIVE	

STUDY STATUS LIST  
SYSTEMICS

APRIL 1987

Description of Study: Loestrin vs Lo-Femenal

Study Number: 8820 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
076	Mukherjee/ Malaysia	86/023	2/87			300						2/87SK	EDI 3/87	
314	Saleh/Cairo, Egypt	86/014	7/86	10/86	6/88	300	107	85	19			4/1/87	3/87PC	Active
633	Lubis/Jakarta, Indonesia	86/016	9/86	1/87	8/88	300	1					3/31/87	3/87MR	Active
8590	Rueda/Bogota, Columbia	86/015	9/86	7/86	5/88	300	10	1				10/7/86 queried	11/86DB	Active
8594	Perez Palacios/ Mexico City, Mexico	86/011	5/86	6/86	5/88	300	44	53	27	6		3/26/87	9/86CC	Active

TOTALS ON THIS LIST REPRESENT THE NUMBER OF FORMS LOADED INTO THE COMPUTER

STUDY STATUS LIST  
SYSTEMICS

April 1987

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
E1	Moreno/Panama	82/013		2/83	6/86	300	300	268	247	221	222	4/86	1/86	CR 571
356	Rahman/Egypt	83/015		8/83	12/86	300	220	220	201	149	109	12/86	7/86	CR in progress
890	Runez/Honduras	82/010		11/82	6/86	300	174	120	75	46	46	5/86	9/85	CR 583
SC03	Albuquerque/Brazil	82/014		10/82	5/86	300	302	284	246	157	95	5/86	4/86	CR in progress

Totals reflect number of forms loaded.

STUDY STATUS LIST  
SYSTEMICS

April 1987

Description of Study: Morinyl 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	Otolarija/Nigeria	83/027		7/84	3/86	100	95	78	74	56	33	3/86	6/85	CR 585
370	Mada/Egypt	83/016		6/84	10/85	300	298	296	291	292	285	1/86	7/86	CR 581
436	Ayangade/Nigeria	83/028		8/84	3/86	100	96	80	72	70	33	3/86	6/85	CR 580
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	Noggia/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	82	12/84	9/84	*

Totals reflect number of forms loaded.

\* Data not to be analyzed.

STUDY STATUS LIST  
SYSTEMICS

APRIL 1987

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			
400	Gerais/Khartoum, Sudan	86/002	2/86	8/86	3/88	300	286	240	1		4/1/87	3/87PG	Active
703	Easnayake/Colombo, Sri Lanka	86/004	2/86	4/86	3/88	300	227	182	111	40	3/30/87	S/86JM	Active
850	Guzman-Serani/ Valdivia, Chile	86/005	3/86	4/86	3/88	300	288	262	192	83	2/11/87 queried	4/87CC	Active
964	Aguayo/Quito, Ecuador	86/024				150							EDI 3/27
8057*	Calventi/ Santo Domingo, Dominican Republic	86/003	6/86	3/87	3/88	300	6				3/12/87	3/87CC	Active

\*forms received, not loaded

TOTALS ON THIS LIST REPRESENT THE NUMBER OF FORMS LOADED INTO THE COMPUTER.

STUDY STATUS LIST  
SYSTEMICS

APRIL 1987

Description of Study: Crossover - Moriday 1/50 to Lo-Femenal; Lo-Femenal to Moriday 1/50

Study Number: 8845 FCO: 3139

Total Number of Cases: 1200

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
							ADN	1 mo FU	3 mo FU	4 mo FU	6 mo FU			
023	Breznik/Maribor, Yugoslavia	85/008	6/85	11/85	12/86	300	297	289	253	189	214	3/12/87	4/87JB	Will close once status is confirmed
602	Benitez/ Metro Manila, Philippines	85/009	9/85	2/86	12/87	300	252	191	107	60	71	3/24/87	2/87SK	Active
340	Ramos/Ciudad Juarez, Mexico	85/010	10/85	3/86	5/87	300	13	7	4	2	2	12/9/86 queried	12/85CC	Follow-up only
843	Eonfim/Fortaleza, Brazil	86/006	2/86	8/86	10/87	300	8	4	1			3/20/87	3/87DB	Active
8593	Remes/Veracruz, Mexico	86/019	9/86	10/86	5/88	300	42	20	2			3/18/87	1/87MN	Active

TOTALS OF THIS LIST REPRESENT THE NUMBER OF FORMS LOADED INTO THE COMPUTER.

STUDY STATUS LIST  
SYSTEMICS

April 1987

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	Pehlilovic/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 574
703	Basnayake/Sri Lanka	83/014		9/84	10/85	500	500	454	450	380	316	10/85	7/86	CR 561
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 576

Totals reflect number of forms loaded.

STUDY STATUS LIST  
SYSTEMICS

APRIL 1987

Description of Study: CC's With vs Without Iron

Study Number: 8856 FCO: 3136

Total Number of Cases: 1280

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/ LAB	6 wks FU	14 wks FU				26 wks FU
085	Bassol/Torrecon, Mexico	86/007	7/86	8/86	11/87	320	27/65	21	15	3	3/23/87	9/86CC	Active
603	Ago/POPCOM Legaspi City, Phillipines	86/022	9/86			320						9/86SK	EDI 3/87
621	BKS PENFIS/Soeprapti Bandung, Indonesia	86/008	11/85	2/87	4/88	320	12/17	4			2/20/87	3/87MK	Active
704	Sarua/BRP Dhaka, Bangladesh	86/020	3/87			320						4/87JM	EDI 4/87

TOTALS OF THIS LIST REPRESENT THE NUMBER OF FORMS LOADED INTO THE COMPUTER.

182

STUDY STATUS LIST  
SYSTEMICS

April 1987

Description of Study: Depo Provera vs Oral Contraceptives (Retrospective)

Study Number: 3880 FCO: 3135

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
							ADH	> 24 mo FU			
340	Etman/Egypt	83/025		6/84	12/85	300	294	290	1/86	7/86	CK 563
703	Basnayake/Sri Lanka	83/021		9/83	7/85	600	600	473	3/85	5/85	CR 554
709	Mongkol/Thailand	84/003		2/84	1/85	300	299	291	7/84	10/84	CR 525
869	Cetina/Mexico	83/024		1/84	12/85	300	300	236	12/85	6/85	CR 573

Totals reflect number of forms loaded.

852

**STUDY STATUS LIST**  
**PROGESTOGEN-ONLY OC VERSUS NON-HORMONAL METHODS**

APRIL 1987

Description of Study: Progestogen-only Oral Contraceptive versus Non-Hormonal Methods in Lactating Women (Repeated Studies)

Study Number: 377, 378 FCO: 3133

Total number of Cases: 800

Total Number of Studies: 3

Center	Investigator/ Country	Index Number	Date Init./Active	Expiration Date	Proposed No. of Cases	ADM	Forms Processed							Date Last Shipment	Date Last Site Visit	Status/ Comments
							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	85	79	75	60	51	31	19	4/1/87	3/87PG	Active	
371	Maggia/Buenos Aires, Argentina	85/004	10/85 10/85	4/87	300	300	249	209	230	217	217	192	92	3/9/87	4/87CC	Active (Adm. closed)
871	Maggia/Buenos Aires, Argentina	86/001	8/86 11/86	4/88	200	65	42	31	9				3/9/87	4/87CC	Active	

THE TOTALS ON THIS LIST REPRESENTS THE TOTAL NUMBER OF FORMS LOADED INTO THE COMPUTER.

STUDY STATUS LIST  
PROGESTOGEN-ONLY ORAL CONTRACEPTIVES

APRIL 1987

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	PT FU			
084	Delgado/Mexico Villahermosa	84/034		11/84	11/87	200	198	194	162	103		3/19/87	9/86 CC	Active (Adm. closed)
102	Guzman/Peru Lima	84/013		7/84	11/87	200	199	139	91	37		2/27/87 queried	1/87 CC	Active (Adm. closed)
110	Nagahata/Peru Lima	84/014		3/84	9/87	200	193	190	183	181		1/15/87	1/87 CC	Closed
400	Gerais/Sudan Khartoum	85/002		2/85	2/87	200	200	199	186	174		5/21/86	2/86 PG	Closed CR in Progress
422	Broquet/Rwanda Gisenyi	84/004		6/85	3/87	200	18	11	1			5/20/86	5/86 RD	Closed
452	Doh/Cameroon Yaounde	84/030		12/84	7/87	200	228	128	98	91		1/6/87	2/87 RD	Closed CR in Progress
453	Wright/Nigeria Jos	84/035		3/86	12/87	100	75	37	5	2		2/10/87 queried	6/86 RD	Active
463	Diaye/Senegal Dakar	84/004		11/84	12/87	200	103	84	55	27		2/22/87 queried	2/87/ED	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 Complete
840	FEMAP/Mexico Ciudad Juarez	84/029		10/84	9/86	200	200	164	134	56	62	5/7/86	12/85 CC	Closed CR in Progress
841	Santoso/Guatemala Guatemala City	84/031		12/84	10/86	200	199	192	162	148		11/11/86	3/87 CC	Will Close once status is confirmed

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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
							ALM	2 mo FU	6 mo FU	12 mo FU	PT FU			
343	Lomfim/Brazil Fortaleza	84/036		12/84	4/87	200	196	159	109	64	52	3/23/87	8/86 DB	Active (Adm. Closed)
865	Barbosa/Brazil Santa Maria	84/038		2/85	4/87	200	191	123	73	26		1/6/87 queried	3/86 DB	Active (Adm. closed)
869	Celina/Mexico Merida	84/015		7/84	6/86	200	200	185	146	93		6/11/86	12/85 CC	Closed CR in progress
871	Hoggia/Argentina Buenos Aires	84/020		8/84	9/86	200	200	162	1	130		4/21/86	4/86 CC	Closed CR Complete
893	Czeresnia/Brazil Sao Paulo	84/037		2/85	4/87	200	133	95	39	18	11	3/23/87	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 CR Complete
3056	Oliveira/Brazil Londrina	84/039		2/85	4/87	200	195	137	88	37	8	1/6/87 queried	8/86 DB	Will close once status is confirmed
8058	Andrade/Brazil Curitiba	84/041		5/85	4/87	200	203	152	80	25	28	1/6/87 queried	8/86 DB	Active (Adm. closed)
3059	Funes/Brazil Porto Alegre	84/040		2/85	4/87	200	200	192	173	126	42	1/20/87 queried	3/86 DB	Will Close once status is confirmed

The totals on this list represent the total number of forms loaded to date.

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STUDY STATUS LIST  
EXPANDED PROGESTOGEN-ONLY OC

APRIL 1987

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./Active	Date 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	4/87	200	198	191	115	3	10/31/86 queried	6/86 PL	Active (Adm. closed)
044	Klufio/Ghana Accra	84/003	10/85	7/87	200	199	189	181	72	3/16/87	6/86 PL	Active (Adm. closed)
440	Doucoure/Traore Bamako/Mali	83/031	1/85	7/87	100	99	78	57	27	2/4/87 queried	3/87 KJ	Active
457	Toure/Traore Kayes/Mali	84/002	9/85	4/87	200	48	6			9/16/86	8/86 KJ	Closed
460	Samake/Traore Bamako/Mali	85/003	9/85	4/87	200	140	83	18	9	3/12/87	3/87 KJ	Active
8060	Russowsky/Brazil Porto Alegre	84/001	3/85	12/86	300	149	98	49	20	7/22/86 queried	8/86 DB	Will Close once status is confirmed

The totals on this list represent the total number of forms loaded to date.

2062

STUDY STATUS LIST  
INVESTIGATOR NETWORK NEEDS  
FCO 3114  
CLOSED STUDIES

APRIL 1987

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	Ekwempu/Nigeria	IUD 85/001	3/85 / 3/85	4/86	150	150	139	113	89		1/86	6/86RD	Closed CR in Progress

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	2/85NB	Closed CR Completed
4000	Akuse/Nigeria	IUD 83/013	9/84 / 9/84	8/85	150	148	130	110	53	33	11/85	10/85PL	Closed CR Completed

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STUDY STATUS LIST  
INVESTIGATOR NETWORK NEEDS  
FCO 3114  
CLOSED STUDIES

Description of Study: ML 250 VS. COPPER T 200B

APRIL 1987

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	
						ADM	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	272	208	180	1	8/86	11/86MR	Closed CR Completed

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	
						ADM	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 in review

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STUDY STATUS LIST  
 INVESTIGATOR NETWORK NEEDS  
 FCO 3114  
 ACTIVE STUDIES

APRIL 1987

Description of Study: TCU 380A VS TCU 200

Study Number: 5550

Total Number of Cases: 600

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			
079	Shrestha/Nepal	IUD 87/001		2/89	200						2/87 SB	Awaiting AID Approval
875	Arboleda/Colombia	IUD 87/005		4/89	400						2/87 DB	Awaiting AID Approval

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STUDY STATUS LIST  
 INVESTIGATOR NETWORK NEEDS  
 FCO 3114  
 ACTIVE STUDIES

APRIL 1987

Description of Study: FS SURVEILLANCE

Study Number: 6900

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	1 mo FU	3 mo FU	6 mo FU	12 mo FU				
040	Otolorin/Nigeria	FS 86/003	6/86	9/86	2/88	200	67		X		X	12/86	9/86 PL	active

967

STUDY STATUS LIST  
 INVESTIGATOR NETWORK NEEDS  
 FCO 3114  
 CLOSED STUDIES

APRIL 1987

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	
						ADM	1 mo FU	3 mo FU	6 mo FU				12 mo FU
893	Czeresnia/Brazil	SYS 83/C01	4/84 / 4/84	7/86	100	93	74	50	44	46	2/86	4/86DB	Closed CR in Progress

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
						ADM	> 24 Mo FU			
4010	Adama Dabo/Gambia	SYS 84/017	7/84 / 7/84	2/86	400	399	352	4/86	4/86RD	Closed CR in Progress

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STUDY STATUS LIST  
 INVESTIGATOR NETWORK NEEDS  
 FCO 3114  
 ACTIVE STUDIES

Description of Study: TRIPHASIC VS LOW-DOSE

APRIL 1987

Study Number: 8841

Total Number of Cases: 400

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	4 mo FU	8 mo FU			
613	Cruz/Phillipines	SYS 87/001	3/87	3/89	200						3/87 SK	Awaiting Supplies
6000	Villamar/ Philippines	SYS 87/002	3/87	3/89	200						3/87 SK	Awaiting Supplies

Description of Study: TRIPHASIC VS LOW-DOSE

Study Number: 8830

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	1 mo FU	4 mo FU	8 mo FU			
7020	Ismail/Malaysia	SYS 86/001	1/86	11/87	200	184	155	135	38	1/87	2/87 SK	Active

STUDY STATUS LIST  
 INVESTIGATOR NETWORK NEEDS  
 FCO 3114  
 ACTIVE STUDIES

APRIL 1987

*BR*

Description of Study: NORIDAY VS. LO-FENENAL

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	
						ADM	1 mo FU	4 mo FU	8 mo FU				12 mo FU
440	Traore/Mali	SYS 83/032	9/84 / 9/84	9/87	200	200	164	136	87	60	2/87	3/87 KJ	FU Only

Description of Study: OVRETTE VS. MICRONOVUM

Study Number: 8877

Total Number of Cases: 1400

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
Multi	Boohene/Zimbabwe	POC 85/006	10/85/10/85	4/87	1400	500	204	135	51	11/86	8/86 RD	Active

STUDY STATUS LIST  
 INVESTIGATOR NETWORK NEEDS  
 FCO 3114  
 ACTIVE STUDIES

APRIL 1987

192

Description of Study: LOW DOSE AND STANDARD DOSE SURVEILLANCE

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
						ADM	1 mo FU	4 mo FU	8 mo FU			
463	Maidouka/Niger	SYS 86/013	9/86	6/88	200	64	40	16		3/87	9/86 KJ	Active

087

STUDY STATUS LIST  
QUINACRINE

April 1987

Description of Study: Quinacrine Pellets, 250 mg, 3 Insertions, with Penothal

Study Number: 640

Total Number of Cases: 200

Total Number of Studies: 1

Center	Investigator/ Country	Index Number	Date Init	Date Actv	Expiration Date	Proposed No. of Cases	ADM	Forms			Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
								Instillations	Follow-ups		Follow-ups							
							1	2	3	1yr	2yr	3yr	4yr	5yr				
088	Zipper/Chile	77/288		4/77	10/87	200	166	166	165	153	143	126	119	105	100	3/87	4/87CC	Active

STUDY STATUS LIST  
QUINACRINE

April 1987

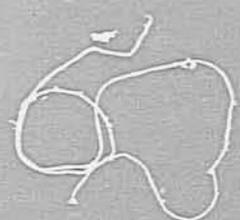
Description of Study: Quinacrine Pellets, 250 mg, 3 Insertions, without Pentothal.

Study Number: 643

Total Number of Cases: 500

Total Number of Studies: 3

Center	Investigator/ Country	Index Number	Date Init	Date Actv	Expiration Date	Proposed		Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments			
						No. of Cases	ADM	Instillations			Follow-ups							
								1	2	3	1yr	2yr	3yr	4yr	5yr			
USP	Zipper/Chile	78/020		10/79	10/87	200	143	143	141	128	108	78	115	109	91	3/87	4/87CC	Active
85U	Guzman-Serani/Chile	78/021		5/79	8/87	150	151	151	151	150	144	132	141	132	129	10/86	4/87CC	Active
05E	Bhatt/India	78/016		10/79	2/82	150	84	84	84	82	77	5	81	81	0	11/83	-	Closed



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