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FAMILY HEALTH INTERNATIONAL • Durham, NC 27713 USA

TABLE OF CONTENTS

|  |     |
|--|-----|
| I. Introduction.....                                       | 1   |
| II. Clinical Trials.....                                   | 9   |
| A. Systemic Contraception.....                             | 15  |
| B. Barrier Contraceptives.....                             | 40  |
| C. Voluntary Surgical Sterilization.....                   | 49  |
| 1. Female Sterilization.....                               | 49  |
| 2. Male Sterilization.....                                 | 75  |
| D. Nonsurgical Female Sterilization.....                   | 77  |
| E. Intrauterine Devices.....                               | 80  |
| F. Investigator Network Needs (INN).....                   | 85  |
| G. Contraceptive Development.....                          | 91  |
| III. Reproductive Epidemiology.....                        | 101 |
| A. Ongoing Projects.....                                   | 101 |
| B. Planned Projects.....                                   | 116 |
| IV. Program Evaluation.....                                | 122 |
| A. Family Planning Evaluation.....                         | 122 |
| B. AIDS Projects.....                                      | 163 |
| C. Maternal and Child Health/Family Planning (MCH/FP)..... | 168 |
| D. Natural Family Planning.....                            | 181 |
| E. Breastfeeding Studies.....                              | 191 |
| V. Field Development and Training.....                     | 202 |
| A. Institutional Development.....                          | 202 |
| B. Training.....   | 235 |
| C. Support for Conferences, Seminars and Expert Meetings.. | 242 |
| D. Contraceptive Technology Transfer.....                  | 246 |
| E. Information Dissemination.....                          | 253 |
| VI. Management.....  | 258 |

APPENDICES:

- A. Publications List
- B. Consultant Reports
- C. Study Status Lists
- D. Expenditures

## I. INTRODUCTION

This report focuses on the six months from April 1988 through September 1988 and complements the semi-annual report covering the first half of 1988 already submitted. Over the past six months, the volume of Family Health International's (FHI) work has grown. There have been solid achievements in the field of long-acting steroids, significant incremental improvements in IUDs and vasectomy, and some exciting work with condoms. Along with improvements in technology, FHI has continued to explore the acceptability of methods to users and the interaction between providers and users. In every area of interest we are trying to transfer skills and build local institutional strengths.

FHI has made uninterrupted progress in the central task of obtaining Food and Drug Administration (FDA) approval for three new products. Phase III clinical trials of the NET 90 injectables have begun at 15 clinical sites in the USA, Latin America and Asia. No unforeseen adverse reactions have been reported, and -- to date -- the pregnancy rate has been slightly over 1 per 100 women years of use. In order to move as rapidly as possible, FHI has made a policy decision to conduct studies on both the 65 and the 100 milligram dose of the injectable. This is expensive in both time and money, but we feel it is essential if the injectable is to be brought to FDA approval early in the 1990s. The sequential investigation of these alternative formulations could have greatly extended the length of time taken to conclude the studies.

The Phase II trials of NET pellets produced by two different manufacturing processes are also under way. All the volunteers have been recruited and if no unforeseen events occur, the study will be expanded to a Phase III trial with a total of 1200 women, early in 1989. As FHI moves forward in these large trials, we are also beginning the necessary long-term planning to conduct introductory trials in selected countries.

The last volunteers were admitted to the Phase III clinical trials of the Filshie Clip in June 1988. The plans for presentation of data to the FDA changed slightly during the reporting period, and some adjustments were made by expanding some aspects of the trial and cutting back on others. The data FHI collects will be provided to FEMCARE Limited who will submit the Investigational Device Exemption (IDE) to the FDA. A detailed follow-up of patients at one site has been planned to try to get further information about the problem of clips migrating once they have been applied to the fallopian tubes.

FHI congratulates the Population Council on the submission of the documents necessary for the FDA approval of NORPLANT<sup>R</sup> in September 1988. The large experience which FHI has now gained with the preintroductory clinical trials and broader programs of technology introduction of NORPLANT<sup>R</sup> in eleven countries is not only of value in its own right, but is building up an experience which will be highly relevant to the other long-acting steroids, as they also come closer to widespread use.

Vasectomy has long been a straightforward and simple technique, and until recently the possibility of a substantial improvement and simplification seemed unlikely. FHI, however, is pleased to have helped introduce a new puncture technique for vasectomy into Thailand. A comparative study of the method compared with the standard technique shows a considerable reduction in complications at the time of surgery and immediately afterwards. FHI has received Investigational New Drug (IND) approval from the FDA to begin clinical trials of the use of iodine given by the FEMCEPT device and inserted in the cervix and is selecting a site for Phase I clinical trials.

Admissions are complete on a large-scale comparative study of the TCu-380-A and the TCu-200. Preliminary results suggest a significantly lower pregnancy rate among the users of the TCu-380-A IUD. FHI welcomes the commercial reintroduction of IUDs into the United States. One product liability problem in the U.S. has revolved around the issue of whether a cervical appendage on a device increases the risk of pelvic inflammatory disease. In a study just completed on more than 1000 women, no difference in pelvic inflammatory disease was found between devices with and without strings. An ongoing study testing the use of prophylactic antibiotics at the time of IUD insertion has not demonstrated a clear difference between those using and those not using an antibiotic and additional cases are being recruited.

Work on the plastic condom has continued at a rapid pace, and prototypes have been tested by volunteers. Issues of manufacture and

cost are being investigated, and expanded human trials will take place in the coming three months. Our goal remains to produce a product which will have a better shelf-life and will be as acceptable -- or more acceptable -- than the latex condom, and which will cost no more -- and possibly somewhat less. FHI is also beginning acceptability trials of the FEMSHIELD, or "female condom," recently invented in Europe.

While working with new barrier methods, FHI has also begun a program to test existing latex condoms. Studies are under way to compare the quality assurance tests which manufacturers conduct on condoms with the possibility of tearing during coital use. Established quality control tests are being applied to condoms which have been distributed to the field in an effort to track possible deterioration with time and to protect users against any condoms which may have become defective in the interval time between them being sent overseas and being used. In addition, new types of quality control tests are being explored.

FHI has demonstrated previously that the commonly used spermicide, nonoxynol-9, is a deterrent to gonorrhea and chlamydia infections. There is an urgent need to establish whether nonoxynol-9 is also an in vivo deterrent to HIV transmission. Technically, this latter question is going to be difficult to address, and the National Institutes of Health (NIH) and the U.S. Agency for International Development (A.I.D.) are in close communication about possible ways of sponsoring studies in this important area. In the short term, FHI is testing the acceptability of various formulations of spermicides in Latin America

and the Caribbean.

It continues to be our judgment that, while nonoxynol-9 is a good spermicide, it is unfortunate that so much of the industry relies exclusively upon this one chemical entity and FHI is please to have conducted a comparative study of nonoxynol-9 and menfegol that shows a very similar pregnancy rate with these two agents. FHI is also working with D-propranolol as a potential spermicide in studies jointly sponsored by NICHD and A.I.D. Problems were met in formulating this compound for human use, but these have now been solved.

We have found the Cooperative Agreement AID/DPE-0537-A-00-4047-00 and the AIDSTECH Cooperative Agreement mutually supportive. We have focused attention on barrier methods of contraception and their interaction with AIDS. The work on plastic condoms has already been referred to; if it can be perfected, is also highly applicable to the work of AIDSTECH. As a contribution to understanding the potential for HIV infection around the world, FHI has used its network of collaborating investigators to conduct a rapid study of the prevalence of genital ulcer disease in a wide range of Third World countries and found previously unexpected high levels in some parts of the world.

FHI continues to implement its broad view that successful contraceptive use demands informed consumers served by honest and committed providers. The pioneer work of Program Evaluation studying oral contraceptive compliance has been extended to Egypt and Zimbabwe. Studies in Honduras show that people who buy pills from commercial

social marketing programs tend to be those who are poor and not normally served by for-profit programs. Attitudes towards condoms have been studied in Haiti where, although nearly everyone knows about this method, only 1 in 20 acceptors use it. FHI has conducted particularly comprehensive studies on several aspects of fertility regulation in Honduras. There has been a marked increase in contraceptive use and a recent rise in breast-feeding. FHI has made studies of breast-feeding a particular priority. As well as studying the impact of breast-feeding on fertility, it has analyzed the possible role of breast-feeding in transmitting HIV infection and concluded in the Third World counseling women not to breast-feed because of fear of AIDS will cause many more deaths from diarrhea than it would save from AIDS transmitted in the milk.

Studies have been completed in the Sukhothai Province of Thailand on causes of infant deaths and pregnancy monitoring has assessed risks of maternal and infant mortality and morbidity in Cote d'Ivoire and Senegal. In Karawa, Zaire the role of TBAs in obstetric care has been studied.

One group that requires particular attention in a great many countries is adolescents. Studies of the health and reproductive patterns of adolescents have been conducted in Mexico, Zimbabwe, The Gambia, Sri Lanka, and the Philippines. In the Philippines it was found that 8 out of 10 unmarried men and 4 out of 10 unmarried women had had premarital intercourse by the age of 25. Approximately half of them relied upon the rhythm method for contraception, but only one-quarter understood

how to use the method.

During the current reporting period, FHI has seen data relating to a possible adverse effect of oral contraceptives contributing to breast cancer. A conflicting and confusing body of data exists in this field, and FHI is attempting to meet A.I.D.'s needs in this important area in two ways. The Division of Reproductive Epidemiology and Sexually Transmitted Diseases (DRESTD) is well-placed to respond rapidly to this area of great potential importance, because they have already embarked on a broader review of the etiology of breast cancer. They are using a computer model to provide an overall perspective by predicting the impact of a variety of adverse and beneficial effects of the pill on cancers and cardiovascular disease. We are using data from all possible sources and preparing material which could be made available to Missions and to overseas family planning programs.

At a less dramatic level, but one which has the potential of a great deal of impact on women's health, FHI is well advanced in a study which compares bone density among women who have used, and those who have never used, oral contraceptives: the hypothesis is that oral contraceptive users will have less osteoporosis than nonusers.

The Field Development and Training Division (FDT) emphasizes institutional development and training in research methods. The Family Health Research Centers (FHRCs) continue to grow in strength and independence. To take a single example, BKS PENFIN in Indonesia is managing a massive multicenter study of three thousand cases comparing

the TCU-380-A with the multiload Cu-375 and the Lippes Loop D. FHI has access to the data on computer disks. FDT works with FHRCs in nine countries, with the recent addition of Nairobi, Kenya through a USAID Mission buy-in.

In this reporting period, information dissemination continued to receive high priority. As a new initiative in this area, FDT sponsored a workshop for journalists who cover health and family planning issues in francophone Africa. The workshop has generated a high level of interest from other countries for similar workshops. These contacts, as well as the FHRCs, can play a key role in providing timely, accurate information on such issues as contraceptive risks and benefits and will be invaluable in controlling negative publicity on oral contraceptives and breast cancer.

The Board held its annual meeting in September. It is looking at the long-term role for FHI. The Board was pleased to elect Dr. Halfdan Mahler to their number at the September meeting.

On August 1, 1988, Family Health International (FHI) (and its associated company, Clinical Research International) moved into a new building with approximately 41,000 square feet (21,000 - CRI) of office, computer and meeting room space. Through the hard work of the relevant staff, FHI and CRI were closed to business for only one day. Along with the new building, FHI began using a VAX mainframe computer with SAS and a microvax. Each professional staff member now has their own workstation with access to All-In-One Office Automation Software.

## II. CLINICAL TRIALS

The Clinical Trials Division of FHI is developing and evaluating several new contraceptive products with the goal of large scale human use of proven products. USFDA marketing approval is being sought for new long-acting steroid delivery systems, the Filshie Clip, an iodine formulation for nonsurgical female sterilization, a new vaginal barrier device and D-propranolol spermicides. Particular attention has been given to the development of a new and better condom. The Division is also conducting a major worldwide program of clinical trials on oral contraceptives, IUDs, female sterilization and vaginal methods. As of September 1988, the Division was conducting 105 studies of contraceptive products in collaboration with about 95 investigators in 40 countries.

Highest priority is being given to obtaining USFDA approval of the new generation of long-acting contraceptive steroid delivery systems. The most advanced product is the NET-90 injectable. FHI holds the IND for 90-day norethindrone (NET) microspheres and has taken the lead role in conducting two multicenter Phase II studies of the NET formulation. 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, but the initiation of the Phase III program was delayed until October 1987 pending the resolution of indemnification problems. Three centers in Latin America, two in Asia and one in the U.S. initiated clinical trials in late 1987. Nine additional U.S. sites began studies in July-August 1988. Three more

U.S. sites and one site in Egypt will initiate studies in the fall of 1988. With the new FDA regulations for steroidal contraception, sufficient clinical data for NDA submission should be available by March of 1991. In collaboration with the Program for Applied Research on Fertility Regulation (PARFR), Stolle Research and Development Corporation, and Ortho Pharmaceutical, FHI has also completed the data analysis of the Phase I evaluation of two 30-day norethindrone injectable formulations, containing 15 and 30 mg of NET.

FHI also holds the IND for the development of subdermal biodegradable pellets. Here again the work was slowed by circumstances outside FHI's control. FHI had to wait for Endocon, Inc., who hold the patent, for more than one year to prepare a satisfactory NET biodegradable pellet. A partial melt system and a flash flow system seem to be the best manufacturing processes for the pellet. A Phase I trial to establish the release rates of these pellets was initiated at CONRAD in March 1988. A new larger pellet prepared by the partial melt system, with higher NET content and a 15-18 month anticipated duration, was included in this trial in April 1988. All the subjects have already been admitted in study. Once the 6-month release rates of these pellets are available, Phase III multicenter trials will be initiated in the U.S., Asia and Latin America.

FHI is collaborating with the National Institute of Nutrition in Mexico City in the development of a macrocrystalline natural progesterone injectable for lactating women. A pharmacokinetic study of this system was initiated in March 1988. The preliminary results indicate the need

for a relatively high progesterone dose per injection to obtain sufficiently high circulating progesterone levels. The product is being formulated to meet this requirement.

Pre-introductory clinical trials of the NORPLANT implant system continue in 11 countries at 37 sites. Studies are now being conducted in Bangladesh, El Salvador, Ghana, Haiti, Nepal, Nigeria, Pakistan, Philippines, Senegal, Singapore and Sri Lanka. The profile of contraceptive efficacy and safety of the product at active study centers is fully consistent with the earlier clinical studies. 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 is to maintain local skills and interest until FDA marketing approval is granted. As a result of FHI trials, NORPLANT was approved by the regulatory agency in Sri Lanka. Due to budget constraints, no new NORPLANT trials with the direct support of FHI have been initiated; however, the follow-up of the participating subjects continues as planned. The support of interested AID Missions and countries has made possible the initiation or enlargement of studies in Bangladesh, El Salvador, Haiti, Pakistan and Senegal.

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 occlusion techniques and approaches including the Wolf clip, the tubal ring, Pomeroy ligation and electrocautery, either by means of minilaparotomy or laparoscopy, in a

total of 33 studies in 17 countries by 28 investigators. The original plans were to present the noncomparative data as pivotal for the FDA submission. However, with the experience of similar, recently approved devices, it was decided to also include comparative data and as a result the trials in some centers had to be extended; conversely, comparative trials not adequate for FDA submission were cancelled. All the admissions to the Filshie Clip trials were terminated in June 1988, and follow-up will terminate in June 1989. The clinical data will be available for PMA organization in the fall of 1989. At the present there are indications that Femcare itself will be directly responsible for the IDE and PMA assembly and submission. 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 these studies will be submitted together with the clinical data in application for marketing approval.

In a planned effort to simplify female sterilization methods, nonsurgical approaches continue to be evaluated. FHI continues to work on quinacrine and iodine formulations as possible sclerosing agents. A Phase I study of the intrauterine placement of slow-releasing quinacrine is nearing completion in Los Angeles. The FDA granted permission to FHI to initiate a Phase I pre hysterectomy study of an iodine formulation to be delivered by means of the FEMCEPT device. Due to changes in the commercial ownership of the products involved, the initiation of these trials has been delayed. One U.S. site will initiate the study in October 1988. Three more U.S. sites will initiate studies in early 1989. The same study protocol was submitted

for the consideration of the Canadian regulatory agency in August 1988. When approval is received from the agency, two other sites in Canada will initiate clinical trials. These activities have been conducted with partial support from the Mellon Foundation.

Comparative trials of the puncture versus the standard incision technique of male sterilization were initiated in February 1988 in Thailand and Sri Lanka. An enlargement of this trial is scheduled to be initiated in these two countries in the fall of 1988.

Intrauterine devices (IUDs) are the method of choice 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 19 countries to compare this product with other IUDs available in their respective countries for the purpose of determining which product is most acceptable for local populations. It is expected that the outcome of these studies will encourage the adoption of the TCu 380A IUD into family planning programs throughout the world. Randomized comparative trials involve close to 10,000 subjects. The largest trials are between the TCu 380A and the TCu 200, and between the TCu 380A, the Multiload Cu375 and the Lippes Loop D devices. The admissions of subjects to these trials ended in fiscal year 1988, and follow-up will be complete by the end of fiscal year 1989.

Since the triphasic oral contraceptives have become available throughout the world, FHI is sponsoring the comparative evaluation of these and the monophasic products USAID currently supplies on a large

scale for less developed countries. The triphasic pill being studied is Triquilar from Schering. Data collection for the noncomparative progestogen-only pill trials will be completed in the autumn of 1988. The multicenter crossover studies between Norinyl 1/50 and Lo-Femenal will terminate in mid-1989. Due to budget constraints several of the contraceptive trials that could be terminated without major effects in the overall results had to be cancelled.

The increasing concern about AIDS and other sexually transmitted diseases has resulted in an important increment in the research activities in the area of barrier and spermicidal contraceptives. A large set of activities is focused on the development of a less expensive and better condom. FHI has contracted a number of individuals and organizations for this purpose. Different materials and manufacturing processes are being tested, and the first prototypes of the new condom became available for consumer preference tests in August 1988. Two materials have proven so far to be the best choices; additional prototypes are being produced and will be submitted to consumer preference tests in the fall of 1988. Different manufacturing processes are also being evaluated for the various alternatives of materials and designs.

Another important area of activity is the clinical testing of condoms and vaginal formulations in populations at high risk of contracting STDs. Two studies of this kind are now being conducted in Colombia and the Dominican Republic.

Under an IND, a Phase I trial of a new vaginal barrier device, Lea's Kap, was initiated in the U.S. in the fall of 1987. This trial had to be cancelled in May 1988 for technical reasons. A new trial in a different U.S. site will be initiated in the fall of 1988.

The comprehensive research program conducted by the Clinical Trials Division is being progressively focused on the development and evaluation of safer and more acceptable contraceptive products, having as its goal their introduction and large-scale use in multiple countries. The trials designed to meet FDA regulatory requirements are a central point in the Division's activities.

#### **A. Systemic Contraception**

##### **1. Long-acting Steroids**

###### **a) NET 90-Day Injectable Microspheres**

The Phase III clinical trial of the NET 90-day injectable microspheres is currently ongoing at 12 U.S. and 6 international study sites. The studies involve 1,200 women using the 100 mg dose and 600 women using the 65 mg dose. As of September 1, 1988, there were 204 women-months of experience with the 65 mg dose and 648 women-months of experience with the 100 mg dose in the Phase III trials. In the Phase II and III trials, one pregnancy was reported in each dose group resulting in pregnancy rates of 1.4 per 100 women-years (95% C.I. 0-4.2) for the 65 mg dose and 1.1

per 100 women-years (95% C.I. 0-3.2) for the 100 mg dose. No serious or unexpected adverse experiences have been reported in the Phase II or III trials.

Based upon the newly recommended guidelines from the FDA for steroid contraceptive NDA submissions, FHI will submit data on 10,000 women-months of use for the 65 and 100 mg dose as well as data on 200 women on the 65 mg dose followed for one year. Therefore, the estimated date of the NDA submission is March 1991.

FHI, Stolle Research and Development Corporation and Ortho Pharmaceuticals are continuing their collaboration on a carcinogenicity study of long-acting norethindrone contraceptives in rats. The study is being conducted at Hazelton Laboratories and the results of the study will be applicable to the NET pellet implant as well as the NET injectable microsphere NDA submission.

b) NET Pellet Implants

A pharmacokinetic study of the NET pellet implants was begun in March 1988 at CONRAD under Dr. David Archer's direction. Twenty women were enrolled to use pellets produced by two different manufacturing processes. Following this, Endocon Inc., the producer of the pellets, manufactured a slightly larger size pellet to ensure a mean duration of action of 15 months. The pharmacokinetic studies of this new pellet implant began in June 1988 among 15 women. Following the collection of data on these 15

subjects for six months, the Phase III trial of the NET pellet implants is planned to begin at eight sites in the U.S. and four sites overseas, involving a total of 1,200 women.

#### Future Plans

The Clinical Trials Division is proceeding with plans to seek regulatory approval of new contraceptives in countries where they are being tested in Phase III trials. Beyond that, FHI has also developed a strategy for introducing new contraceptives to a large number of users (e.g. 3,000 per county) over a 5 year period. Besides large clinical trials, the strategy involves seeking local regulatory approval, training providers, producing educational material, maintaining a registry of all users and conducting acceptability research.

#### c) NORPLANT Implants

In its effort to evaluate worldwide acceptability of NORPLANT contraceptive subdermal implants, FHI continues to monitor a number of ongoing pre-introductory, Phase III clinical trials. During this reporting period, new studies in El Salvador and Pakistan were initiated at nine centers, bringing the total number of NORPLANT insertions to over 4,100 cases at 37 sites in 11 countries. A summary of admissions is given in Table 1.

The objectives of these studies are to introduce the NORPLANT six-capsule 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. FHI, using USAID and non-USAID support, is providing data for local regulatory approval of NORPLANT in several countries. As a direct result of FHI's support of pre-introductory clinical trials, NORPLANT has now been approved for marketing in Sri Lanka.

All investigators participating in the clinical trials received standardized training in the proper insertion and removal techniques at a regional training site or at in-country training centers established at existing study sites. Twenty investigators from Asia have been trained at Raden Saleh Clinic in Jakarta, Indonesia, and 21 investigators from West Africa, El Salvador, Haiti and Venezuela have been trained in Santo Domingo, Dominican Republic. Additional investigators have been trained at local training centers.

In countries where the initial pre-introductory clinical trial caseload has already been enrolled, expanded trials have been initiated to attempt to meet the strong demand for the NORPLANT system and to bridge the gap until local regulatory approval of

the method is obtained and wider distribution can be undertaken. The objectives of these studies are 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 research activities 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 PIACT.

Several expanded clinical trials projects (e.g. Bangladesh, Haiti, Senegal) and new pre-introductory trial efforts (El Salvador, Pakistan) are being supported directly by the local USAID Missions.

Insertions have been performed in 4,118 women to date. There have been a total of 873 removals, 15 due to accidental pregnancy, 325 for menstrual problems, 154 for medical reasons, 185 for planned pregnancies and 194 for other personal reasons. All 15

pregnancies were intrauterine, and in all 15 cases the implants were removed. Of the 15, six are possible method failures; in the others, the women were likely pregnant at admission. Nine pregnancies resulted in live births, one ended in stillbirth, and three in abortion. Two pregnant women have been lost to follow-up, although the pregnancy outcome in one case was believed to be a live birth. Three of the nine live births ended in neonatal death within six weeks of delivery; however, the cause of death of two infants was acute respiratory distress and the third contracted gastroenteritis. None were considered to be related to their mothers' previous NORPLANT use.

A summary of cumulative life-table event rates across all study sites is presented in Table 2. The one-year pregnancy rate is 0.4 per 100 users. Removals for menstrual-related problems account for the greatest number of discontinuations with the method. The rate is 2.9 per 100 users. The pooled continuation rates are 99.9, 96.7, 91.3 and 76.7, respectively, after 1, 6, 12 and 24 months of use. The corresponding follow-up rates are 94.4, 80.9, 70.4 and 48.0.

A 100-case study of the second-generation NORPLANT-2 covered rods was initiated in Singapore in June 1987. In August 1987, manufacture of NORPLANT-2 rods was discontinued. Recruitment of NORPLANT-2 acceptors into this study was therefore suspended, although follow-up of those women already inserted with NORPLANT-2 sets (12 cases) will continue for three years, the effective

use-duration, or until removal of the implants.

d) Egypt: Introduction of Long-Acting Steroids

A major, interdepartmental project involving the introduction of long-acting steroids in Egypt has been designed to evaluate the performance of NORPLANT subdermal implants in a broad population. The project was originally developed with the support of an in-country FHI field office and staff member jointly with the National Population Council (NPC) of Egypt and the Egyptian Fertility Care Society (EFCS). In January 1988, this phase of the work was completed, the FHI field office was dissolved and management responsibility for the project was assigned fully to EFCS with technical assistance support from FHI staff based in North Carolina.

The objectives of the project are: 1) to establish at least two in-country training centers (Assiut and Alexandria), 2) to initiate a multicenter university-based 1,500-case clinical trial of NORPLANT implants, and 3) to initiate a comparative cohort study to evaluate long-term side effects.

Although originally designed to evaluate NORPLANT-2 covered rods, since NORPLANT-2 has been discontinued, the EFCS and NPC, in consultation with FHI, the Population Council and Egyptian physicians and government officials, have opted to substitute NORPLANT capsules for NORPLANT-2 covered rods in the

university-based clinical trial. Initiation of the clinical trial began in July 1988; initiation of the cohort study is targeted for fiscal year 1989.

TABLE 1  
Status of Ongoing NORPLANT Clinical Trials

|                    | Initiation<br>Date | Planned<br>Caseload | Insertions<br>Performed |
|--------------------|--------------------|---------------------|-------------------------|
| <b>Bangladesh</b>  |                    |                     |                         |
| Center 166         | Apr. 1988          | 200                 | 12                      |
| Center 704         | Feb. 1985          | 450                 | 249                     |
| Center 718         | Feb. 1985          | 450                 | 249                     |
| Center 721         | Feb. 1985          | 450                 | 267                     |
| Center 722         | Apr. 1988          | 200                 | 27                      |
| Center 766         | Apr. 1988          | 300                 | 7                       |
| <b>El Salvador</b> |                    |                     |                         |
| Center 800         | Feb. 1988          | 50                  | 11                      |
| Center 821         | Feb. 1988          | 100                 | 29                      |
| Center 823         | Feb. 1988          | 150                 | 47                      |
| Center 824         | Feb. 1988          | 100                 | 49                      |
| <b>Ghana</b>       |                    |                     |                         |
| Center 041         | Oct. 1985          | 100*                | 4                       |
| Center 468         | Jun. 1987          | 100                 | 93                      |
| <b>Haiti</b>       |                    |                     |                         |
| Center 8017        | Nov. 1985          | 550                 | 175                     |
| Center 8331        | Nov. 1985          | 550                 | 151                     |
| Center 8332        | Nov. 1985          | 50                  | 50                      |
| <b>Nepal</b>       |                    |                     |                         |
| Center 729         | Feb. 1985          | 500                 | 507                     |
| Center 731         | May 1985           | 100                 | 100                     |
| Center 735         | Feb. 1987          | 200                 | 181                     |
| Center 736         | Feb. 1987          | 200                 | 89                      |
| Center 742         | Feb. 1987          | 200                 | 126                     |
| <b>Nigeria</b>     |                    |                     |                         |
| Center 040         | Oct. 1985          | 120                 | 123                     |
| Center 042         | Oct. 1985          | 105                 | 71                      |
| Center 435         | Jan. 1986          | 105                 | 100                     |
| Center 437         | Oct. 1985          | 105                 | 94                      |
| Center 453         | Nov. 1985          | 100                 | 96                      |

TABLE 1 (continued)

|             | Initiation<br>Date | Planned<br>Caseload | Insertions<br>Performed |
|-------------|--------------------|---------------------|-------------------------|
| Pakistan    |                    |                     |                         |
| Center 674  | Sep. 1988          | 100                 | 0                       |
| Center 675  | Sep. 1988          | 100                 | 0                       |
| Center 676  | Sep. 1988          | 100                 | 0                       |
| Center 677  | Sep. 1988          | 100                 | 0                       |
| Center 678  | Sep. 1988          | 100                 | 0                       |
| Philippines |                    |                     |                         |
| Center 600  | Feb. 1985          | 150                 | 150                     |
| Center 602  | Feb. 1985          | 150                 | 150                     |
| Senegal     |                    |                     |                         |
| Center 482  | Dec. 1986          | 60                  | 56                      |
| Singapore   |                    |                     |                         |
| Center 798  | Feb. 1985          | 100                 | 100                     |
| Sri Lanka   |                    |                     |                         |
| Center 703  | May 1985           | 355                 | 355                     |
| Center 749  | May 1985           | 200                 | 200                     |
| Center 758  | May 1985           | 200                 | 200                     |
| Total       |                    | 7,250               | 4,118                   |

\*Study has been cancelled.

TABLE 2

**NORPLANT Clinical Trials**  
**Cumulative Life-table Event Rates**

| Event                          | Rate per 100 users |
|--------------------------------|--------------------|
| Accidental pregnancy           |                    |
| 1 month                        | 0.0                |
| 6 months                       | 0.4                |
| 12 months                      | 0.4                |
| 24 months                      | 0.4                |
| Removal for menstrual problems |                    |
| 1 month                        | 0.0                |
| 6 months                       | 0.7                |
| 12 months                      | 2.9                |
| 24 months                      | 10.4               |
| Removal for medical reasons    |                    |
| 1 month                        | 0.1                |
| 6 months                       | 1.4                |
| 12 months                      | 2.4                |
| 24 months                      | 4.6                |
| Continuation                   |                    |
| 1 month                        | 99.9               |
| 6 months                       | 96.7               |
| 12 months                      | 91.8               |
| 24 months                      | 76.7               |
| Follow-up*                     |                    |
| 1 month                        | 94.4               |
| 6 months                       | 80.8               |
| 12 months                      | 70.4               |
| 24 months                      | 48.0               |

\*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.

## 2. Oral Contraceptives

FHI has continued to compare the efficacy, safety and acceptability of oral contraceptive formulations. The evaluation of the safety and efficacy of low-estrogen-dose pills and their acceptability in the developing world continues, but recent emphasis has been on evaluating progestogen-only pills in breastfeeding women, triphasic pills, and the clinical impact of changing from standard- to low-estrogen-dose products.

### a) Loestrin versus Lo-Femenal

FHI is conducting a comparative evaluation of two low-estrogen-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 centers located in Mexico, Egypt, Thailand and Malaysia. The active studies have a total of 801 admissions. Total discontinuation rates at 8 months are 59.8 in the Loestrin group and 56.8 for the Lo-Femenal group (Table 3), with over half of the women having returned for the eight-month follow-up visit. Most discontinuations among women in the Loestrin group were for "other personal" reasons, such as the method was not needed or the husband objected to the method, followed by menstrual problems (amenorrhea) and side effects (headaches, dizziness, etc). Most discontinuations among women in

the Lo-Femenal group were for "other personal" reasons and "method unrelated" reasons such as the patient moved or was unable to return to the center.

b) Crossover Pill Studies

FHI is evaluating the acceptability and possible consequences of switching large numbers of users from a standard- to a low-dose estrogen pill. Concern has been expressed that a switch from one oral contraceptive formulation to another might result in an increase or change in side effects leading to discontinuation. The objective of the study is to determine the acceptability of switching from Noriday 1/50 (Syntex) to Lo-Femenal (Wyeth) in comparison with switching from Lo-Femenal to Noriday 1/50. The 1,200-case trial is being conducted at four centers located in Yugoslavia, the Philippines, Mexico and Thailand. Two sites have completed the study; the other two centers are active. A total of 835 women have been admitted. Women were assigned either Noriday 1/50 or Lo-Femenal for three months and then crossed to the other pill. Total discontinuation rates at three months after crossover are 33.1 for the Noriday 1/50 to Lo-Femenal group and 36.8 for the Lo-Femenal to Noriday 1/50 group, with over half of the women having returned for the six-month follow-up visit. Most discontinuations among women in both the Lo-Femenal to Noriday 1/50 group and the Noriday 1/50 to Lo-Femenal group were for menstrual problems (intermenstrual bleeding) and "other personal" reasons such as forgetfulness, not needing the method or a desire

to change to another method.

c). Progestogen-only Oral Contraceptives

USAID is now making progestogen-only pills available to programs that request them and FHI continues to evaluate 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. Eighteen of these centers have now completed the study; the remaining two centers have completed admissions. Final data on 3,549 women from 20 centers in Latin America and Africa show a six-month total discontinuation rate of 40.6 and a 12-month discontinuation rate of 59.0 (Table 4). Most discontinuations were for "other personal reasons", such as the women changing to another method or not needing contraceptive protection; this type of change was foreseen and expected. Three-quarters of the women have returned for the six-month visit and over half have returned for the twelve-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 was developed to distribute and evaluate Ovrette in several countries, often through a community-based or health post system, and is nearing completion. Of the five centers which began the study in Mali, Ghana and Brazil, one center is active

and has completed admissions and four centers have completed the study. Data on 915 women show a six-month total discontinuation rate of 42.0 and a twelve-month total discontinuation rate of 83.7 (Table 5). The majority of discontinuations were for the same "other personal reasons" as described above; 48.1 percent of the women have returned for the twelve-month visit. In Thailand, an 850-case multicenter introduction of progestogen-only pills has been completed by the Thailand Fertility Research Association (TFRA). The purpose of the study was to evaluate overall acceptability and efficacy of progestogen-only oral contraceptives, to examine the contraceptive practices of breastfeeding women and to assess the attitudes of health personnel to the introduction of the progestogen-only pill. Follow-up visits were scheduled at 2, 6 and 12 months after admission. A total of 829 women were admitted to the study; 190 women (22.9%) discontinued by the six-month follow-up visit, mainly for side effects (most frequently, headaches) or other personal reasons.

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. Two centers in Argentina have completed the study. The objectives of this trial are to evaluate and compare the overall acceptability and reported side effects of the progestogen-only oral contraceptive Ovrette with the nonhormonal methods used. Additionally, the differences over time in the weight of

breast-fed infants for both groups are being compared. To date, 743 women have been admitted to the study, and 586 women have completed six months of use with a six-month follow-up rate of 78.9. Table 6 presents preliminary data on the complications and complaints reported for 743 women participating in the trial and their infants. Complaints, such as cystitis, were similar in both groups, with the exception that more IUD users complained of some pain in the iliac area of the abdomen. Table 7 shows preliminary data on mean infant weight for women and their infants followed-up thus far in both groups. Data from the Egyptian center is undergoing reanalysis. As a result, data reported in the future may differ slightly. One infant death was reported in the nonhormonal group due to Sudden Infant Death Syndrome. The mother was an IUD user and the death was not related to the contraceptive method. Two additional deaths were reported in the nonhormonal group due to pneumopathy. In both cases the mother was an IUD user and the death was not related to the contraceptive method. The physician related the infants' worsening condition to decreased weight and diarrhea, possibly related to the use of supplemental foods.

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 May 12, 1988, 26 women had completed the project. Two more women were expected to complete the study. Data from two subjects was excluded due to difficulty in following the protocol. In a preliminary assessment, the Principal

Investigator has concluded that "the relationship between pre-yield and post-yield is similar for the test and control groups".

d) Triquilar versus Lo-Femenal

Triphasic formulations vary the ratio of progestogen and estrogen to simulate natural hormonal changes in the menstrual cycle. They are less tolerant of mistakes in daily use than combined OCs and careful clinical research is required to determine whether USAID should offer triphasic pills under its commodity purchases. 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 six centers in Ecuador, the Dominican Republic, Chile, Sri Lanka, Brazil and the Sudan. Five of the centers are active; the center in Chile has completed the study and 1,071 women have been admitted. The 8-month cumulative life-table total discontinuation rates are similar, 34.2 for the Triquilar group and 35.6 for the Lo-Femenal group (Table 8). Two-thirds of the women have returned for the 8-month visit and over one-third have returned for the 12-month visit. Most discontinuations in the Triquilar group were for common side effects (headaches, nausea, etc.) and "other personal" reasons such as the husband objecting to the method or the fact the woman no longer required contraceptive protection, while in the Lo-Femenal group most of the discontinuations were for common side effects, followed by

"other personal" reasons and planned pregnancy.

#### Future Plans

Insufficient resources are available to permit any new oral contraceptive acceptability, safety, and efficacy studies to be initiated by FHI. Emphasis has shifted to clinical testing of contraceptive methods for ultimate FDA approval. FHI will, however, evaluate research proposals from USAID field centers on a project-by-project basis.

Table 3

## Cumulative Life-table Rates for Loestrin versus Lo-Femenal Studies

| Event                             | Loestrin<br>(N = 391 ) | Lo-Femenal<br>(N = 410 ) |
|-----------------------------------|------------------------|--------------------------|
| <b>Discontinuation For:</b>       |                        |                          |
| Accidental Pregnancy              |                        |                          |
| 1 month                           | 0.0                    | 0.0                      |
| 4 month                           | 0.0                    | 0.0                      |
| 8 month                           | 0.5                    | 0.0                      |
| Menstrual Problems                |                        |                          |
| 1 month                           | 0.3                    | 0.0                      |
| 4 month                           | 3.8                    | 0.3                      |
| 8 month                           | 8.9                    | 1.5                      |
| Side Effects                      |                        |                          |
| 1 month                           | 1.1                    | 0.8                      |
| 4 month                           | 4.7                    | 2.0                      |
| 8 month                           | 5.6                    | 3.8                      |
| Other Medical Reasons             |                        |                          |
| 1 month                           | 0.0                    | 0.8                      |
| 4 month                           | 0.3                    | 1.1                      |
| 8 month                           | 1.9                    | 3.5                      |
| Planned Pregnancy                 |                        |                          |
| 1 month                           | 0.0                    | 0.0                      |
| 4 month                           | 0.3                    | 0.3                      |
| 8 month                           | 0.8                    | 3.2                      |
| Other Personal Reasons            |                        |                          |
| 1 month                           | 3.0                    | 2.1                      |
| 4 month                           | 6.2                    | 4.2                      |
| 8 month                           | 10.2                   | 8.6                      |
| Method Unrelated Reasons          |                        |                          |
| 1 month                           | 1.1                    | 2.9                      |
| 4 month                           | 2.7                    | 4.1                      |
| 8 month                           | 4.0                    | 6.4                      |
| <b>Lost-to-Follow-up Rate</b>     |                        |                          |
| 1 month                           | 5.5                    | 4.8                      |
| 4 month                           | 11.0                   | 11.2                     |
| 8 month                           | 31.1                   | 30.1                     |
| <b>Total Discontinuation Rate</b> |                        |                          |
| 1 month                           | 7.4                    | 7.8                      |
| 4 month                           | 21.7                   | 19.3                     |
| 8 month                           | 59.8                   | 56.8                     |

Table 4

Cumulative Life-table Rates for Progestogen-Only Studies (Ovrette)  
in Lactating Women

| Event                       | Ovrette<br>(N = 3,549) |
|-----------------------------|------------------------|
| <b>Discontinuation For:</b> |                        |
| Accidental Pregnancy        |                        |
| 2 month                     | 0.1                    |
| 6 month                     | 0.5                    |
| 12 month                    | 1.6                    |
| Menstrual Problems          |                        |
| 2 month                     | 1.8                    |
| 6 month                     | 5.0                    |
| 12 month                    | 7.7                    |
| Side Effects                |                        |
| 2 month                     | 1.2                    |
| 6 month                     | 3.4                    |
| 12 month                    | 4.4                    |
| Other Medical Reasons       |                        |
| 2 month                     | 1.1                    |
| 6 month                     | 2.4                    |
| 12 month                    | 3.2                    |
| Planned Pregnancy           |                        |
| 2 month                     | 0.2                    |
| 6 month                     | 0.5                    |
| 12 month                    | 1.0                    |
| Other Personal Reasons      |                        |
| 2 month                     | 3.9                    |
| 6 month                     | 10.0                   |
| 12 month                    | 17.2                   |
| Method Unrelated Reasons    |                        |
| 2 month                     | 1.6                    |
| 6 month                     | 5.2                    |
| 12 month                    | 7.4                    |
| Lost-to-Follow-up Rate      |                        |
| 2 month                     | 10.5                   |
| 6 month                     | 21.6                   |
| 12 month                    | 31.8                   |

TABLE 4 Continued

| Event                        | Ovrette<br>(N = 3,549) |
|------------------------------|------------------------|
| <b>Total Discontinuation</b> |                        |
| 2 month                      | 14.9                   |
| 6 month                      | 40.6                   |
| 12 month                     | 59.0                   |
| <b>Follow-up</b>             |                        |
| 2 month                      | 89.6                   |
| 6 month                      | 75.8                   |
| 12 month                     | 59.7                   |

Table 5

**Cumulative Life-Table Rates  
for Expanded Progestogen-Only Study (Ovrette)**

| Event                       | Ovrette<br>(N = 915) |
|-----------------------------|----------------------|
| <b>Discontinuation For:</b> |                      |
| Accidental Pregnancy        |                      |
| 2 month                     | 0.0                  |
| 6 month                     | 0.4                  |
| 12 month                    | 0.6                  |
| Menstrual Problems          |                      |
| 2 month                     | 1.0                  |
| 6 month                     | 1.8                  |
| 12 month                    | 2.5                  |
| Side effects                |                      |
| 2 month                     | 0.8                  |
| 6 month                     | 1.1                  |
| 12 month                    | 1.8                  |
| Other Medical Reasons       |                      |
| 2 month                     | 1.6                  |
| 6 month                     | 3.6                  |
| 12 month                    | 5.1                  |
| Planned Pregnancy           |                      |
| 2 month                     | 0.1                  |
| 6 month                     | 0.3                  |
| 12 month                    | 0.5                  |
| Other Personal Reasons      |                      |
| 2 month                     | 6.0                  |
| 6 month                     | 10.2                 |
| 12 month                    | 14.1                 |
| Method Unrelated Reasons    |                      |
| 2 month                     | 2.5                  |
| 6 month                     | 6.8                  |
| 12 month                    | 9.6                  |
| Lost-to-Follow-up           |                      |
| 2 month                     | 15.8                 |
| 6 month                     | 24.8                 |
| 12 month                    | 61.1                 |

TABLE 5 Continued

| Event                        | Ovrette<br>(N = 915) |
|------------------------------|----------------------|
| <b>Total Discontinuation</b> |                      |
| 2 month                      | 19.7                 |
| 6 month                      | 42.0                 |
| 12 month                     | 83.7                 |
| <b>Follow-up</b>             |                      |
| 2 month                      | 84.2                 |
| 6 month                      | 71.7                 |
| 12 month                     | 48.1                 |

Table 6

**Complications and Complaints Reported for Women and Infants  
in Comparative Study of POCs versus Nonhormonal Methods**

| Event                          | POC<br>(N=394) |      | Nonhormonal<br>(N=349) |      |
|--------------------------------|----------------|------|------------------------|------|
|                                | No.            | %    | No.                    | %    |
| <u>Complications</u>           |                |      |                        |      |
| Pain in iliac area             | 0              | 0.0  | 47                     | 13.5 |
| Endometritis                   | 1              | 0.3  | 0                      | 0.0  |
| Pain in adnexa                 | 0              | 0.0  | 1                      | 0.3  |
| Diarrhea                       | 4              | 1.0  | 5                      | 1.4  |
| Cystitis                       | 20             | 5.1  | 27                     | 7.7  |
| Small abcess in<br>breast      | 1              | 0.3  | 3                      | 0.9  |
| Pruritus                       | 1              | 0.3  | 0                      | 0.0  |
| Vaginitis                      | 1              | 0.3  | 0                      | 0.0  |
| Vaginal discharge              | 0              | 0.0  | 1                      | 0.3  |
| <u>Intermenstrual Bleeding</u> |                |      |                        |      |
| Staining/spotting              | 107            | 27.2 | 101                    | 28.9 |
| Moderate                       | 107            | 27.2 | 85                     | 24.4 |
| Heavy                          | 8              | 2.0  | 7                      | 2.0  |
| <u>Complaints</u>              |                |      |                        |      |
| Nipple abrasion                | 110            | 27.9 | 103                    | 29.5 |
| Flu-like symptoms              | 34             | 8.6  | 22                     | 6.3  |
| Abdominal pain                 | 0              | 0.0  | 18                     | 5.2  |
| Cough/cold                     | 0              | 0.0  | 2                      | 0.6  |
| Sore throat                    | 1              | 0.3  | 0                      | 0.0  |
| <u>Infant Health</u>           |                |      |                        |      |
| Gains little weight            | 59             | 15.0 | 82                     | 23.5 |
| Gastrointestinal               | 1              | 0.3  | 0                      | 0.0  |
| Flu/fever                      | 11             | 2.8  | 11                     | 3.2  |
| Ear infection                  | 4              | 1.0  | 6                      | 1.7  |
| Diarrhea                       | 15             | 3.8  | 27                     | 7.7  |
| Renal colic                    | 0              | 0.0  | 1                      | 0.3  |
| Intestinal colic               | 0              | 0.0  | 1                      | 0.3  |
| Whooping cough/fever           | 1              | 0.3  | 1                      | 0.3  |
| Dystrophy                      | 1              | 0.3  | 0                      | 0.0  |
| Pneumopathy                    | 0              | 0.0  | 10                     | 2.9  |
| Death (pneumopathy)            | 0              | 0.0  | 2                      | 0.6  |
| Death (SIDS)*                  | 0              | 0.0  | 1                      | 0.3  |
| <u>Milk Volume</u>             |                |      |                        |      |
| Increase                       | 53             |      | 2                      |      |
| Decrease                       | 157            |      | 191                    |      |

\*Sudden Infant Death Syndrome

Table 7

Mean Infant Weight at Follow-up for Ovrette versus  
Nonhormonal Methods in Lactating Women

| Time | Mean Infant Weight (g) |                        |
|------|------------------------|------------------------|
|      | Ovrette<br>(N=298)     | Nonhormonal<br>(N=249) |
| FU 1 | 5723                   | 5189                   |
| FU 2 | 6465                   | 6375                   |
| FU 3 | 6872                   | 6537                   |
| FU 4 | 7469                   | 7108                   |
| FU 5 | 7945                   | 7559                   |
| FU 6 | 8406                   | 8223                   |
| FU 7 | 9672                   | 9466                   |
| FU 8 | 9991                   | 9985                   |

Table 8

**Cumulative Life-table Rates for Triquilar versus Lo-Femenal Studies**

| Event                       | Triquilar<br>(N = 538 ) | Lo-Femenal<br>(N = 533 ) |
|-----------------------------|-------------------------|--------------------------|
| <b>Discontinuation For:</b> |                         |                          |
| Accidental Pregnancy        |                         |                          |
| 1 month                     | 0.0                     | 0.0                      |
| 4 month                     | 0.0                     | 0.0                      |
| 8 month                     | 0.5                     | 0.0                      |
| Menstrual Problems          |                         |                          |
| 1 month                     | 0.0                     | 0.0                      |
| 4 month                     | 0.0                     | 0.0                      |
| 8 month                     | 0.3                     | 0.0                      |
| Side Effects                |                         |                          |
| 1 month                     | 1.6                     | 2.4                      |
| 4 month                     | 3.0                     | 3.9                      |
| 8 month                     | 5.1                     | 5.7                      |
| Other Medical Reasons       |                         |                          |
| 1 month                     | 0.2                     | 0.4                      |
| 4 month                     | 0.2                     | 0.6                      |
| 8 month                     | 1.3                     | 1.7                      |
| Planned Pregnancy           |                         |                          |
| 1 month                     | 0.2                     | 0.2                      |
| 4 month                     | 0.4                     | 3.3                      |
| 8 month                     | 2.0                     | 3.8                      |
| Other Personal Reasons      |                         |                          |
| 1 month                     | 0.4                     | 0.2                      |
| 4 month                     | 1.3                     | 1.6                      |
| 8 month                     | 3.7                     | 3.5                      |
| Method Unrelated Reasons    |                         |                          |
| 1 month                     | 0.6                     | 0.0                      |
| 4 month                     | 1.1                     | 1.2                      |
| 8 month                     | 2.1                     | 2.3                      |
| Lost-to-Follow-up           |                         |                          |
| 1 month                     | 9.5                     | 10.7                     |
| 4 month                     | 16.4                    | 17.5                     |
| 8 month                     | 24.0                    | 22.3                     |
| Total Discontinuation       |                         |                          |
| 1 month                     | 10.8                    | 11.8                     |
| 4 month                     | 20.4                    | 24.0                     |
| 8 month                     | 34.2                    | 35.6                     |

## B. Barrier Contraceptives

### 1. Acceptability Trials

The evaluation of barrier contraceptives, especially among women exhibiting high risk sexual behavior, is of special interest for FHI, although the evaluation of vaginal contraceptives in more traditional settings continues. With increasing concern about infection from sexually transmitted diseases (STDs), especially AIDS, more attention is now being given to spermicidal agents that are topically germicidal. Nonoxynol-9 has been demonstrated in in vitro laboratory investigations to destroy the pathogens of many STDs, including the human immunodeficiency virus (HIV). As a prelude to addressing these findings in clinic-based studies, FHI is currently investigating the acceptability of various contraceptive products containing nonoxynol-9 when used as prophylaxes against STDs among women at high risk for these infections.

An acceptability and sensitivity trial comparing Delfen spermicidal foam and Conceptrol spermicidal (nonoxynol-9) gel among women at high risk of contracting gonorrhea was initiated in January 1988 in Bogota, Colombia and in July 1988 in Ibaque, Colombia. A similar trial comparing Delfen spermicidal foam and Profam gel ovules (Profamilia, Mexico) containing nonoxynol-9 was recently initiated in Santo Domingo, Dominican Republic. A trial comparing Ortho vaginal foaming tablets containing nonoxynol-9

(OVT-n) and menfegol (OVT-m) was completed and final data are reported below. FHI is continuing its trial comparing the diaphragm without spermicides (Ortho All-Flex) to the diaphragm with spermicides (Gynol-II Jelly), and Delfen spermicidal foam containing nonoxynol-9.

Interim data from the two Colombia sites are presented in Table 9. Thus far, 68 women have been assigned to use Delfen foam and 64 women to use Conceptrol gel. Two women in the foam group have been discontinued for contracting an STD (trichomonas and chancroid), compared to four women (two for trichomonas, one each for bacterial vaginosis and gonorrhea) in the gel group. Overall, 43 women (63.2%) in the foam group have completed the required four weeks of product use, while 35 women (54.7%) have done so in the gel group. Ten subjects, four foam users and six gel users, have been lost to follow-up. In general, both of the study products have been well-received by the women. Product-related complaints most often reported at the two-week follow-up visit by gel users were: too wet or watery vagina (4 women); male discomfort or irritation (4 women); and vaginal rash (4 women). Too wet or watery vagina (4 women) and male discomfort or irritation (3 women) also were reported by foam users. At the four-week visit, too wet or watery vagina and male discomfort or irritation continued to be the product-related complaints reported most often by both treatment groups.

## 2. Contraceptive Efficacy Trials

Table 10 presents final results from trials completed in Ghana and Thailand evaluating Ortho vaginal foaming tablets containing nonoxynol-9 (OVT-n) and Ortho vaginal foaming tablets containing menfegol (OVT-m). Overall, the twelve-month cumulative life-table rates for women discontinuing from the study for accidental pregnancy were 19.3 per 100 women among OVT-n users and 17.5 per 100 women among OVT-m users. Product-related complaints most often reported at follow-up visits were failure of the products to dissolve upon insertion, messiness or inconvenience, and burning or stinging. Continuation rates at twelve months were 64.4 per 100 women for OVT-n and 66.3 for OVT-m. Follow-up rates at twelve months were 80.9 per 100 women for OVT-n and 84.9 for OVT-m. A total of sixteen OVT-n users were lost to follow-up, compared to seven OVT-m users.

## 3. Comparative Diaphragm Study

Interim data for the study being conducted at the Margaret Pyke Center in London comparing the fitted diaphragm with or without spermicide and spermicide alone (foam) are presented in Table 11. Enrollment has increased to a total of 119 women. Eight accidental pregnancies have so far been reported in the diaphragm with spermicide group (two due to method failure, five due to user failure and one due to a combination of method and user failure), twelve in the diaphragm alone group (seven due to method failure

and five due to user failure), and seven in the spermicide only group (three due to method failure and four due to user failure). The center continues to recruit informed volunteers who are willing to risk the potential of higher failure rates and who have not decided to end their childbearing. As a result, a number of the volunteers have withdrawn from the study before their scheduled twelve-month end-of-study visit because they wish to become pregnant. In order to improve the pace of recruitment, random assignment to the spermicide only group was discontinued in July 1988, primarily because potential volunteers indicated an unwillingness to use this method. This product is now being offered only to interested volunteers as a separate component of the study.

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

Preclinical studies of D-propranolol as a spermicide continue and are described in Section G, Contraceptive Development. An Investigational New Drug (IND) application was submitted to the FDA and approved. The first clinical trial was delayed due to formulation problems as described in Section G. It is anticipated that these will be rectified so that the first clinical trial will begin in November 1988.

#### 5. Condom Quality Assurance

FHI is carrying out a program to assess the quality of condoms in

current stocks that are being distributed by USAID Missions, and to develop policies and testing procedures that will assist USAID in assuring the procurement of uniform high-quality products. It is well known that natural rubber deteriorates with age, and that the deterioration accelerates at higher temperatures, on exposure to light, and possibly from other factors as well. Largely because of programming complexities, some lots of condoms are delayed at one or more stages along the distribution channels, and may then be warehoused under severe conditions. One objective of the program is therefore to identify condom lots that no longer provide adequate protection of users, so that these lots can be destroyed. Another objective is to evaluate the present testing methods in attempts to demonstrate correlations between these methods and also between methods and end-use results. A further objective is to develop accelerated aging conditions that will permit predictions of resistance to deterioration in storage.

Each of the three test methods--tensile, water, and air burst--offers advantages and suffers disadvantages. The tensile test, which measures the strength and elongation of a ring which is cut from a condom under prescribed conditions, provides useful information about the quality of the rubber, but it examines only a small portion of a condom, and fails to detect defects that are localized in the closed end, where failure commonly occurs. The water test is simplistic, consisting of finding out whether a condom is strong enough to hold 300 ml of water and will do so without leaking. The gradations in quality which occur on aging

are unlikely to be detected until deterioration has become sufficiently advanced. The air-burst test would appear to be especially useful, because it is a product test which examines the entire condom. Concerns have been expressed, however, that failures in the air-burst test occur at the neck of the condom due to nonuniform stress distribution, and that the results are therefore not related to actual usage. FHI will examine all of these tests and explore variations that may overcome disadvantages.

#### Future Plans

FHI will continue to study the effectiveness and acceptability of several vaginal contraceptives in the coming year. The diaphragm comparative study in England will continue. Pilot studies on the acceptability of spermicides as protection against STDs are well under way in Colombia and another was initiated recently in the Dominican Republic. Other sites also are under consideration. In addition, plans for an efficacy trial of nonoxynol-9 products against STDs is being planned for initiation in early 1989. A request from the field for a contraceptive efficacy study of vaginal spermicide tablets was received recently. The initiation of this study is being planned for early 1989. D-propranolol will be studied for its safety and efficacy in Phase I trials in women not at risk for pregnancy. The testing and evaluation of condoms will also continue in the coming years.

TABLE 9

**Reason for Discontinuations and Primary Method-related Complaints:  
Acceptability and Sensitivity Trials of Vaginal Contraceptives  
Among Women at High Risk of Sexually Transmitted Diseases  
(Study 799) in Bogota and Ibagu , Colombia**

|  | Delfen<br>Foam<br>(n=68) | Conceptrol<br>Gel<br>(n=64) |
|--|--------------------------|-----------------------------|
| <b>Reasons for Discontinuation</b>           |                          |                             |
| Sexually transmitted disease                 | 2                        | 4                           |
| Partner(s) object to product                 | 0                        | 1                           |
| Dysplasia on Pap (Class III)                 | 1                        | 1                           |
| Too wet/watery vagina                        | 1                        | 0                           |
| Lost to follow-up                            | 4                        | 6                           |
| Completed study                              | 43                       | 35                          |
| <b>Product-related Complaints (2-weeks)*</b> |                          |                             |
| Too wet/watery vagina                        | 4                        | 4                           |
| Male discomfort/irritation                   | 3                        | 4                           |
| Vaginal rash                                 | 1                        | 4                           |
| Burning/stinging                             | 2                        | 1                           |
| Dislikes odor                                | 0                        | 1                           |
| Abdominal pain                               | 0                        | 1                           |
| Unspecified complaint                        | 1                        | 0                           |
| <b>Product-related Complaints (4 weeks)*</b> |                          |                             |
| Too wet/watery vagina                        | 4                        | 4                           |
| Male discomfort/irritation                   | 3                        | 1                           |
| Vaginal rash                                 | 1                        | 0                           |
| Burning/stinging                             | 2                        | 0                           |
| Frequent urination                           | 0                        | 1                           |
| Abdominal pain                               | 1                        | 0                           |
| Itching                                      | 0                        | 1                           |
| Sensation of illness                         | 0                        | 1                           |
| Ejaculation delayed                          | 0                        | 2                           |
| Unspecified complaint                        | 1                        | 0                           |

\*Ever reported at follow-up. Totals reflect only women reporting complaints at follow-up visits.

TABLE 10

**Reasons for Discontinuation, Primary Method-related Complaints  
and Twelve-month Cumulative Life-table Rates per 100 Women  
for OVT Comparative Trials (Study 7798) in Ghana and Thailand**

|   | OVT-nonoxynol-9<br>(n=139) | OVT-menfegol<br>(n=129) |
|---|----------------------------|-------------------------|
| <b>Reasons for Discontinuation</b>                                |                            |                         |
| Accidental pregnancy  | 22                         | 19                      |
| Planned pregnancy   | 3                          | 1                       |
| Medical   |                            |                         |
| abdominal pain  | 0                          | 3                       |
| other   | 2                          | 4                       |
| Discomfort  |                            |                         |
| burning   | 8                          | 7                       |
| other   | 1                          | 1                       |
| Product-related   | 2                          | 1                       |
| Other personal  |                            |                         |
| partner objects to product  | 4                          | 1                       |
| irregular intercourse   | 2                          | 4                       |
| other   | 3                          | 2                       |
| Lost to follow-up   | 16                         | 7                       |
| Completed study   | 76                         | 79                      |
| <b>Primary Method-related Complaints*</b>                         |                            |                         |
| Male irritation   | 4                          | 5                       |
| Messy/inconvenient  | 15                         | 4                       |
| Burning/stinging  | 22                         | 31                      |
| Abdominal pain  | 4                          | 3                       |
| Tablets did not dissolve  | 10                         | 1                       |
| Vaginal discharge   | 3                          | 1                       |
| Vagina too wet  | 6                          | 1                       |
| Other   | 3                          | 4                       |
| <b>Twelve-month Cumulative Life-table<br/>Rates per 100 Women</b> |                            |                         |
| Discontinuation   |                            |                         |
| Accidental pregnancy  | 19.3                       | 17.5                    |
| Planned pregnancy   | 3.1                        | 0.9                     |
| Other medical   | 1.7                        | 7.0                     |
| Discomfort  | 7.4                        | 6.7                     |
| Product-related   | 1.5                        | 0.8                     |
| Other personal  | 8.2                        | 5.9                     |
| Continuation rate   | 64.4                       | 66.3                    |
| Follow-up rate  | 80.9                       | 84.9                    |
| <b>Woman Months of Use (12 months)</b>                            | 1188.5                     | 1184.0                  |

\*Ever reported at follow-up. Totals reflect only women reporting complaints at follow-up visits.

TABLE 11

**Reasons for Discontinuation, Primary Method-related Complaints  
and Twelve-month Cumulative Life-table Rates per 100 Women  
for Diaphragm Comparative Trial (Study 7788) in England**

|   | Diaphragm<br>w/spermicide<br>(n=39) | Diaphragm<br>only<br>(n=41) | Spermicide<br>only<br>(n=39) |
|---|-------------------------------------|-----------------------------|------------------------------|
| <b>Reasons for Discontinuation</b>                                |                                     |                             |                              |
| Accidental pregnancy  | 8                                   | 12                          | 7                            |
| Planned pregnancy   | 6                                   | 4                           | 8                            |
| Medical   | 0                                   | 0                           | 1                            |
| Discomfort  | 0                                   | 0                           | 1                            |
| Product-related   | 0                                   | 0                           | 1                            |
| Other personal  | 2                                   | 1                           | 6                            |
| Completed study   | 15                                  | 12                          | 8                            |
| <b>Primary Method-related Complaints*</b>                         |                                     |                             |                              |
| Method lessens spontaneity  | 1                                   | 1                           | 0                            |
| Male discomfort/irritation  | 0                                   | 0                           | 2                            |
| Itching in and around vagina                                      | 1                                   | 1                           | 3                            |
| Messy/inconvenient  | 1                                   | 0                           | 4                            |
| Dislikes odor   | 1                                   | 1                           | 0                            |
| Pain/soreness   | 0                                   | 0                           | 1                            |
| Vaginal dryness   | 0                                   | 1                           | 0                            |
| Partner feels diaphragm   | 0                                   | 2                           | 0                            |
| Other   | 0                                   | 1                           | 2                            |
| <b>Twelve-month Cumulative Life-table<br/>Rates per 100 Women</b> |                                     |                             |                              |
| Discontinuation   |                                     |                             |                              |
| Accidental Pregnancy  | 25.4                                | 38.8                        | 27.6                         |
| Planned pregnancy   | 22.4                                | 13.9                        | 28.5                         |
| Other medical   | 0.0                                 | 0.0                         | 8.3                          |
| Discomfort  | 0.0                                 | 0.0                         | 2.6                          |
| Product-related   | 0.0                                 | 0.0                         | 3.2                          |
| Other personal  | 6.0                                 | 3.9                         | 27.1                         |
| Continuation rate   | 54.4                                | 50.6                        | 32.6                         |
| Follow-up rate  | 66.7                                | 50.0                        | 52.9                         |
| <b>Woman Months of Use</b>  | 318.0                               | 315.0                       | 286.5                        |

\*Ever reported at follow-up. Totals reflect only women reporting complaints at follow-up visits.

## 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 other methods of tubal occlusion. The Filshie Clip is being compared with the tubal ring, the Wolf Clip, the Secuclip, bipolar electrocautery and the Pomeroy method of tubal ligation. Comparisons will examine the ease of use, and the complications and pregnancy rates as reported by 33 centers in which trials are being conducted. Select comparative trials and noncomparative trials in England, Canada and Mexico will provide the basis for requesting FDA approval for marketing.

#### a) Filshie Clip versus Wolf Clip

The Filshie Clip is being compared with the Wolf Clip in minilaparotomy procedures in interval women in the Dominican Republic, Malaysia and Mexico. Another center in Panama completed follow-up; a short report was completed. To date 819 interval procedures have been performed. There have been four technical failures among planned Filshie Clip procedures. Table 12 details the surgical difficulties. Fourteen women, five from the Filshie group and nine from the Wolf group, were reported as having surgical injuries or major complications. These are also detailed in Table 12.

Early follow-up visits (<30 days post-sterilization) have approximated 89.4% for both groups. Forty-eight Wolf Clip cases (13.3%) and 63 Filshie Clip cases (17.2%) reported one or more complications, mostly minor, at early follow-up visits. However, one luteal phase pregnancy was reported in the Filshie group, and one woman in the Filshie Clip group and two women in the Wolf Clip group were readmitted to the hospital. One woman in the Wolf group had additional pelvic/abdominal surgery for metrorrhagia. Over seventy percent of the women in both groups have returned for long-term follow-up (>30 days post-sterilization). Seven women in the Filshie Clip group were readmitted to the hospital as were two women in the Wolf Clip group. In all, 32 (9.7%) Filshie Clip cases and 26 (8.0%) Wolf Clip cases reported one or more complications at long-term follow-up. One case of a migrating Filshie Clip was reported at the Dominican Republic center. The patient reported pain of the right pelvic region and leg. An x-ray report identified the right clip in a subdermic mass which suggested a migratory process from the adnexal adhesion area; surgery showed the clip to be lodged in a granuloma where the clip had pushed through the abdominal wall and was interposed between muscle layers. The clip could not be removed at that time. A similar case report involving the Hulka Clip has been published in the medical literature. The patient is being followed up with periodic x-ray reports.

The two clips are also being compared in laparoscopic procedures. Two sites in Mexico and Venezuela are now active. Two sites in Guatemala and Haiti have completed follow-up; a short report was prepared for the latter. Interval sterilizations have been performed on 1,189 patients. Surgical difficulties were reported in 10.6% of the Wolf Clip cases and in 6.9% of the Filshie Clip cases (Table 13). Eleven women, five from the Filshie Clip group and six from the Wolf Clip group, were reported as having sustained surgical injuries. Approximately 90% of the women in both groups have returned for early follow-up visits (<30 days post-sterilization). Thirty-seven Filshie Clip cases (6.8%) and 54 Wolf Clip cases (10.1%) reported one or more complications at early follow-up. There have been two hospital readmissions. Over 60% of the women have returned for their long-term follow-up visits (>30 days post-sterilization). There have been six hospital readmissions and eight pregnancies, one luteal in a Wolf Clip patient, as shown in Table 13.

TABLE 12

**Filshie Clip versus Wolf Clip  
via Minilaparotomy**

|  | Filshie Clip<br>(N=410) |     | Wolf Clip<br>(N=409) |     |
|--|-------------------------|-----|----------------------|-----|
|  | No.                     | %   | No.                  | %   |
| <b>A. Events at Surgery</b>                                |                         |     |                      |     |
| <u>Surgical difficulties</u>                               |                         |     |                      |     |
| With equipment   | 0                       | -   | 1                    | 0.2 |
| Entering the peritoneum                                    | 2                       | 0.5 | 5                    | 1.2 |
| Visualizing/grasping tubes                                 | 6                       | 1.5 | 5                    | 1.2 |
| Occluding tubes  | 2                       | 0.5 | 1                    | 0.2 |
| Occlusive technique to wrong<br>structure                  | 1                       | 0.2 | 0                    | -   |
| Ovarian Cyst   | 0                       | -   | 1                    | 0.2 |
| More anesthesia required                                   | 1                       | 0.2 | 0                    | -   |
| <u>Surgical Injuries</u>                                   |                         |     |                      |     |
| Tubal injury without bleeding                              | 1                       | 0.2 | 1                    | 0.2 |
| Tubal bleeding   | 1                       | 0.2 | 2                    | 0.5 |
| Uterine tear   | 1                       | 0.2 | 1                    | 0.2 |
| Apnea  | 0                       | -   | 1                    | 0.3 |
| Uterine perforation  | 1                       | 0.2 | 4                    | 1.0 |
| Bowel injury   | 1                       | 0.2 | 0                    | -   |
| Total women with 1+<br>surgical injuries/<br>complications | 5                       | 1.2 | 9                    | 2.2 |

TABLE 12 (Continued)

|   | Filshie Clip<br>(N=410) |      | Wolf Clip<br>(N=409) |      |
|---|-------------------------|------|----------------------|------|
|   | No.                     | %    | No.                  | %    |
| <b>B. Events Reported at<br/>Early Follow-up*</b>     |                         |      |                      |      |
| Women returning                                       | 371                     | 90.5 | 361                  | 88.3 |
| Readmissions  | 1                       | 0.3  | 2                    | 0.6  |
| Pregnancy   | 1**                     | 0.3  | 0                    | -    |
| <u>Complications</u>                                  |                         |      |                      |      |
| Serous discharge                                      | 16                      | 4.4  | 16                   | 5.0  |
| Hematoma  | 8                       | 2.2  | 4                    | 1.1  |
| Inflammation at incision                              | 20                      | 5.4  | 13                   | 3.6  |
| Abscess   | 6                       | 1.6  | 3                    | 0.8  |
| Perineo-plastic surgery                               | 0                       | -    | 1                    | 0.3  |
| Bleeding  | 1                       | 0.3  | 0                    | -    |
| Complete dehiscence                                   | 0                       | -    | 1                    | 0.3  |
| Other infection                                       | 3                       | 0.9  | 7                    | 2.0  |
| Urinary tract infection                               | 1                       | 0.3  | 2                    | 0.6  |
| Vaginal bleeding                                      | 9                       | 2.5  | 4                    | 1.1  |
| Women with 1+<br>complications                        | 63                      | 17.2 | 48                   | 13.3 |
| <b>C. Events Reported at<br/>Long-term follow-up*</b> |                         |      |                      |      |
| Women returning for 6-month<br>follow-up              | 318                     | 77.6 | 307                  | 75.1 |
| Women returning for 12-month<br>follow-up             | 277                     | 67.6 | 269                  | 65.8 |
| Readmissions  | 7                       | 2.4  | 2                    | 0.6  |
| Total women with 1+<br>complications                  | 32                      | 9.7  | 26                   | 8.0  |

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

\*\*Luteal phase

TABLE 13

**Filshie Clip versus Wolf Clip  
via Laparoscopy**

|  | Filshie Clip<br>(N=594) |     | Wolf Clip<br>(N=595) |      |
|--|-------------------------|-----|----------------------|------|
|  | No.                     | %   | No.                  | %    |
| <b>A. Events at Surgery</b>                            |                         |     |                      |      |
| <u>Surgical difficulties</u>                           |                         |     |                      |      |
| With equipment   | 0                       | -   | 4                    | 0.7  |
| Entering peritoneum                                    | 6                       | 1.0 | 14                   | 2.4  |
| Visualizing/grasping tubes                             | 15                      | 2.5 | 19                   | 3.2  |
| Occluding the tubes                                    | 8                       | 1.3 | 16                   | 2.7  |
| Occlusive technique to wrong structure                 | 7                       | 1.2 | 6                    | 1.0  |
| Adhesions/occluded additional structure                | 1                       | 0.2 | 1                    | 0.3  |
| Dropped clips  | 4                       | 0.7 | 1                    | 0.3  |
| Total  | 41                      | 6.9 | 61                   | 10.6 |
| <u>Surgical injuries/complications</u>                 |                         |     |                      |      |
| Cervical laceration                                    | 0                       | -   | 2                    | 0.3  |
| Tubal bleeding   | 4                       | 0.7 | 0                    | -    |
| Clip left in pelvis                                    | 0                       | -   | 1                    | 0.2  |
| Soft tissue emphysema                                  | 2                       | 0.3 | 7                    | 1.2  |
| Apnea  | 1                       | 0.2 | 0                    | -    |
| Uterine perforation                                    | 0                       | -   | 1                    | 0.2  |
| Two incisions necessary                                | 0                       | -   | 1                    | 0.2  |
| Other  | 1                       | 0.2 | 1                    | 0.2  |
| Total women with 1+ surgical injuries or complications | 8                       | 1.3 | 13                   | 2.2  |

TABLE 13 (continued)

|  | Filshie Clip<br>(N=594) |      | Wolf Clip<br>(N=595) |      |
|--|-------------------------|------|----------------------|------|
|  | No.                     | %    | No.                  | %    |
| <b>B. Events Reported at<br/>Early Follow-up*</b>              |                         |      |                      |      |
| Women returning  | 545                     | 91.8 | 535                  | 89.9 |
| Readmissions   | 2                       | 0.4  | 0                    | -    |
| Luteal phase pregnancies                                       | 1                       | 0.2  | 2                    | 0.4  |
| <u>Complications</u>   |                         |      |                      |      |
| Serous discharge   | 10                      | 1.8  | 8                    | 1.5  |
| Hematoma   | 5                       | 0.9  | 6                    | 1.1  |
| Inflammation at incision                                       | 8                       | 1.5  | 17                   | 2.9  |
| Bleeding at incision   | 0                       | -    | 4                    | 0.7  |
| Ecchymona  | 4                       | 0.7  | 7                    | 1.3  |
| Vaginal bleeding   | 12                      | 2.3  | 15                   | 2.9  |
| Abscess  | 1                       | 0.2  | 2                    | 0.4  |
| Urinary tract infection  | 2                       | 0.4  | 7                    | 1.3  |
| Other  | 2                       | 0.4  | 4                    | 0.7  |
| Total women with 1+<br>complications at follow-up              | 37                      | 6.8  | 54                   | 10.1 |
| <b>C. Events Reported at<br/>Long-Term Follow-up**</b>         |                         |      |                      |      |
| Women returning at 6 months                                    | 385                     | 64.8 | 417                  | 69.8 |
| Women returning at 12+ months                                  | 378                     | 63.7 | 385                  | 64.7 |
| Readmission  | 5                       | 1.0  | 1                    | 0.2  |
| Pregnancy  | 2                       | 0.4  | 6***                 | 1.3  |
| Total women with 1+<br>complications at long-term<br>follow-up | 54                      | 11.7 | 53                   | 11.2 |

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

\*\*> 31 days post-sterilization

\*\*\*1 luteal phase

b) Filshie Clip versus Tubal Ring

The Filshie Clip is being compared with the Tubal Ring via laparoscopy in interval women in Indonesia, Mexico and the Dominican Republic. Two centers in Thailand are also conducting this comparison under the direction of the Thailand Fertility Research Association; their data is being sent to FHI, but is not included here. Another center in Panama has completed follow-up and a report has been written. To date 1,027 procedures have been performed. Surgical injuries and complications were reported in 16 (3.2%) of the clip patients and 28 (5.5%) of the ring patients and surgical difficulties were reported in 35 Filshie Clip procedures (7.1%) and in 25 ring procedures (4.9%) (Table 14).

Over 83% of the women in each group have returned for early follow-up (<30 days post-sterilization). In both groups the most frequently reported complication/complaint was serous discharge from the incision site. Fifty-four percent of the women have returned for 12-month follow-up visits. There have been seven readmissions in the Filshie Clip group and five in the ring group. Five pregnancies have been reported.

Two cases of migrating clips were noted in the previous report. A third case of a migrating clip was reported at the Panama center. This patient reported expelling a Filshie Clip vaginally during sexual intercourse after a total abdominal hysterectomy. The patient is being observed and remains asymptomatic. A pelvic

x-ray or ultrasound will be performed as well as a diagnostic laparoscopy in order to locate the position of the second clip. A similar case has been reported with the Hulka Clip in the medical literature.

Two centers, one in Mexico and one in Kenya, are completing follow-up for the comparative study of the Filshie Clip and Tubal Ring via minilaparotomy. Three centers in Latin America have completed follow-up. Of the 763 interval procedures performed thus far (Table 15), 20 have resulted in technical failures which occurred between three centers: six in Filshie Clip procedures and 14 in Tubal Ring procedures. Surgical difficulties were reported for 34 women in the Filshie Clip group and for 55 women in the Tubal Ring group; the most common difficulties were visualizing or grasping tubes and occluding tubes. Tubal injury or tubal bleeding were the most frequently reported surgical injuries for both groups.

Over 90% 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 17.3% in the clip group and 16.1% in the ring group. Two luteal phase pregnancies, one in each group, were reported at early follow-up. Twelve-month follow-up exams have been completed for over 55% of the patients; the rate of complications reported at long-term follow-up visits was 14.7% in the clip group and 17.2% in the ring group. There have been seven readmissions

reported including one for an ectopic pregnancy in a ring patient.  
The majority of reported complications are for menstrual problems  
and adnexal pain.

TABLE 14

Filshie Clip versus Tubal Ring  
Via Laparoscopy

|   | Filshie Clip<br>(N=510) |     | Tubal Ring<br>(N=517) |     |
|---|-------------------------|-----|-----------------------|-----|
|   | No.                     | %   | No.                   | %   |
| <b>A. Events at Surgery</b>                   |                         |     |                       |     |
| <u>Technical Failures</u>                     |                         |     |                       |     |
| Change in approach                            | 2                       | 0.4 | 0                     | -   |
| Change in technique                           | 0                       | -   | 2                     | 0.4 |
| Two techniques used                           | 0                       | -   | 3                     | 0.6 |
| <u>Surgical Difficulties</u>                  |                         |     |                       |     |
| Entering the peritoneum                       | 8                       | 1.6 | 5                     | 1.0 |
| Visualizing/grasping the tubes                | 13                      | 2.6 | 15                    | 2.9 |
| Occluding tubes                               | 6                       | 1.2 | 4                     | 0.8 |
| With equipment                                | 4                       | 0.9 | 1                     | 0.2 |
| Occluding wrong structure                     | 4                       | 0.8 | 0                     | -   |
| Total   | 35                      | 7.1 | 25                    | 4.9 |
| <u>Surgical injuries/complications</u>        |                         |     |                       |     |
| Cervical laceration                           | 6                       | 1.2 | 3                     | 0.6 |
| Uterine perforation                           | 3                       | 0.6 | 1                     | 0.2 |
| Tubal bleeding                                | 1                       | 0.2 | 14                    | 2.7 |
| Bladder injury                                | 1                       | 0.2 | 0                     | -   |
| Lesions                                       | 0                       | -   | 1                     | 0.2 |
| Soft tissue emphysema                         | 5                       | 1.0 | 6                     | 1.2 |
| Blood loss > 100 ml                           | 0                       | -   | 1                     | 0.2 |
| Tubal injury without bleeding                 | 0                       | -   | 2                     | 0.4 |
| Total   | 16                      | 3.2 | 28                    | 5.5 |
| Total women with 1+<br>injuries/complications | 15                      | 2.9 | 26                    | 5.0 |

TABLE 14 (Continued)

|  | Filshie Clip<br>(N=510) |      | Tubal Ring<br>(N=517) |      |
|--|-------------------------|------|-----------------------|------|
|  | No.                     | %    | No.                   | %    |
| <b>B. Events Reported at Early Follow-up*</b>              |                         |      |                       |      |
| Women returning  | 424                     | 83.1 | 449                   | 86.8 |
| Readmissions   | 1                       | 0.2  | 1                     | 0.2  |
| <u>Complications</u>                                       |                         |      |                       |      |
| Serous discharge   | 19                      | 4.5  | 16                    | 3.6  |
| Hematoma   | 0                       | -    | 2                     | 0.5  |
| Incomplete dehiscence                                      | 2                       | 0.5  | 3                     | 0.7  |
| Inflammation/infection                                     | 4                       | 0.9  | 9                     | 2.0  |
| Eczema   | 1                       | 0.2  | 0                     | -    |
| Vaginal bleeding   | 3                       | 0.7  | 5                     | 1.1  |
| Complete dehiscence  | 0                       | -    | 1                     | 0.2  |
| Bleeding   | 1                       | 0.2  | 1                     | 0.2  |
| Ecchymosis   | 1                       | 0.2  | 0                     | -    |
| Total women with 1+ complications at early follow-up       | 31                      | 7.3  | 36                    | 8.1  |
| Luteal phase pregnancies                                   | 1                       | 0.2  | 1                     | 0.2  |
| <b>C. Events Reported at Long-Term Follow-up</b>           |                         |      |                       |      |
| Women reporting for 6-month follow-up*                     | 366                     | 71.8 | 350                   | 67.7 |
| Women reporting for 12+month follow-up*                    | 273                     | 53.5 | 279                   | 54.0 |
| Pregnancy  | 2                       | 0.5  | 1                     | 0.3  |
| Total women with 1+ complications at long-term follow-up** | 17                      | 4.3  | 14                    | 3.6  |
| Readmissions**   | 7                       | 1.9  | 5                     | 1.4  |

\*Excludes technical failures and non-interval women.

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

TABLE 15

## Filshie Clip versus Tubal Ring Via Minilaparotomy

|   | Filshie Clip<br>(N=382) |      | Tubal Ring<br>(N=381) |      |
|---|-------------------------|------|-----------------------|------|
|   | No.                     | %    | No.                   | %    |
| <b>A. Events at Surgery</b>                               |                         |      |                       |      |
| <u>Technical Failures</u>                                 |                         |      |                       |      |
| Change in approach  | 2                       | 0.5  | 2                     | 0.5  |
| Two techniques used                                       | 4                       | 1.0  | 7                     | 1.8  |
| Change in technique                                       | 0                       | -    | 4                     | 1.0  |
| Only one tube occluded                                    | 0                       | -    | 1                     | 0.3  |
| Total   | 6                       | 1.6  | 14                    | 3.7  |
| <u>Surgical Difficulties</u>                              |                         |      |                       |      |
| With equipment  | 1                       | 0.3  | 2                     | 0.5  |
| Visualizing and/or grasping tubes                         | 26                      | 6.8  | 31                    | 8.1  |
| Occluding tubes   | 2                       | 0.5  | 12                    | 3.1  |
| Entering peritoneum                                       | 3                       | 0.8  | 8                     | 2.1  |
| Closing incision  | 0                       | -    | 1                     | 0.3  |
| Ovarian cyst  | 1                       | 0.3  | 0                     | -    |
| Ectopic Pregnancy   | 1                       | 0.3  | 1                     | 0.3  |
| Total   | 34                      | 12.1 | 55                    | 14.4 |
| <u>Surgical Injuries/Complications</u>                    |                         |      |                       |      |
| Tubal injury without bleeding                             | 9                       | 2.4  | 10                    | 2.6  |
| Tubal injury with bleeding                                | 7                       | 1.8  | 12                    | 3.1  |
| Uterine perforation                                       | 4                       | 1.0  | 1                     | 0.3  |
| Cervical laceration                                       | 0                       | -    | 3                     | 0.8  |
| Spasm of larynx   | 0                       | -    | 3                     | 0.8  |
| Blood loss > 100 ml                                       | 1                       | 0.3  | 0                     | -    |
| Vasovagal reaction  | 1                       | 0.3  | 0                     | -    |
| Lesions   | 2                       | 0.6  | 0                     | -    |
| Laceration of ligament                                    | 0                       | -    | 2                     | 0.5  |
| Laceration of ovary                                       | 1                       | 0.3  | 0                     | -    |
| Cardiorespiratory arrest                                  | 1                       | 0.3  | 0                     | -    |
| Bowel injury  | 1                       | 0.3  | 0                     | -    |
| Total women with 1+ surgical injuries/complications       | 24                      | 6.3  | 30                    | 7.9  |
| Total women reporting major complications during recovery | 15                      | 4.0  | 14                    | 3.8  |

TABLE 15 (continued)

|  | Filshie Clip<br>(N=382) |      | Tubal Ring<br>(N=381) |      |
|--|-------------------------|------|-----------------------|------|
|  | No.                     | %    | No.                   | %    |
| <b>B. Events Reported at<br/>Early Follow-up*</b>                    |                         |      |                       |      |
| Women returning for early follow-up                                  | 347                     | 90.8 | 348                   | 91.3 |
| Readmissions   | 3                       | 0.9  | 3                     | 0.9  |
| Pregnancy (luteal phase)   | 1                       | 0.3  | 1                     | 0.3  |
| <u>Complications/Complaints</u>                                      |                         |      |                       |      |
| Serous discharge/abscess   | 9                       | 2.6  | 8                     | 2.4  |
| Inflammation   | 20                      | 5.8  | 13                    | 3.9  |
| Hematoma   | 10                      | 2.9  | 5                     | 1.5  |
| Incomplete dehiscence  | 6                       | 1.8  | 13                    | 3.9  |
| Complete dehiscence  | 2                       | 0.6  | 0                     | -    |
| Infections   | 3                       | 0.8  | 3                     | 0.8  |
| Vaginal bleeding   | 2                       | 0.6  | 3                     | 1.0  |
| Bleeding   | 2                       | 0.6  | 3                     | 0.8  |
| Other complications  | 6                       | 1.6  | 8                     | 2.4  |
| Total women reporting 1+ complications<br>at early follow-up visit   | 59                      | 17.3 | 54                    | 16.1 |
| <b>C. Events Reported at<br/>Long Term Follow-up</b>                 |                         |      |                       |      |
| Women returning for 6-month<br>follow-up*                            | 283                     | 74.1 | 291                   | 76.4 |
| Women returning for 12+month<br>follow-up*                           | 222                     | 58.1 | 243                   | 63.7 |
| Readmissions   | 2                       | 0.6  | 5                     | 1.6  |
| Pregnancy  | 0                       | -    | 1                     | 0.3  |
| Total women reporting 1+ compli-<br>cations at long-term follow-up** | 43                      | 14.7 | 52                    | 17.2 |

\*Excludes technical failures and non-interval women.

\*\*Includes 6- and 12-month follow-up visits.

c) Filshie Clip versus Pomeroy Method

The Filshie Clip is being compared with the modified Pomeroy method via minilaparotomy in postpartum women in Thailand and Panama. A total of 1,394 procedures have been performed to date. The centers in Taiwan and the Philippines have completed follow-up and a short report is in progress for the latter center. Surgical difficulties were reported for 35 women (5.0%) in the Filshie Clip group and for 38 women (5.4%) in the Pomeroy group (Table 16); the most common difficulty was visualizing or grasping the tubes. Tubal bleeding was the most frequently reported surgical injury in both groups. Early follow-up visits (<30 days post-sterilization) are now complete for more than 90% of the women. During the early follow-up period, 68 (10.7%) Filshie Clip patients and 77 (12.5%) Pomeroy patients reported one or more complications. Two hospital readmissions were reported among Filshie Clip cases and three readmissions were reported among Pomeroy cases.

Approximately 73% of the women in each group have also returned for their six-month follow-up visit; 94 women in the Filshie Clip group (15.6%) and 98 women in the Pomeroy group (15.8%) have experienced one or more complications since one-month post-surgery. During long-term follow-up visits, 16 women, 12 in the Pomeroy group and 4 in the Filshie Clip group, were readmitted to the hospital.

53.5% women in the Filshie Clip group and 50.4% in the Pomeroy group have returned for their 24-month follow-up visit. Nine pregnancies have been reported, seven in Filshie Clip cases and two in the Pomeroy group.

TABLE 16

## Filshie Clip and Modified Pomeroy

|   | Filshie Clip<br>(N=695) |      | Modified Pomeroy<br>(N=699) |      |
|---|-------------------------|------|-----------------------------|------|
|   | No.                     | %    | No.                         | %    |
| <b>A. Events at Surgery</b>                       |                         |      |                             |      |
| <u>Technical Failures</u>                         |                         |      |                             |      |
| Change in technique                               | 1                       | 0.1  | 1                           | 0.1  |
| Change in approach                                | 0                       | -    | 1                           | 0.1  |
| Two techniques used                               | 2                       | 0.3  | 2                           | 0.3  |
| Total   | 3                       | 0.4  | 4                           | 0.5  |
| <u>Surgical Difficulties</u>                      |                         |      |                             |      |
| Entering peritoneum                               | 4                       | 0.6  | 0                           | -    |
| Visualizing/grasping tubes                        | 21                      | 3.0  | 35                          | 5.0  |
| Occluding tubes                                   | 7                       | 1.0  | 0                           | -    |
| Uterine involution                                | 0                       | -    | 2                           | 0.3  |
| Obesity   | 1                       | 0.1  | 0                           | -    |
| Mesosalpinx varicose                              | 0                       | -    | 1                           | 0.1  |
| PID complicated by incision                       | 2                       | 0.3  | 0                           | -    |
| Total   | 35                      | 5.0  | 38                          | 5.4  |
| <u>Surgical injuries/complications</u>            |                         |      |                             |      |
| Tubal injury without bleeding                     | 1                       | 0.1  | 1                           | 0.1  |
| Tubal injury with bleeding                        | 8                       | 1.2  | 6                           | 0.9  |
| Soft tissue emphysema                             | 0                       | -    | 1                           | 0.1  |
| Total women with 1+<br>injuries/complications     | 9                       | 1.3  | 9                           | 1.3  |
| <b>B. Events Reported at<br/>Early Follow-up*</b> |                         |      |                             |      |
| Women returning for follow-up*                    | 640                     | 92.1 | 617                         | 88.3 |
| Readmissions                                      | 2                       | 0.3  | 3                           | 0.5  |
| <u>Incision Complications</u>                     |                         |      |                             |      |
| Serous discharge                                  | 32                      | 5.0  | 38                          | 6.2  |
| Inflammation                                      | 17                      | 2.7  | 17                          | 2.8  |
| Abscess   | 8                       | 1.3  | 11                          | 1.8  |
| Bleeding  | 1                       | 0.2  | 1                           | 0.2  |
| Hematoma  | 1                       | 0.2  | 0                           | -    |
| Incomplete dehiscence                             | 4                       | 0.6  | 8                           | 1.3  |
| Other   | 1                       | 0.2  | 0                           | -    |
| Total women with 1+ complications*                | 68                      | 10.7 | 77                          | 12.5 |

TABLE 16 (Continued)

|  | Filshie Clip<br>(N=695) |      | Modified Pomeroy<br>(N=699) |      |
|--|-------------------------|------|-----------------------------|------|
|  | No.                     | %    | No.                         | %    |
| <b>C. Events Reported at<br/>Long Term Follow-up**</b> |                         |      |                             |      |
| Women returning for 6-month<br>follow-up visit*        | 506                     | 72.8 | 514                         | 73.5 |
| Women returning for 12-month<br>follow-up visit*       | 493                     | 70.9 | 506                         | 72.4 |
| Women returning for 24+-month<br>follow-up visit       | 372                     | 53.5 | 352                         | 50.4 |
| Total women with 1+ complications**                    | 94                      | 15.6 | 98                          | 15.8 |
| Readmission to the hospital**                          | 4                       | 0.7  | 12                          | 1.9  |
| Pregnancy  | 7                       | 1.2  | 2                           | 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 a center in Brazil. A second center in Latin America completed follow-up contacts; a brief report was written on the 75 case study. 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.

At the Brazilian center, long-term (> 31 days post-surgery) follow-up data were collected for 49 of the 50 (98.0%) Filshie Clip cases and 31 of the 33 (93.9%) Secuclip cases. One pregnancy was reported among Secuclip patients and one luteal phase pregnancy was reported in the Filshie Clip group. At long-term follow-up visits, 4 Secuclip patients (12.9%) and 8 Filshie Clip patients (16.3%) reported complications. Most of these were keloids or adnexal pain. About 46% of the Secuclip patients and 58% of the Filshie Clip patients have returned for two-year follow-up visits. One readmission to the hospital for a colestectomy was reported at this time.

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 underway at five sites. The site in Taiwan has decided to stop admissions at 75 cases. To date 421 bipolar procedures and 440 Filshie Clip procedures have been done. One Filshie Clip procedure resulted in a technical failure (Table 17). Surgical difficulties were reported for seven women in the Filshie Clip group and for 12 women in the cautery group; the most common difficulty was entering the peritoneum. Two surgical injuries were reported for each group.

Over 92% 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 2.9% in the clip group and 7.7% in the cautery group. One readmission for observation was reported in the cautery group. There have been five cases (1.1%) of incision complications reported among clip patients and thirteen (3.3%) among cautery patients. Twelve-month follow-up exams have been completed for over 36% of the patients; the rate of complications reported at long-term follow-up visits was 4.7% in the clip group and 10.8% in the cautery group. One readmission was reported for observation in the cautery group. Adnexal pain was the major complaint recorded at the long-term follow-up visit. One pregnancy was reported in each group.

Table 17

## Filshie Clip versus Bipolar Electrocoagulation

|  | Filshie Clip<br>(N=440) |      | Bipolar<br>Electrocoagulation<br>(N=421) |      |
|--|-------------------------|------|--|------|
|  | No.                     | %    | No.                                      | %    |
| <b>A. Events at Surgery/Recovery</b>                         |                         |      |  |      |
| <u>Technical Failures</u>                                    |                         |      |  |      |
| Change in approach   | 1                       | 0.1  | 0  | -    |
| <u>Surgical Difficulties</u>                                 |                         |      |  |      |
| Entering peritoneum  | 4                       | 0.9  | 7  | 1.7  |
| Visualizing tubes  | 3                       | 0.7  | 2  | 0.5  |
| Grasping tubes   | 1                       | 0.2  | 2  | 0.5  |
| Occluding tubes  | 0                       | -    | 1  | 0.2  |
| <u>Surgical Injuries/Complications</u>                       |                         |      |  |      |
| Uterine perforation  | 1                       | 0.2  | 0  | -    |
| Soft tissue emphysema  | 1                       | 0.2  | 2  | 0.5  |
| Bowel injury   | 1                       | 0.2  | 0  | -    |
| Blood loss > 100 ml  | 0                       | -    | 1  | 0.2  |
| Tubal bleeding   | 0                       | -    | 1  | 0.2  |
| Omental bleeding   | 0                       | -    | 1  | 0.2  |
| Total women with 1+ surgical<br>injuries/complications       | 3                       | 0.7  | 5  | 1.2  |
| Total women reporting major<br>complications during recovery | 8                       | 1.8  | 25                                       | 5.9  |
| <b>B. Events Reported at<br/>Early Follow-up*</b>            |                         |      |  |      |
| Women returning for follow-up*                               | 409                     | 93.0 | 389                                      | 92.4 |
| Readmissions   | 0                       | -    | 1  | 0.3  |
| <u>Complications/Complaints</u>                              |                         |      |  |      |
| Serous discharge   | 1                       | 0.2  | 4  | 1.0  |
| Inflammation   | 1                       | 0.2  | 4  | 1.0  |
| Bleeding   | 2                       | 0.5  | 0  | -    |
| Hematoma   | 1                       | 0.2  | 3  | 0.7  |
| Incomplete dehiscence  | 0                       | -    | 1  | 0.3  |
| Complete dehiscence  | 0                       | -    | 1  | 0.3  |
| Infections   | 3                       | 0.7  | 15                                       | 3.6  |
| Vaginal bleeding   | 4                       | 1.0  | 3  | 0.8  |
| Total women with 1+ complications*                           | 12                      | 2.9  | 30                                       | 7.7  |

TABLE 17 (Continued)

|  | Filshie Clip<br>(N=440) |      | Bipolar<br>Electrocoagulation<br>(N=421) |      |
|--|-------------------------|------|--|------|
|  | No.                     | %    | No.                                      | %    |
| <b>C. Events Reported at<br/>Long Term Follow-up**</b> |                         |      |  |      |
| Women returning for 6-month<br>follow-up visit*        | 359                     | 81.6 | 358                                      | 85.0 |
| Women returning for 12-month<br>follow-up visit*       | 163                     | 37.0 | 150                                      | 35.6 |
| Total women with 1+ complications**                    | 17                      | 4.7  | 39                                       | 10.8 |
| Readmission to the hospital**                          | 0                       | -    | 1  | 0.3  |
| Pregnancy  | 1                       | 0.3  | 1  | 0.3  |

\*Excludes technical failures

\*\*Includes 6-, 12- and 24-month follow-up visits

f) Noncomparative Filshie Clip Studies

One investigator in Brazil undertook a comparison of the minilaparotomy and laparoscopic techniques using the Filshie Clip. Admissions have been completed and one-year follow-up visits have been completed. Results were summarized in the previous report.

Long-term follow-up is being completed for a noncomparative trial of the Filshie Clip applied via laparoscopy in four Canadian centers, six centers in the United Kingdom and one in Mexico. Sterilization procedures have been completed on 1,222 interval patients. There were eight technical failures. Table 18 details events at surgery and at follow-up. Surgical difficulties have included 22 cases of difficulty with the equipment, 9 cases of difficulty entering the peritoneum, 34 cases of difficulty visualizing or grasping the tubes, 53 cases of difficulty in occluding the tubes and 10 cases of clip application to the wrong structure. In 73 cases two clips were used on one tube. The rate of surgical injuries/complications is 1.6%. Over 80% of the patients have returned for the early follow-up visit, 14.4% of the 994 women returning reported one or more complications. There were three readmissions. There was one reported pregnancy. Three luteal phase pregnancies were reported among the 783 women who returned more than 30 days post-sterilization. One pregnancy was reported by a woman who had been sterilized 2 years previously. Hospital readmissions occurred for: hysterectomy (at 12 months post-sterilization), bronchitis, pelvic pain (2 cases), urethral dilation, foot problems, stress incontinence, pregnancy

termination, cervical stenosis, a D&C (3 cases), draining of an ovarian cyst (3 cases), re sterilization, blackouts, cone biopsy, a blood transfusion for menorrhagia, an ulcer (2 cases), and gallstones. Seventy-three (9.3%) patients reported complications at a long-term follow-up visit. Over half of these were adnexal pain or menstrual problems.

TABLE 18

Noncomparative Filshie Clip Trials

|   | Filshie Clip<br>(N=1222) |     |
|---|--------------------------|-----|
|   | No.                      | %   |
| <b>A. Events at Surgery</b>                         |                          |     |
| <u>Technical Failures</u>                           |                          |     |
| Change in Approach                                  | 6                        | 0.5 |
| Two Techniques Used                                 | 2                        | 0.2 |
| <u>Surgical Difficulties</u>                        |                          |     |
| With equipment                                      | 22                       | 1.8 |
| Entering peritoneum                                 | 9                        | 0.7 |
| Visualizing/grasping tubes                          | 34                       | 2.8 |
| Occluding tubes                                     | 53                       | 4.3 |
| Occluding wrong structure                           | 10                       | 0.8 |
| More than 2 clips needed                            | 73                       | 6.0 |
| <u>Surgical Injuries/Complications</u>              |                          |     |
| Cervical laceration                                 | 2                        | 0.2 |
| Uterine perforation                                 | 2                        | 0.2 |
| Tubal bleeding                                      | 9                        | 0.7 |
| Tubal injury w/o bleeding                           | 2                        | 0.2 |
| Ruptured ovarian cyst                               | 1                        | 0.1 |
| Vasovagal reaction                                  | 1                        | 0.1 |
| Other perforation                                   | 1                        | 0.1 |
| Cardiac arrest                                      | 1                        | 0.1 |
| Soft tissue emphysema                               | 1                        | 0.1 |
| Total women with 1+ surgical injuries/complications | 20                       | 1.6 |

TABLE 18 (Continued)

|   | Filshie Clip<br>(N=1222) |      |
|---|--------------------------|------|
|   | No.                      | %    |
| <b>B. Events Reported at Early Follow-Up*</b>       |                          |      |
| Women returning for early follow-up                 | 994                      | 81.3 |
| Readmissions  | 3                        | 0.3  |
| <u>Complications</u>                                |                          |      |
| Serous discharge                                    | 39                       | 3.9  |
| Inflammation/Abcess                                 | 39                       | 3.9  |
| Bleeding  | 6                        | 0.6  |
| Incomplete dehiscence                               | 5                        | 0.5  |
| Pregnancy   | 1**                      | 0.1  |
| Hematoma  | 9                        | 0.9  |
| Infection   | 13                       | 1.3  |
| Complete dehiscence                                 | 1                        | 0.1  |
| Other   | 2                        | 0.8  |
| Women reporting 1+ complications at early follow-up | 143                      | 14.4 |
| <b>C. Events Reported at Long-Term Follow-Up*</b>   |                          |      |
| Women returning for 6-month follow-up               | 753                      | 61.6 |
| Women returning for 12-month follow-up              | 456                      | 37.3 |
| Total women with 1+ complications                   | 73                       | 9.3  |
| Readmissions  | 22                       | 2.7  |
| <u>Pregnancies</u>                                  |                          |      |
| Luteal  | 3                        | 0.2  |
| Possible method failure                             | 1                        | 0.8  |

\*Technical failure cases are excluded

\*\*Luteal

g) Other Sterilization Studies

A retrospective evaluation of the Filshie Clip is underway 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 are being made to contact these women and ask them to return for a long-term follow-up visit. Data transfer has been completed on 636 sterilization procedures. Nine surgical difficulties, two surgical injuries and eleven cases of blood loss greater than 100 ml were recorded. Five pregnancies have been reported at 84, 82, 69, 12 and 6 months post-surgery. One readmission for post-cautery bleeding and the following complications have been noted at 6- or 12-month visits: pelvic pain (1), wound discharge (2), backache (1), scar tenderness (1), dyspareunia (1) and lower abdominal pain (1). One hundred eighty women have returned for exams at 12 or more months after surgery. No subsequent readmissions have been noted.

Future Plans

In order to establish the frequency and significance of migration of Filshie Clips the following is planned:

- to conduct a follow-up study to determine if placed Filshie Clips have migrated after one year post-sterilization

on approximately 400 patients; and to interview these cases on the nature of any adverse experiences.

## 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 puncture and ligation technique developed in China has been transferred to other areas of Asia. Reports from physicians trained by AVSC (Association for Voluntary Surgical Contraception) have been enthusiastic. The puncture approach results in less blood loss and in many cases does not require a suture. Comparison will examine the standard incision and ligation technique with the puncture and ligation technique, also known as the "Li" technique.

### a) Puncture Method versus Standard Incision

The two selected sites in Thailand and Sri Lanka are now active. Sterilizations have been performed on 276 patients. Surgical difficulties were reported in 33.0% of the standard incision group and in 12.4% of the puncture group (Table 19). Approximately 86.3% of the men in the standard incision group and 84.7% in the puncture group have returned for early follow-up visits (<15 days post-sterilization). Fifty complications were reported, 43 among standard incision patients and 7 among puncture patients. Approximately 25% of both groups have returned for long-term follow-up.

TABLE 19

## PUNCTURE METHOD VERSUS STANDARD INCISION TECHNIQUE

|  | Puncture Method<br>(N=137) |      | Standard Incision<br>Technique<br>(N=139) |      |
|--|----------------------------|------|---|------|
|  | No.                        | %    | No.                                       | %    |
| <b>A. Events at Surgery</b>                          |                            |      |   |      |
| <u>Surgical Difficulties</u>                         |                            |      |   |      |
| With Equipment                                       | 2                          | 1.8  | 3   | 2.6  |
| Isolating Vas  | 8                          | 7.0  | 3   | 2.6  |
| Entering Scrotum                                     | 1                          | 0.9  | 1   | 0.9  |
| Occluding Vas  | 2                          | 1.8  | 4   | 3.5  |
| Closing Incision                                     | 0                          | -    | 7   | 6.1  |
| Mild Bleeding  | 0                          | -    | 19  | 13.7 |
| Short Scrotum  | 0                          | -    | 2   | 1.8  |
| Fatty tissue   | 1                          | 0.9  | 0   | -    |
| Restless patient                                     | 0                          | -    | 1   | 0.9  |
| Nausea   | 0                          | -    | 1   | 0.9  |
| Total  | 14                         | 12.4 | 41  | 33.0 |
| <b>B. Event Reported at<br/>Early Follow-up</b>      |                            |      |   |      |
| Men returning  | 116                        | 84.7 | 120                                       | 86.3 |
| <u>Complications</u>                                 |                            |      |   |      |
| Hematoma   | 1                          | 0.9  | 14  | 11.7 |
| Incision infection                                   | 0                          | -    | 1   | 0.8  |
| Scrotal bruise/swelling                              | 1                          | 0.9  | 24  | 20.0 |
| Serous discharge                                     | 0                          | -    | 1   | 0.8  |
| Bleeding   | 2                          | 1.7  | 1   | 0.8  |
| Backache   | 1                          | 0.9  | 0   | -    |
| Combination  | 2                          | 1.7  | 2   | 1.7  |
| <b>C. Events Reported at<br/>Long-term Follow-up</b> |                            |      |   |      |
| Men returning for 10-week<br>follow-up               | 34                         | 24.8 | 35  | 25.2 |
| <u>Complications/complaints</u>                      |                            |      |   |      |
| Scrotal pain   | 6                          | 17.6 | 6   | 17.1 |
| Wound pain   | 0                          | -    | 1   | 2.9  |

### Future Plans

Plans are for two additional sites for studies using the "Li" technique to be initiated after appropriate physician training has occurred. Other plans include comparative trials of chemical male sterilization via puncture vs incision and ligation techniques

#### **D. Nonsurgical Female Sterilization**

FHI continues to develop rapid, effective and safe nonsurgical methods of sterilization that can be performed by paramedical personnel. FHI holds an IND from the FDA for quinacrine hydrochloride pellet insertions (IND #19163) and for iodide/iodine (IND # 29262) to be inserted with the FEMCEPT device.

##### **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 96-month, cumulative life-table pregnancy rates for the three active studies shown in Table 20 range from 6.4 to 8.8 per 100 women. Nine-year follow-up (108 months) is available for some women; no additional pregnancies and no long term complications of the procedure have been reported.

A Phase I study conducted under an IND to determine the effect of intrauterine insertion of 250 mg of ten-minute releasing quinacrine hydrochloride pellets in ten women one month before hysterectomy is active at the University of Texas Health Sciences Center in San Antonio. The study includes histological evaluation of uterine and fallopian tube tissue in addition to a determination of quinacrine pharmacokinetics. Four women have completed the study.

An independent study conducted by Dr. Jaime Zipper of the Hospital Sotero del Rio in Santiago, Chile has provided evidence that 100-minute releasing quinacrine pellets, 250 mg, may be as effective as the ten-minute releasing product when given with only two insertions rather than with three. Two insertions in 107 women have resulted in a 36-month pregnancy rate of 3.0 per 100 women. Eighty percent of the women have completed 36-month follow-up. A Phase I 30-day pre-hysterectomy study of this slower releasing formulation was conducted at the University of Southern California. Six women completed the study; data analysis is in progress.

## 2. Iodine

FHI has received IND approval to initiate clinical trials of an iodine containing tubal sclerosing formulation. Documentation has been sent to the Health Review Board of Canada for pre-marketing approval to study iodine administered in the FEMCEPT device.

Sites for a 20-case Phase I pre-hysterectomy study in the U.S. and Canada are under consideration. The study will be initiated this year, with support from the Mellon Foundation.

#### Future Plans

FHI is the only institution doing research in the area of nonsurgical sterilization. Priority will be given to clinical studies of iodine.

Upon successful completion of the 30-day pre-hysterectomy studies of quinacrine hydrochloride, FHI will meet with the FDA to discuss initiation of Phase II and III studies to evaluate the safety and efficacy of the method.

## 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. Evaluation of the TCU 380A

A 10,000 case multicenter trial of the TCU 380A IUD has been underway since 1984 to assess acceptability of this most recent 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 2,322 cases have been received from Brazil, Cameroon, Chile, Costa Rica, Egypt, El Salvador, Honduras, Mexico, Pakistan and Sudan. Admissions are now complete at all sites. It is therefore expected that 12-month follow-up of all study patients will be completed by the end of next fiscal year. Twelve-month follow-up rates are currently 50.9 and 52.0 for TCU 380A and TCU 200 users, respectively. The corresponding life-table pregnancy rate is significantly lower for the TCU 380A group at 0.9 than for the TCU 200 group at 2.8 ( $p < 0.05$ ). All other event rates are comparable for the two IUD groups.

The Egyptian Fertility Care Society (EFCS) is also coordinating a randomized, multicenter trial of these two devices. Data

concerning their 1,000 cases are being managed and analyzed with the EFCS computer facilities. Follow-up rates at each of the five sites are high. No significant differences have yet been noted between device groups. Although 12-month follow-up is scheduled for completion during the spring of 1989, EFCS hopes to continue follow-up through 24 months postinsertion in order to provide requested information to the Egyptian Ministry of Health.

Four studies were designed to evaluate the TCU 380A in comparison with the TCU 220; one was completed recently in Mexico and three were initiated July 1987 in the Philippines. A total of 732 patients of a planned 900 caseload have now enrolled in the trial. With respective 6-month follow-up rates of 64.7 and 66.9, no significant differences have been detected 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) will close during the next fiscal year in Nigeria, Peru and Turkey. A total of 757 interval category patients have been admitted so far and their twelve-month follow-up rate is approximately 56%. Although the six-month expulsion rate is significantly lower ( $p < 0.05$ ) for the TCU 380A (2.1) than for the LLD (5.5), the difference at twelve months is not statistically significant. All other event rates and overall continuation rates are comparable for the two IUD groups.

Twelve-month follow-up is now complete in Venezuela, where the TCU 380A was compared to the Nova T. With twelve-month follow-up rates of 55.9 and 53.2 for the respective groups, more removals for bleeding/pain were reported for TCU 380A users than for Nova T users ( $p < 0.10$ ). No other differences were detected between the two groups of IUD users.

Studies comparing the TCU 380A with the Multiload Cu 250 are still underway in Malaysia, Sri Lanka and Thailand. A total of 2,144 women have now been admitted with 12-month follow-up rates of 80.3 for those using a TCU 380A and 82.0 for those using a Multiload Cu 250. The twelve-month pregnancy rate remains significantly lower for the TCU 380A at 0.2 than for the Multiload Cu 250 at 1.1 ( $p < 0.05$ ). The two devices have performed comparably in terms of all other event rates and overall continuation rates.

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. All 3,000 patients have been enrolled and their overall follow-up rates are high. BKS PENFIN expects to complete 24-month follow-up during the summer of 1989. For both BKS PENFIN and EFCS studies, data on printouts and disks are made available to FHI periodically.

## 2. 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 planned cases was initiated in Thailand in May 1985. As reported previously, FHI decided to terminate admissions to this study. A total of 172 patients were admitted and follow-up of these active subjects will continue through 12 months postinsertion. No significant differences between the devices are apparent at this time.

## 3. 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 in Mexico is now complete. The Mexican Institute of Social Security (IMSS), who managed this multicenter trial, are currently analyzing the data. The planned caseload of 1,800 cases was surpassed: 2,344 women were admitted to the study and three-month follow-up rates were higher than IMSS had originally anticipated. FHI hopes to

collaborate with IMSS on report preparation in the next few months.

#### 4. 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 initial results suggested a trend towards less intrauterine infection with IUD use when prophylactic antibiotics are used, but the basal level of Pelvic Inflammatory Disease was lower than believed when the sample size was first calculated. Additional cases were needed to arrive at a definitive result before setting major new health policies in this important area. The 1,800-case study in Nigeria was included in order to provide an adequate sample size to detect a difference between the two groups should one exist. Data have been received for total of 1,275 women in the Nigeria study to date and 86.7% have completed the three-month follow-up visit. Sufficient data are not yet available to detect any significant differences between the two groups of women; seventeen cases of PID have been diagnosed, eight occurring in placebo users and nine occurring in the doxycycline users. Eleven were diagnosed at the one-month follow-up visit and six were diagnosed at the three month follow-up visit.

## 5. 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, may be evaluated initially at one or two sites in the U.S. or Europe in a small pilot study. In January 1987, the FDA approved FHI's application for an Investigational Device Exemption (IDE). Since that time, FHI has been exploring manufacturing possibilities.

### Future Plans

The planned long-term follow-up, up to ten years, of the 1,400 patients enrolled in Thailand's multicenter trial of TCU 380A and Multiload Cu 250 IUDs will be reevaluated during the upcoming fiscal year in terms of organizational priorities.

## 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 strategy helps medical practitioners gain experience with various methods of contraception in many different parts of the world as well as permitting 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 ten 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

Two investigators trained at FHI-sponsored Clinical Trials Workshops are conducting IUD studies under the INN strategy, one in Nepal and one in Colombia. Each is a programmatic evaluation of the TCu 380A vs the TCu 200 encompassing a planned total of 600 cases. Data have been received for 540 cases to date. With respective 6-month follow-up rates of 42.5 and 43.4, no differences between groups are evident at this point.

2. Sterilization Studies

A surveillance study of 200 sterilization procedures is progressing slowly in Nigeria. To date, 196 women have been enrolled in the study; follow-up data are not yet sufficient to note any significant differences among techniques.

### 3. Systemics Studies

A study in Mali, at the Maternal and Child Health Center associated with the Ministry of Health, designed to compare Noriday and Lo-Femenal, two locally available oral contraceptives, has recently closed. Two hundred women were admitted into this study. With respective twelve-month follow-up rates of only 48.1 and 52.6, there appeared 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. One thousand one hundred twenty-five women have been admitted to this study. Six-month follow-up rates are 49.7 and 45.4 for the respective groups; there are no group differences at this time.

An additional systemic study was recently completed in Malaysia. This study was designed to compare the triphasic pill, Triquilar, with the low-dose combination pill, Marvelon. One hundred ninety-eight women were enrolled in the study, and although follow-up rates were high through 8 months postadmission (approximately 93%), by 12 months after admission the rates fell to approximately 37% in each group. No significant differences were demonstrated between the two types of pill users.

In Niger, a surveillance study is underway to collect data on the

use of locally available standard- and low-dose oral contraceptives, Minidril and Stediril. A total of 141 patients have been admitted to the trial so far. Eight-month follow-up rates are 44.3 in the Stediril group and 57.6 in the Minidril group, with no significant differences evident between the two groups.

Two investigators in the Philippines who were Clinical Trials Workshop participants are progressing steadily with studies of locally available oral contraceptives. Of a combined planned total caseload of 400, 283 have been admitted. The studies are evaluating Triquilar, a triphasic pill, and Lo-Ovral, a low-dose combination pill. One-month follow-up rates of active study subjects are quite high at 90.5 and 89.7 for the respective groups.

One additional systemic study, a noncomparative study of Lo-Femenal, was initiated in Indonesia during the past fiscal year. Eighty-three patients have been admitted to this 100-case study, and their one-month follow-up rate is 92.8.

#### Future Plans

FHI's policy continues to be to attempt, whenever possible, to meet local needs, as identified by AID Missions and/or local investigators. In addition to answering locally defined questions, Investigator Network Needs studies also assist FHI in continuing

to recruit proven investigators for new studies. It is anticipated that additional studies will be identified for the INN strategy by Clinical Trials Workshops to be held during the upcoming fiscal year.

TABLE 20

Gross Life Table Pregnancy Rates for  
Women Who Completed Three Administrations of  
Quinacrine Hydrochloride  
(250 mg per Administration)

|                                   | 12-mo.<br>rate | 24- mo.<br>rate | 36-mo.<br>rate | 48-mo.<br>rate |
|-----------------------------------|----------------|-----------------|----------------|----------------|
| Pellets with Sodium Thiopental    |                |                 |                |                |
| Santiago, Chile                   |                |                 |                |                |
| N=148                             | 4.2            | 6.4             | 8.8            | 8.8            |
| Active trial                      | (94.4)*        | (88.5)          | (84.7)         | (79.4)         |
| Pellets without Sodium Thiopental |                |                 |                |                |
| Santiago, Chile                   |                |                 |                |                |
| N=123                             | 3.3            | 6.7             | 6.7            | 6.7            |
| Active trial                      | (96.6)         | (96.5)          | (93.9)         | (93.0)         |
| Pellets without Sodium Thiopental |                |                 |                |                |
| Valdivia, Chile                   |                |                 |                |                |
| N=149                             | 0.7            | 3.4             | 4.1            | 5.6            |
| Active trial                      | (99.3)         | (99.3)          | (96.5)         | (95.0)         |

TABLE 20 (continued)

|                                    | 60-mo.<br>rate | 72-mo.<br>rate | 84-mo.<br>rate | 96-mo.<br>rate | 108-mo.<br>rate |
|------------------------------------|----------------|----------------|----------------|----------------|-----------------|
| Pellets with Sodium Thiopenthal    |                |                |                |                |                 |
| Santiago, Chile                    |                |                |                |                |                 |
| N=148                              | 8.8            | 8.8            | 8.8            | 8.8            | 8.8             |
| Active trial                       | (77.9)         | (77.2)         | (77.2)         | (75.0)         | (66.9)          |
| Pellets without Sodium Thiopenthal |                |                |                |                |                 |
| Santiago, Chile                    |                |                |                |                |                 |
| N=123                              | 7.6            | 7.6            | 7.6            | 7.6            | -               |
| Active trial                       | (86.8)         | (68.4)         | (34.2)         | (20.2)         | -               |
| Pellets without Sodium Thiopenthal |                |                |                |                |                 |
| Valdivia, Chile                    |                |                |                |                |                 |
| N=149                              | 5.6            | 6.4            | 6.4            | 6.4            | -               |
| Active trial                       | (94.3)         | (90.7)         | (73.4)         | (18.7)         | -               |

\*Follow-up rate

## G. Contraceptive Development

### 1. Plastic Condoms

FHI has embarked on an intensive program to develop a new condom utilizing synthetic thermoplastic elastomers instead of natural rubber. The use of synthetic materials offers many advantages. For example, they can be extruded and thermoformed by inexpensive processes in high volume with low capital investment and low operating costs. Furthermore, the materials when appropriately chosen offer superior durability, being resistant to puncture and tear, and retaining their properties under adverse aging conditions. And yet further, they are amenable to modification to alter their physical and mechanical properties and their surface characteristics. Their principal shortcoming is their lack of compliance: in general, they are not as soft and extensible as natural rubber. As in the case of any engineering materials, one designs around the deficiencies, by changing physical parameters and geometries.

To accomplish its objectives, FHI is working with three major resin suppliers, two design firms, a research, development, and testing laboratory, two equipment manufacturers, and a patent law firm. The last is significant in expressing FHI's dedication to protecting its technology through ownership of patents, thus insuring the eventual availability of products.

Numerous prototypes have been prepared for functionality test which are now under way, and the preliminary results are enlightening, suggesting the viability of new design concepts. In pursuing its course, FHI has had to evaluate the test methods which are now commonly employed, and attempt to develop new ones which will be more meaningful. These efforts are providing a greater understanding of the physical, mechanical, and chemical properties of condoms, and should thus contribute to improvements in condoms in general, including natural rubber as well as the synthetics.

## 2. D-Propranolol as a Spermicide

NICHD awarded FHI a contract for a formal evaluation of D-propranolol as a potential new advance in vaginal contraception. Development and partial funding is being coordinated with AID. The work specified in the original work plan is being actively pursued, although the sequence in which certain sub-projects will be implemented has been modified.

Earlier studies under this contract demonstrated in monkeys and rabbits that D-propranolol is highly spermicidal, is less irritating to the vaginal mucosa when formulated in a cream, and is consistently efficacious when the concentration of D-propranolol in the cream is 6% or more.

The most recent preclinical efficacy studies were designed to

identify improved formulations of D-propranolol. Two sets of experiments were conducted. In the first, cream formulations containing 3% D-propranolol and increasing concentrations of nonoxynol-9, ranging from 0% to 4%, were tested in macaque monkeys by Dr. L. Zaneveld at Rush Presbyterian/St. Luke's Medical Center. Early results revealed that the creams containing the D-propranolol and 3% or 4% nonoxynol-9 were highly spermicidal, but those containing lesser concentrations of nonoxynol-9 were not. The results, however, were inconsistent. The testing of these formulations in additional animals did not clarify the results. The animal-to-animal data remained highly variable. The experiments were inconclusive and were terminated.

In the second set of experiments, modifications to the cream formulation were made in an attempt to increase retention of the cream in the vagina, and thereby lengthen the duration of spermicidal action. The first modification consisted of incorporating various concentrations of methocel, ranging from 1% to 50% into the creams. Initially, 1%, 10% and 50% were tested with 1% showing the greatest spermicidal activity. The results, however, were again erratic with three animals showing high spermicidal activity and three showing little activity. Because of these inconsistencies, it was decided to suspend all further studies with methocel and other additives and to focus on the reliability of the monkey as a model for evaluating spermicidal contraceptives.

To determine whether these inconsistencies were due to the novelty of the formulations or to erratic performance of the monkey experiments, it was decided that proven formulations yielding consistent results in past experiments would be tested blindly. Four formulations were prepared, coded, and sent to Dr. Zaneveld for blind evaluation. One was a 7% D-propranolol cream, another a 5% D-propranolol gel and the remaining were placebos for each formulation. The active cream and gel had always been completely spermicidal in all previous experiments conducted throughout the development of the formulations. In the present experiments, the 5% D-propranolol gel was completely spermicidal in one monkey but showed little or no activity in the other two tested. In vitro evaluation of this formulation ("No-Mix Assay") revealed it to be spermicidal. The 7% D-propranolol cream was highly spermicidal in three of four monkeys tested, but showed no activity in the fourth. This formulation also was spermicidal when tested in vitro, but the cream required more time than the gel to exert its spermicidal action. This latter result is consistent with earlier findings in vitro by Dr. P. Saling.

The beta-blocking activity of D-propranolol was studied at Pharmakon Research International in a series of experiments in anesthetized dogs. The ability of D-propranolol to antagonize isoproterenol stimulation of the cardiovascular system was compared to that of DL-propranolol.

The initial experiment consisted of administering 2.5 ml or 5.0 ml

of an 8% D-propranolol cream intravaginally to anesthetized dogs (two dogs for each dose) that had received 0.125 ug/kg of isoproterenol intravenously. The D-propranolol doses approximated 20 and 40 mg/kg respectively or approximately 160,000 and 320,000 times the dose of isoproterenol. This resulted in a blockade of isoproterenol that commenced 15-30 minutes after D-propranolol cream administration and persisted for the duration of the experiment, four hours. Two additional dogs, one treated with D-propranolol and the other with DL-propranolol, were studied to establish the relative potency of the two drugs following intravenous administration. Anesthetized dogs stimulated by isoproterenol were given increasing doses of either drug until complete beta-adrenergic blockade could be established. The highest doses at which no beta-adrenergic blocking activity was observed were 100 ug/kg of D-propranolol and 3 ug/kg of DL-propranolol. Initial effects upon beta-adrenergic stimulation were evident following a 300 ug/kg dose of D-propranolol and a 10 ug/kg dose of DL-propranolol. These effects continued in a dose-related manner until complete beta-adrenergic blockade was observed following a 3 mg/kg dose of D-propranolol and a 100 ug/kg dose of DL-propranolol. This suggests that the beta-blocking activity of the former is approximately 33 times less potent than that of the latter.

The final series of experiments were designed to confirm the findings of the intravenous experiments and attempted to identify the relative potency of DL-propranolol and D-propranolol

administered intravaginally in a cream. Administration of either 3 ug/kg DL-propranolol or 100 ug/kg D-propranolol failed to antagonize 0.125 ug/kg of isoproterenol given intravenously. When the doses of DL- and D-propranolol were increased to 10 and 300 ug/kg, respectively, the cardiovascular response to isoproterenol was reduced in one out of two dogs for each compound. Thus, these latter two doses were interpreted as the lowest possible doses of each compound that antagonized 0.125 ug/kg of isoproterenol and confirmed observations of the earlier experiments that D-propranolol has approximately 3% of the beta adrenergic receptor blocking activity of DL-propranolol.

Plans were made to conduct the first clinical trial of D-propranolol at Quincy Research Center in Kansas City in January 1988. In preparation for this, the Pharmaceutical Service of the University of Iowa was commissioned in October 1987 to produce clinical supplies of D-propranolol creams under GMP regulations following the procedures developed at the University of North Carolina at Chapel Hill. Although the creams were manufactured, they were not released due to difficulty in analyzing the concentrations of D-propranolol. After several months, the creams were assayed successfully, but by this time, were reported by the Pharmaceutical Service to have separated, ie, cracking occurred and aqueous liquid oozed from the creams. Close inspection of older creams prepared in Dr. Swarbrick's laboratory at the University of North Carolina showed similar problems with some of their preparations. In addition, the Pharmaceutical Service of

the University of Iowa found the analytical procedure developed at the University of North Carolina to be difficult to conduct. Because of this, the clinical studies were postponed until these problems could be rectified at the University of North Carolina. Dr. Swarbrick is the principal investigator responsible for developing and modifying the various D-propranolol formulations. Thus, correcting these problems proved difficult while Dr. Swarbrick was on sabbatical. Since his return, several minor variations to the creams have been made and these are on short-term stability testing to determine if the altered formulations are improved. In addition, an expert in the science of emulsions and ointment preparation, Dr. P. Becher, is being consulted. Appropriate personnel from the Pharmaceutical Service of the University of Iowa also will be brought to Chapel Hill to observe the procedures in Dr. Swarbrick's laboratory to assure accurate and reliable transfer of the technology to Iowa. It is anticipated that the formulation problems will be rectified by October 1988 so that clinical supplies will be manufactured shortly thereafter and the clinical investigation can be initiated in November.

### 3. Filshie Clip Preclinical Toxicity Studies

Studies on potential tumorigenic effects of the silicone ring (Falope Ring) and the titanium/silicone clip (Filshie Clip) in mice and rats have been requested by the FDA. As a result FHI, Cabot Medical Corporation and Femcare Ltd. are jointly sponsoring

a study to assess the potential tumorigenic effects of these two devices. FHI manages the study and monitors the progress. The testing facility for this study is the Department of Pathology, University of Nottingham Medical School, Queen's Medical Centre, Nottingham, England. The Study Director is Dr. Graham Robinson, Senior Lecturer in the Pathology Department. Quality Assurance for the study was contracted out to a third party, Toxicol Laboratories Ltd., of Herefordshire, England. The studies are being conducted under Good Laboratory Practices.

Each treatment group involved 200 animals and the study involved two devices--the silicone ring and the Filshie Clip. Four hundred female mice of the Charles River CD-1 strain (approximately 6-7 weeks old) underwent laparotomy and either a silicone ring or a Filshie Clip was implanted around their Fallopian tube-anterior uterus region. Also, two hundred female mice underwent a sham operation with nothing being implanted; these animals served as controls. Surgery began on these mice on April 21, 1986. All mice have undergone post-mortems as of December 21, 1987. All tissues have been fixed and are being prepared for histological evaluation.

Four hundred Sprague-Dawley (approximately 6-7 week old) rats also underwent laparotomy during which either a silicone ring or a Filshie Clip was placed on their Fallopian tubes, and 200 control animals underwent a sham operation with nothing being implanted. Post-mortems on the rats were completed as of June 26, 1988.

The most recent quarterly report from Dr. Robinson extends up to July 12, 1988 and includes the initial results on the post mortems of the rats. In rats with the devices implanted, there were 45 interim deaths among the 200 rats with Filshie Clips and 94 interim deaths among the 200 control rats. As previously noted in the mice, the predominant reaction to treatment was the presence of hydroceles, a total of 79 being noted. It was also noted that there were 94 cystic ovaries in 400 treated rats as compared to 19 cystic ovaries in 200 control rats. At post mortom 15 clips were found internalized within the uterine horn.

Histological studies are in progress on the samples taken from the mice which were autopsied in December 1987. At the present stage of this study, there have not been any untoward findings to report other than that mentioned above.

Quality assurance inspections took place on May 12, 13; June 13, 14; and July 8, 1988. There were no major discrepancies. Also, five inspections of the animals and animal facilities were conducted by Dr. J. Roberts of His Majesty's Home Office.

#### Norethindrone (NET) Preclinical Carcinogenicity Study

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. The pharmacokinetics of the drug will be evaluated simultaneously in additional groups treated under the same protocol. As a result of competitive bids submitted by several laboratories, a contract was awarded to Bio Dynamics in New Jersey and the study began in late August 1987. It will take two years to complete the animal experiments and approximately one additional year to analyze all tissues and prepare the final report. To date, the study is progressing well and uneventfully. Food intake, body weight gain and gross observations are all normal. A few animals have died of natural causes and this is to be expected in a study of this duration.

#### Future Plans

Acceptability trials for the new condom will continue in the coming year. The production of D-propranolol creams for clinical trials will be completed in the fall and the clinical safety trials will be initiated shortly thereafter. Initiation of efficacy trials is planned for early 1989.

The carcinogenicity studies for the Filshie Clip and for the NET products will continue.

### III. 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 evaluates the non-contraceptive consequences of contraceptive use, including adverse pregnancy outcomes, sexually transmitted diseases (STDs), cancer, cardiovascular disease and longevity. An emphasis over the past few years has been to integrate 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. Recent findings on OCs and cardiovascular disease and breast cancer will be evaluated in this way in the coming year. Achievements of the last fiscal year include completion of data collection in studies of osteoporosis and cervical cancer, development of a study of liver cancer, and initiation of a study on spermicide use and HIV infection.

#### A. Ongoing Projects

##### 1. 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.

Work is in progress to use the life-table program to estimate the number of deaths caused or averted by oral contraceptives for each of the nine broad categories of cause of death. Among women who use the pill before age 30, two deaths are averted for each death caused, while among women taking the pill after age 30, oral contraceptive use causes more deaths than it averts due to the increased risk of cardiovascular disease associated with the pill. The model can also be used to assess the consequences of OC use on a disease among subgroups of women at different hypothetical risks (e.g., breast cancer in those under age 25 at first birth). We continue to use this analytic technique to evaluate the effects of newly reported associations between OC use and specific diseases. FHI is disseminating up-to-date perspectives on the pill to users and providers working with other AID-funded agencies in this task.

## 2. 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 made 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 the women in unions use contraception, and approximately 15% of the women have used depomedroxyprogesterone acetate. (DMPA).

Study personnel were trained by staff from FHI and Survey Research Associates in October 1985. A total of 581 women were interviewed (212 cases and 369 controls). Two of the 41 physicians who were asked to participate refused. Neither of these had more than 2 case patients who were eligible for the study. Of the 493 cases of cervical cancer diagnosed between 1982 and 1988 who met the eligibility criteria, physician consent was obtained for 92%. Consent was denied for seven women who were believed to be too ill or too sensitive to be interviewed. Three were known by their physician to be deceased. Of the 433 cases to whom recruitment letters were sent, 214 (47%) agreed to participate, 15 (3%) refused, 59 (13%) were found to be deceased during the case recruitment phase, 23 (5%) had moved out of the study area and 79 (17%) did not reply. Of the 802 controls selected for whom physician consent was obtained and to whom recruitment letters were sent, 336 (42%) agreed to participate, 14 (2%) refused, none were deceased, 34 (4%) had moved out of the study area and 3 were excluded because they did not meet the age criteria. Letters were returned undelivered for many potential respondents (43 cases and 167 controls) because they had moved and no forwarding address could be found. Home visits were initiated in September 1987 as part of the efforts to follow-up nonrespondents, and recruitment efforts were focused on incident cases. Response rates improved significantly after these changes were implemented.

The data collection phase for this study ended in July 1988, and all data have been transferred to FHI for processing and analysis. Data management and cleaning have been initiated. This is a large data set for which a number of analysis variables must be constructed from the questionnaire data. It is expected that the data file will be clean and ready for bivariate and multivariate analysis in January 1989.

Colleagues in the Viral Disease Division of the Centers for Disease Control (CDC) had planned to look for evidence of human papillomavirus (HPV) in the tumors of the case women and in the cervical scrapings of certain respondents taken at the time of interview. However, the CDC and the Department of Pathology and Microbiology of the University of the West Indies were not able to agree on the collaboration. A limited number of cervical scrapings were obtained and are being stored at the University of the West Indies. The interested colleague at CDC has now left that organization and efforts are underway to find a laboratory which can perform DNA hybridization to identify HPV subtypes in the scrapings which show evidence of HPV.

### 3. Contraception and 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. In this randomized double-blind crossover study, thirty patients are being followed through six months on OCs and six months on placebo, with a three month "washout" period between the two phases. The last two patients were entered in the trial in March 1988; 22 have completed the first phase, and 14 have completed the second phase. By the end of September 1988 all patients are expected to have completed the first phase. At that time we will begin analyzing the results of the first phase. Results from the completed study should be available by mid-1989.

Patients with sickle cell disease typically have frequent episodes of illness; in this study there have been four patients with attacks of gallbladder disease (three have had cholecystectomies), three episodes of acute chest syndrome, one case of duodenal ulcer, one case of intermittent dyspnea, 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; this patient was four weeks into the washout period at the time of the procedure. She had been taking the active medication for the 6 months preceding that. The investigator believes that the medication did not

contribute to her illness or death.

A study in Nigeria of women with sickle cell disease who use the NORPLANT contraceptive system has begun. The active ingredient of NORPLANT is levonorgestrel, a synthetic progesterone. The study is neither randomized nor a crossover; volunteers' hematologic and biochemical parameters will be evaluated for three months while using a nonhormonal method of contraception before NORPLANT insertion, and for up to five years of observation after insertion. The first seven participants have had the implants inserted, but the investigator is unsure whether the planned 30 participants can be enrolled.

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

In Thailand, approximately 1,200 children have been identified who were exposed to DMPA and 200 who were exposed to OCs 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 almost complete. The study is being conducted in collaboration with the Johns Hopkins University and is jointly funded by the World Health Organization (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. The Hebrew

University in Jerusalem is the collaborating institution. Data collection was completed in 1986; analysis is now underway. Preliminary results show no significant differences in height, weight, sexual development, measures of intelligence or psychosocial development in children exposed to MPA in utero. These results support the hypothesis that MPA poses no threat to progeny when inadvertently given during pregnancy.

#### 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 chlamydial infection and ectopic pregnancy, investigators in Boston performed a hospital-based case-control study. The study examined the prevalence of serologic evidence of active (IgM) or previous (IgG) chlamydial infection among ectopic pregnancy patients compared with matched prenatal controls. Preliminary results from multiple logistic regression analysis indicate that previous chlamydial infection increases the risk of ectopic pregnancy by about two-fold.

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

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 male occupational 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 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 was completed in December 1987. The crude analysis showed no association between paternal exposure and risk of spontaneous abortion. An exposure classification system was developed to assign specific exposures to men on the basis of their occupation. In the spring of 1988, our Finnish collaborators completed analyses which examine this association in occupational subgroups, controlling for the effects of other risk factors. These analyses showed no association between paternal exposure to specific exposures and the risk of spontaneous abortion. The investigators have prepared a manuscript summarizing the study findings which will be reviewed at FHI upon receipt.

#### 7. 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) contraceptives is well recognized. Since the first report in the 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 OCs 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 not been demonstrated.

FHI is contributing to a case-control study of young women with myocardial infarction being conducted by the Department of Community and General Practice, Radcliffe Infirmary of Oxford, England. The study began in early 1986. To date, 101 cases and 202 controls have been identified. Information on contraceptive history and other risk factors for myocardial infarction are collected from family members and the deceased's physician. Data collection is continuing.

#### 8. Hysterectomy Following Tubal Sterilization

Debate continues about whether higher rates of hysterectomy among sterilized women are due to the sequelae of tubal ligation, an increased propensity to seek medical care, or the physicians' reduced need to preserve reproductive function. FHI conducted a case-control study of women undergoing hysterectomies at the University of Monterrey, Mexico. Controls were women seeking treatment for a dermatologic condition. Data collection was completed in 1986 and a data tape has been made which we expect to receive shortly.

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

A study was begun in February 1987 in Zacatecas, Mexico to measure

the number and severity of side effects associated with oral contraceptive use. Two groups are compared: women who also take 150 mgs of Vitamin B6 daily, and women taking a placebo. Approximately 95 of the 200 women have been enrolled. An interim analysis was done at FHI in October 1988 by an epidemiologist with the Mexican research group GIMIESAR. The study is progressing well.

#### 10. 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. If oral contraceptive use helps prevent premenopausal bone loss, the public health impact is potentially enormous, because osteoporosis affects millions of U.S. women and has an economic cost in the billions of dollars each year.

In 1987, FHI began 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 or are taking OCs is greater than the bone density of women who have never used OCs. The bone mineral density of the lumbar spine is measured by dual photon absorptiometry; two sites on the radius are measured by the single photon method. Information on other risk factors for osteoporosis and a contraceptive history is collected on a self-completed questionnaire. The bone density will be compared by duration of use and recency of use. Three hundred and forty women have been enrolled as of September 1988. Data preparation began in August 1988.

## 11. Prospective Studies of Barrier Contraception and HIV Infection

FHI is supporting three studies of barrier contraception and infection with human immunodeficiency virus (HIV, the AIDS virus). One study is a clinical trial of the efficacy of the nonoxynol-9 vaginal sponge in reducing the risk of HIV infection among a group of high-risk women in Nairobi, Kenya. This study is in collaboration with colleagues at the Universities of Nairobi, Washington and Manitoba. Preliminary results showed that while the sponge protects against several STDs, the risk of genital ulcers was higher in sponge users, and the incidence of HIV infection was roughly equal in the sponge and placebo groups.

The second study is in Kigali, Rwanda, and is being conducted in collaboration with the University of California at San Francisco. Two large cohorts of women have been formed there and will be followed semi-annually for three years. Cohort A comprises 600 healthy, sexually active seronegative women; this portion of the study will examine sexual behaviors and the incidence of HIV infection. Cohort B consists of 600 healthy seropositive women; this arm of the study will determine factors associated with progression to AIDS-related conditions and AIDS. FHI earlier supported at the site an acceptability trial of compliance with use of condoms and with three types of vaginal spermicides. The current cohort studies will evaluate the efficacy of these barrier contraceptives in preventing HIV infection and progression of HIV disease.

The third study is in Lusaka, Zambia. The investigator at the University Teaching Hospital has identified a cohort of over 200 HIV-discordant couples (i.e. couples in which one partner is HIV-positive and the other is HIV-negative). The seronegative partners are at high risk of sexual acquisition of HIV infection. These couples are already making regular clinic visits, are fully aware of each partner's serostatus, and receive risk-reduction counseling. Past exhortations failed to convince more than 10% of the couples to use condoms, however, and the investigator was eager to offer them spermicides as an alternative means of protection.

In September 1988 FHI initiated a case-control study of spermicide use by these couples, with prospective ascertainment of cases. After the informed consent process, the couples are counseled on the use of the spermicidal gel, film and suppository, and are urged to use condoms as well. Blood is drawn for ELISA and confirmatory IFA HIV antibody tests, and for syphilis serology. Physical examinations focus on STDs and genito-urinary conditions; specimens are taken for gonorrhea culture. A short admission questionnaire collects information on sociodemographic characteristics of the seronegative partner. The couple is given a Coital Log to maintain between visits, which pictorially represents days on which intercourse occurred and whether a barrier method was used.

At follow-up visits these procedures will be repeated. Information on sexual activity will be summarized from the Coital Log, and the physical status of the seropositive partner will be assessed. When a

new seroconversion occurs, the person will be designated a case and three controls will be selected. Cases and controls will then undergo a detailed interview on exposures and behaviors relevant to HIV infection. Follow-up will continue for one year or more, or until HIV infection occurs.

## 12. Genital Ulcer Disease in Women

HIV infection is not evenly distributed throughout the world. One proposed explanation for the large number of heterosexually infected persons in Africa is the high prevalence of genital ulcers, which are thought to provide easier access for the virus. FHI conducted a quick prevalence survey of 40 sites around the world to estimate the prevalence of genital ulcers in women. The survey was done in STD, family planning, and prenatal clinics with one hundred or more women from each site.

As expected, STD clinic patients had a higher prevalence of genital ulcers (11.6%) than did prenatal/gynaecological (4.5%) or family planning (1.9%) clinics. STD clinics had a range of prevalences from 0 to 29%. Bangladesh had the highest prevalence (29%); Colombia had a prevalence of 25.5%; Sri Lanka 20.8% ulcers; Zimbabwe 18.4% ulcers; Kenya 13% ulcers; Thailand 6.6% ulcers; Panama 5% ulcers; and the U.S. 3% ulcers. Overall there were 242 women diagnosed with a genital ulcer out of the 4056 examined. Herpes was the presumptive cause for 24.8%, fungus or yeast caused 21.1%, syphilis caused 17.4%, chancroid caused 15.3%, an unknown cause was assigned to 8.3% and the remaining (13.1%)

were given a variety of diagnoses. Ulcers on the external genitalia accounted for 75.2% of the ulcers. STD clinics diagnosed 100% of the chancroid, 76.7% of the herpes, and 90.2% of the syphilis. These data have been submitted for publication in The Lancet.

### 13. Prevalence of HIV, HTLV-1, and Anemia in Gonaives, Haiti

Between 1979 and 1987, 1,155 causes of AIDS were reported in Haiti. It is difficult to know the true prevalence or incidence of AIDS in Haiti because no systematic surveillance of the general population has been undertaken. Data on the prevalence of HIV are also scarce; most information has been collected in Port-au-Prince, the capital, and on specific groups such as prostitutes, tuberculosis patients, and blood donors. Whether the pattern of disease and HIV infection is the same in areas of Haiti outside of Port-au-Prince is unclear. Before planning intervention programs, information must be obtained about the magnitude of the problem in the community and the population characteristics which can be targeted for risk-reduction programs.

Beginning in April 1988, a cross-sectional clinic-based study was initiated to determine the prevalence of antibodies against HIV and HTLV-1 among 2,000 adults aged 15-45 who attend two comprehensive health centers in Gonaives, Haiti. Gonaives was selected because it is a stable semi-urban community in which the effect of subsequent intervention programs on the incidence of the disease could be evaluated.

In April and May 1988, a study questionnaire, fact sheet and consent form were designed and translated into Creole. Two nurses and two laboratory technicians were trained to interview participants and collect blood samples. A nurse specialized in STD education was hired as the field coordinator for the study.

Data collection started at the end of May 1988. Blood specimens and information on demographic characteristics and risk factors are being collected. By the end of July 1988, questionnaires were completed and blood specimens were obtained for 1,040 individuals. 966 of the blood specimens have been tested for HIV by ELISA. All specimens positive by first ELISA are being retested and then sent to the AIDS Research Laboratory at the Johns Hopkins University in Baltimore for confirmation by Western blot. To date, 10% have been HIV positive on first ELISA, 9% by repeat ELISA, and 9% have been confirmed positive by Western blot. As of this writing, we expect that data collection will be complete by the end of October 1988.

#### 14. Study To Increase Condom Use Among Male Bar Workers in Bangkok

There are many male bar workers in Bangkok, Thailand who work in clubs that encourage on-site and off-site sexual contact. Many of Thailand's reported cases of AIDS and HIV infected persons have occurred in homosexually active males. Many of the male bar workers are homosexually active at work and heterosexually active outside of work, frequently with female prostitutes. FHI is evaluating the acceptability of spermicidal condoms among this group of high-risk

males. The study includes a knowledge-attitudes-practice (KAP) survey, a workshop (AIDS information, condom use, and condom use strategies), a trial period of condom use, and a condom acceptability survey of the bar workers and their clients. The first KAP and workshop have been completed and the second KAP is underway. The first KAP demonstrated that the bar workers know about AIDS, its transmission and how to prevent transmission, but that condom use was low.

## 15. Maternal Mortality

FHI's Maternity Care Monitoring data bank is a rich source of information on the determinants of maternal mortality and morbidity. From this data bank, three files have been created: 577 maternal deaths; controls matched for age and parity; and unmatched controls randomly selected from the same institution. Preliminary analysis of the crude effect of birth interval shows no difference in either the mean birth interval, or the distribution of birth intervals, between the women who died and those who did not.

## B. Planned Projects

### 1. Breast Cancer

Breast cancer is the first or second most common cancer of women worldwide. It is increasing rapidly in countries undergoing economic development. Its incidence is related to diet, possibly mediated through changes in estrogen metabolism. It is also affected by changes

in patterns of reproduction: the timing of childbirth in relation to menarche and the duration of breastfeeding. In addition, there are unanswered questions about the long-term safety of oral contraception in relation to breast cancer.

FHI is developing a corporate strategy for public service and research in breast cancer with the long-term aim of providing women, and their advisors and health planners, with information which will allow them to take this disease into account when making reproductive choices.

Research on two topics will soon begin.

a) Estrogen metabolites and diet. In a three-way collaboration which FHI catalyzed with scientists at the Rockefeller University and the National Institute of Environmental Health Sciences (NIEHS), we will study the prevalence of the estrogen metabolites 16 $\alpha$  hydroxy estrone, 2 hydroxy estrone and their ratio in the urine of 98 post-menopausal women. Our aims are to determine the day-to-day variation of these compounds and to gain experience in the technical problems of their measurement. In addition, the NIEHS team conducted a randomized control trial of a soy diet intervention and we are testing the 24-hour urines collected to determine how these estrogen metabolites are changed by the diet. Sixteen alpha hydroxy estrone is a metabolite which appears related to breast cancer in a way similar to cholesterol in heart disease; we expect that study of this hormone will revolutionize the epidemiology of breast cancer.

b) Female reproductive cancers and oral contraceptives. We have

initiated a collaborative study with CDC, NICHD and WHO, will calculate the probability of endometrial, ovarian, cervical and breast cancer under various strategies for reproduction. We are undertaking a decision analysis to compare the expectation of all cancers with or without OC use. We will explore utilities and values deriving from mortality and quality of life of women with reproductive cancers. The purpose of this research is to determine how oral contraceptive use should be viewed, weighing the known benefits of preventing endometrial and ovarian cancer with a hypothetical, though small, risk of breast cancer.

## 2. Oral Contraceptives, Hepatitis B and Hepatocellular Carcinoma

Two recent studies published in Britain showed an association between hepatocellular carcinoma (HCC) and oral contraceptive use. In Britain and the United States, HCC is extremely rare, and the association with OC use has little public health impact. In developing countries, however, HCC is much more common. In some areas of Africa and Asia, HCC is the third leading cancer. The high prevalence of liver cancer in developing countries is attributed to the high prevalence of hepatitis B virus (HBV) infection as well as to aflatoxins in some staple foods. Since the British studies excluded the few cases with evidence of exposure to HBV, it is not known whether OC use increases the risk of development of liver cancer in women exposed to HBV. FHI has developed a case-control study of liver cancer in Hong Kong. Hong Kong has an excellent health care system with the necessary expertise for definitive diagnosis and a sufficient number of cases to complete

data collection in two years. Additional outside funding is being sought for this study.

### 3. Triphasic Oral Contraceptives in Perimenopausal Women

Contraceptive options for older women are limited. Many physicians are reluctant to give OCs because of fear of cardiovascular side effects. Data are emerging which suggest this risk is not as great as originally thought. Furthermore, a study in Israel has shown that women treated for symptoms of menopause with triphasic OCs not only had complete remission of symptoms, but also had greater bone mineral density compared with women presenting with menopausal symptoms but not treated. We plan to develop a replication of the Israeli study, and a potential investigator has been identified. Outside funding may be sought for his study.

### 4. Acceptability of Spermicidal Products

Laboratory and clinical data suggest that spermicides can reduce the risk of a variety of STDs. But there will be little public health benefit attributable to spermicide use unless persons at high risk of STD acquisition actually use the products. FHI will test the acceptability of several spermicidal products among women attending a Nigerian family planning clinic that provides STD services.

### 5. Program to Reduce the Incidence of Chancroid

Chancroid is the leading cause of genital ulcers in Kenya, and genital ulcers are a major risk factor for HIV infection. An area that is an important source of chancroid infection will be identified from the records at Nairobi's only STD clinic. A satellite clinic will be established in this area and will treat STDs, distribute condoms, be a base for a community outreach program, and provide information and education on the prevention of STDs, including HIV. Public Health nurses will be used in an outreach program to identify, treat, and educate women at high risk for infection in the community. The outreach nurses will also distribute condoms and spermicides.

#### 6. Spermicidal Foaming Tablets and Sexually Transmitted Disease

One completed FHI study determined that use of the contraceptive vaginal sponge reduced the risk of gonorrhea and chlamydial infection. Another ongoing study examines the relationship between use of the sponge and the incidence of HIV infection. To study the association between spermicide use and STD infection, however, the sponge is an inappropriate spermicidal vehicle for two reasons. First, from the scientific standpoint, it is not possible to separate the sponge's physical barrier effect from its chemical barrier effect. Second, from the practical standpoint, the sponge is a costly product and is unlikely to be widely available in the developing world.

The Division intends to conduct a clinical trial of spermicidal foaming tablets and the incidence of STDs. These products are inexpensive, are distributed by USAID, and have already become popular in some

countries. Priority in site selection will be given to areas with a high incidence of HIV infection.

#### **IV. PROGRAM EVALUATION**

The Program Evaluation Division supports research in four areas: family planning evaluation, AIDS, 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. Others evaluate the performance of delivery systems and the knowledge and attitudes providers have toward the methods they deliver. One broad goal is to understand the various factors associated with contraceptive acceptance and continuation within the **general population**. Another is to evaluate condom distribution programs for AIDS prevention and conduct studies on the acceptability of methods (condoms, spermicides) thought to have a protective effect against HIV transmission. A third priority is to evaluate breastfeeding promotion programs in developing countries. The Division is one where the opportunities for needed research exceed the available resources by a wide margin.

##### **A. Family Planning Evaluation**

Many of the studies of the Program Evaluation Division 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 projects assess the family planning knowledge and attitudes of providers (such as physicians) or commercial distributors. Others 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 of 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, including NORPLANT contraceptive implants and spermicidal-lubricated condoms, female condoms, condoms made from new materials and studies of patterns of pill compliance in the general population. Development strategies to study the consumer aspects of other new FHI products, such as NET-90 injectables, is also underway.

#### 1. Provider/Client Surveys

Throughout much of the developing world, oral contraceptives (OCs) are often acquired without first making a visit to a physician. Retailers and community-based distributors play an important role in determining what clients know about OCs and other methods. This 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 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 doubled its market share to 42%. The study found that Perla users were of lower socio-economic status than users of other brands.

This study, which provides objective documentation of the usefulness of one of USAID's social marketing programs, was presented at the American Public Health Association (APHA) meeting in Las Vegas, September 1986. The final report was distributed in October 1987 and an article describing the findings will appear in Studies in Family Planning in

January, 1989.

b) Mexico: Promoter's Knowledge of Contraceptives

This survey of community-based distributors involved in promoting family planning among adults and youths was conducted in Juarez, Mexico. One goal of the study was to provide Federacion Mexicana de Asociaciones Privadas de Planificacion Familiar (FEMAP) with recommendations on how to improve training programs for promoters.

Results of this survey were described in detail in the previous semiannual report. The findings reinforced the need for educating providers of OCs and underscore once more the misunderstandings about OCs that exist in many parts of the world.

The final draft report for this study has been sent to FEMAP for review. It will be finalized and distributed in late 1988.

2. Accessibility, Acceptability, and Effectiveness of Selected Methods

The studies in this section deal with the range of contraceptive methods including sterilization, implants, pills, and condoms. Studies on OC compliance are a comparatively new field, but if we can understand why and how people measure a method, then it should be possible to design interventions to improve use. Sterilization is one of the two most prevalent contraceptive 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 particularly low, programs to provide information and counseling may be necessary for men and women to overcome their fears and misinformation and adopt this method.

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

A.I.D. 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 sought to determine whether such cash payments were perceived by clients as coercive and whether they had a measurable effect on an individual's capacity to give informed consent, on the decision to accept sterilization, and on long-term satisfaction or regret with the method.

The research staff of the Community Development Service (CDS) selected a sample of 1,350 acceptors of female sterilization from the 16,301 women served by 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.

Subsequent regret over being sterilized was not associated with the amount of the reimbursement payment. Nor did clients feel the cash payments were coercive. But a logistic model did suggest that regret was 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. The study suggests 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 counseling for women who can be predicted, based on the current study, of being at high risk for regretting the operation.

Results were presented at the annual meeting of the APHA in October 1987 and a final report was completed May of 1988.

b) Egypt: NORPLANT Acceptability

As part of a new series of clinical trials of NORPLANT contraceptive implants in Egypt, the acceptability of NORPLANT to previous users and new acceptors is being assessed. The purpose of the study is to assess the reactions of users to the product, identify any problems with insertion or removal, and evaluate user perceptions of any counseling

before and during use.

The study is being conducted by five local universities in Egypt, coordinated by public health physicians working closely with the clinical trials investigators. Data collected from 270 previous users in Alexandria and Assiut are now being analyzed. Data from new acceptors in all five regions will be collected over the next two years, using surveys, focus group discussions, observations of client-provider interactions, interviews with husbands, and community surveys. Data collection on new acceptors will start in the Fall of 1988. The Egyptian Fertility Care Society is coordinating this research.

c) Bangladesh: NORPLANT Acceptability Research

This project has three phases that relate to both the first cohort of NORPLANT acceptors and a second cohort representing an expanded clinical investigation.

The first cohort of NORPLANT acceptors was recruited during February 1985-March 1986, with a total of 673 NORPLANT acceptors in three clinics. An in-depth follow-up of the discontinuers of the first cohort of NORPLANT users and a sample of those still continuing with the implants were interviewed at their homes. A small sample of husbands was also interviewed. The survey instrument was designed to investigate the relative roles of a host of potential factors affecting the discontinuation and continuation with the implants.

A total of 121 discontinuers were successfully followed-up. This represented a follow-up rate of 87%. The median duration of use of the implants among these women was 18 months.

The preliminary results (N=121) showed that the discontinuers' mean age was 28 years with an average of three living children. About half of them did not want to have any more children. Among those who had discontinued, 51% said they were satisfied with the implants. The most important reasons (compiled from an open-ended question) given for removal were: menstrual related (38%); general weakness and unspecified illness (22%); dizziness/headache (8%); and desire for pregnancy (9%).

In answer to the open-ended question, "When you made the request for removing NORPLANT implants, what did the clinic staff tell you?", the following responses were found: the woman was told that the implant would be removed (25%), she was advised to try and keep the implant longer (36%), she was given medicine and asked to come back again (23%), the doctor was unavailable (3%), the staff didn't take the request seriously (4%) and other (8%).

In response to the question, "Overall, how much effort did you have to exert to get the implants removed," the women said: very little (38%), some effort (52%), and a lot of effort (10% i.e., 12 women). Overall, 18% of the women said they did not like the advice given by the clinic person regarding their request for removal. Nearly 45% of the

discontinuers reported using a contraceptive method at the follow-up interview; the pill was used by one-quarter of these discontinuers.

d) Sri Lanka: Demand for NORPLANT in the General Population

The promising results on safety, efficacy and acceptability of NORPLANT based on clinical studies on the one hand, and the dearth of studies which assess the demand for NORPLANT in the general population on the other, provided the rationale for developing a methodology to assess demand for NORPLANT.

A special questionnaire module on NORPLANT was included in the 1985-86 Rural Family Planning Survey in Sri Lanka. Eligible respondents for this module were women who were not sterilized and whose husbands were not sterilized. Since NORPLANT is a new method and most rural women would not have heard of it, a pictorial brochure on NORPLANT was given to each respondent. The brochure used was the same one used in pre-introductory clinical trials in Sri Lanka. The interviewers first introduced each eligible respondent to NORPLANT by guiding her through the brochure; then the respondent was asked questions regarding her interest in using the method, willingness to pay, and reasons for not being interested.

The findings showed that the demand for NORPLANT is high in Sri Lanka; 35% of the married women ages 15-44 expressed interest in using the implants. Another 13% were unsure with the remainder (52%) not interested. The demand was found greatest among women from lower

socioeconomic status and those who had previously used a contraceptive. The demand was higher among women with more children and those who were interested in spacing their pregnancies for more than four years.

A section of the paper was presented at the 1987 Annual Conference of the National Council for International Health. It is being revised for publication.

e) Sri Lanka: Is the NORPLANT Implant System a Substitute for Sterilization?

This paper analyzes data from a population-based survey fielded in Sri Lanka which showed that almost half of the women interested in using NORPLANT contraceptive implants were actually those who wanted to limit childbearing, a pattern also found in other international NORPLANT clinical studies. A comparison between recently sterilized women and women interested in using NORPLANT to limit their family size showed the limiters to be socioeconomically and demographically different from the sterilized women. Among several variables analyzed, the most important factor distinguishing the two groups was their economic status. Further comparison of the limiters with professed spacers interested in using NORPLANT showed that the spacers were yet another distinct category of women, the most important characteristic distinguishing between the two groups being the total number of living children. The paper concludes that NORPLANT is not a substitute for sterilization; it appears potentially a popular method among those who want no more children, but are not ready to accept sterilization. The finding that the potential NORPLANT users represent two very different types of women in the population has implications for provider

counseling and user satisfaction as well as continuation.

This paper has been submitted to Studies in Family Planning.

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 has increased.

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. A joint effort between FHI and the Centre Haitiano-Arabe, this investigation assessed reasons for use or non-use, and obtained information on the sources of condoms used by men residing in the study area. Results will be used to design more effective approaches to increase condom use among Haitian couples who are not otherwise protected against unwanted pregnancy.

Analysis was completed during the reporting period, and shows near universal knowledge yet very low use of condoms in Cite Soleil. Even among men whose wives or partners had obtained condoms at the local family planning center during the previous three months, fewer than one

half had ever used them and only five percent said they were current users. Condoms appear to be considerably less popular than systemic methods--pills and injectables--in Cite Soleil. Among those not currently practicing any method of contraception, only one percent said they planned to use condoms in the future, compared with one fourth who plan to accept oral contraception and over half who intend to use Depo provera. A final report, currently in preparation, will discuss the findings of this study in the context of improving the acceptability of family planning among males in urban settings such as Cite Soleil. This ought to be useful for planned AIDS prevention programs to promote condoms.

g) Colombia: Pill Compliance

Although oral contraceptives (OCs) have been used by tens of millions of women in LDCs, there has been very little systematic effort to try and understand how women actually use the pill and what mistakes may be most common. In many settings, poor compliance may contribute to increased side effects, discontinuation and method failure.

The first of a series of studies on pill compliance that FHI intends to conduct began in Magdalena, Colombia in 1986. Magdalena is the only Department (State) in Colombia in which all rural health promoters have been trained by the Ministry of Health (MOH) to provide oral contraceptives. This served as an ideal site to investigate the relationship between OC compliance and user, method and service system characteristics.

Using focus groups and interviews, data were obtained from new acceptors and providers on knowledge, attitudes and practices with special emphasis on daily compliance (using a recall calendar) and the affects of the service delivery system (including the providers) on correct and continued use of the pill. Data collection was completed in June 1987.

Of the 572 new OC acceptors first interviewed, complete data were available for 500 women or 87% of the initial sample. Four out of ten (41%) of the new OC users had discontinued the pill by the end of the study, primarily because of side effects. Of those who remained on the pill (59%), fewer than half took it correctly. Roughly half of the incorrect users made errors in their transition from one pill packet to the next, and half took the pill incorrectly during the cycle (e.g., only when they had sex, alternate days, simply forgot, etc). In response to specific questions, neither the new users nor the rural health promoters who deliver their OCs fully understood how to take the pill correctly. In fact, of those making errors, 71% were due to incorrect knowledge of pill use, 7% to side effects or illness, 10% to running out and 7% to simply forgetting. Current analysis concerns the relationship of other promoter characteristics and service system variables to compliance, and further, compliance with discontinuation.

This study has shown that OC users's level of knowledge about the pill is positively associated with compliance and continuation. The data further suggest that the most common reason for discontinuation and

non-compliance is the presence of perceived side effects.

Surprisingly, no direct association between compliance and continuation was discovered using bivariate analysis. The final report will be completed in the Fall, 1988. A paper on OC knowledge of providers and users and their relationship to compliance was published in the March 1988 issues of International Family Planning Perspectives.

Multi-variate analysis is now in progress to further examine the association between compliance and continuation and between service delivery and OC use. Those results will be presented in upcoming papers.

h) Zaire: Contraceptive Continuation and Reasons for Discontinuation

In recent years, government and privately-funded family planning programs in sub-Saharan Africa have attempted to increase acceptance of contraceptive methods. These efforts have been successful in gaining new acceptors, however, the drop-out rates are thought to be substantial and follow-up studies are urgently needed to learn the extent and causes of poor compliance and discontinuation.

With local USAID Mission funding, FHI has developed projects in Senegal and Zaire to study the reasons for discontinuation of contraceptive methods. These projects seek 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 change in the service delivery program: client charges; screening practices; including laboratory work requirements; education

and counseling programs; method availability; clinic hours and accessibility; and knowledge and attitudes of clinic staff.

In the Spring of 1986, the Regional Family Planning Association (CRND) in Kinshasa expressed a concern about the high dropout rate from clinic services--50% of acceptors did not return for services after the first six months. Site visits were made to ten clinics in March 1987 in order to have a better idea of the organization of the clinics and to finalize the protocol. Five clinics were selected as study centers.

All women coming to the clinic for the first time are interviewed at admission to gather information on socio-demographic characteristics, obstetric history, motivation for family planning and preferred method. Women accepting the pill, IUD or injectables are followed up at regular intervals during six months. Those who do not return for a scheduled follow-up visit are visited at home by a trained interviewer. The study began in April 1987, and has completed admission of 1,300 proposed study participants. As determined during the retrospective study of clinic records, drop out rates are high--over 50%. Data collection was completed in September 1988.

Data will be entered and analyzed by the Family Planning Services Project (PSND) with the technical assistance of FHI. The final report will be prepared by FHI and the PSND. Field costs are being provided by PSND through their operations research grant with Tulane University.

i) Senegal: Contraceptive Acceptance and Discontinuation: "Les Inactives"

Services statistics from the Projet Sante Familiale (PSF) program in Senegal 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 "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 interested in improving both the number of new acceptors and their satisfaction and continued use of their chosen method. With technical assistance from FHI, a study is being conducted to determine the proportion of clients at a sample of PSF centers who do not become acceptors of a modern method of contraception; to understand why non-acceptors do not choose to use a contraceptive method; to ascertain the six-month continuation rate among acceptors; and to understand the factors associated with early discontinuation. Field work for this investigation began in September, 1988.

j) West Africa: Laboratory Requirements

Hormonal contraceptives (orals and injectables) are the most popular modern methods of contraception in Africa. However, as a result of conservative biases derived from a longstanding interaction and partial misunderstanding of French medical practices, excessive laboratory tests are required in many Francophone African countries before prescribing these methods, thus severely limiting access to systemic methods. The required laboratory tests are expensive, difficult to

obtain and scientifically unjustified use of scarce resources on desperately poor countries. They are virtually unavailable outside of the capitals and large urban areas and divert medical resources from much more important health care problems. These illogical requirements appear to represent an anachronistic and substantial barrier to the accessibility of family planning services without any commensurate contribution to the health of women.

The Regional Economic Development Services Office/West Central Africa (REDSO/WCA) requested that Family Health International (FHI) design and implement an assessment of the prevalence of laboratory testing requirements for hormonal methods in West African francophone countries.

Initial baseline data on laboratory test requirements were obtained through a questionnaire administered at the Quality Child Spacing Services Conference in Abidjan in 1987. More specific information is being gathered in a review of clinic records and through discussions with clinic personnel during site visits to eight francophone countries. Burkina Faso is being used as a case study since it has recently changed its obligatory laboratory test requirements. Information has been gathered on previous clinic practices, impetus for the change and the change process. In Senegal, where systematic laboratory tests are still required, a prospective study to compare the results of laboratory tests with a straightforward evaluation based on a medical history, examination and simple diagnostic procedures such as taking the client's blood pressure will be carried out for 300 women.

The questions to be addressed are:

- (1) Do the laboratory tests or family planning providers identify a higher percentage of women as poor risks for systemic contraceptive use? Do laboratory tests and family planning providers identify the same women as poor risks?
- (2) If the laboratory tests identify a larger percentage of women as poor risks, how many women need to be screened in order to identify one additional poor risk? What is the total cost of identifying that one additional case?

Assessment visits began in February, 1988, and FHI will provide a complete report including policy alternatives to REDSO/WCA when the study is completed. It is proposed that this report be used in other francophone countries, such as Togo and the Cote d'Ivoire, which still require lab exams before prescription of hormonal contraception, to facilitate changing these requirements.

#### k) Acceptability and Use of New Barrier Contraceptives

Given the tremendous investment required to develop new methods of contraception, it is important to evaluate the acceptability of these methods early in the development process, or before procurement of large scale supplies for program distribution. The first FHI effort of this kind involved spermicidally-lubricated condoms. (See section

on AIDS studies.) During the past six months, FHI has begun several small in-house studies to examine the acceptability of the contraceptive patch (non-A.I.D. funded), a prototype plastic condom and a stronger latex condom. These studies will provide valuable preliminary information that will allow improvements to be made before these methods are tested in the field. In subsequent phases of the evaluation process, increasing emphasis will be placed on marketability of the new methods at all levels in developing countries, with studies focusing on planners and providers as well as users.

Condom breakage is an issue that has increased in importance, especially in the context of the global AIDS epidemic. FHI currently is conducting an in-house study to examine whether users can distinguish between two condoms of differing strengths, and whether the stronger condoms is acceptable. This trial may eventually be expanded into a three-country study, and the results of these tests will be used to recommend possible changes in A.I.D.'s condom procurement policy.

The AIDS epidemic has also led to efforts focusing on improved condom design and construction. FHI has developed a prototype plastic condom that may provide a stronger and more comfortable alternative to the latex condom. An in-house acceptability trial of the prototype condom is currently underway at FHI. This trial is the first stage of an iterative evaluation process that will incorporate user feedback into subsequent versions of the prototype.

### 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 sectors to meet this demand. Surveys of women, men and young adults provide data to plan and evaluate service delivery for different groups in the population.

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 projects described below involve data collection and analysis, as well as secondary analysis of existing data.

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

In 1984, a survey of 5,500 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 have been prepared. A paper entitled "Contraceptive Use and Fertility" summarizing results was published in Studies in Family Planning in September/October 1987.

Contraceptive prevalence in Honduras increased from 27% of women in union ages 15-49 in 1981 to 35% of those 15-44 in 1984 and the increase was most marked in rural areas (from 16% to 24%). Information from questions on place of purchase, price, and brand of oral contraceptive demonstrated the important role played by the Honduran Family Planning Association. Efforts have been made to promote breastfeeding in urban areas. The duration of breastfeeding had increased by 1984, with the greatest changes occurring among women in urban areas and women with the highest levels of education.

Further analysis is focusing on birth intervals. Among women who have had two or more children, 35% of the last live births were born within 24 months of the previous birth and these results show a negative relationship with age. That is, the largest proportion of short birth intervals is found among the youngest women.

A paper entitled "Modeling Determinants of Diarrheal Disease: Relative Effects of Demographic, Environmental and Child Correlates in Honduras Children," was given at the annual APHA meeting in October 1987. An additional paper "Management and Treatment of Diarrhea in Honduran Children: Factors Associated with Mothers' Experience" has been submitted for presentation at the 1988 APHA annual meeting to be held in Boston, Massachusetts on 13-17 November.

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

USAID/Honduras asked FHI to provide technical assistance in carrying out the 1987 MCH/FP Survey. Funds to carry out activities were provided to FHI through a buy-in from the bilateral USAID program.

The primary purpose of the 1987 Survey is to update the information gathered from the 1984 Survey. Specifically, this survey measures contraceptive prevalence, duration of breastfeeding and fertility among women ages 15-44 and infant mortality. There are also several questions on AIDS. Among children less than five years of age, the impact of health services is measured by immunization coverage and the prevalence and treatment of diarrhea and acute respiratory infections. In an effort to provide a more precise estimate of infant mortality, this survey includes approximately 11,700 households--about double the number in 1984.

The agencies involved in the 1984 Survey (Ministry of Public Health, Honduran Association for Family Planning, FHI and Management Sciences for Health) also carried 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 is 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 began in June 1987, and

was completed in November 1987. Data entry and editing utilized the CDC Data Entry and Edit System called Survey which produces very clean data as they are input.

Preliminary results became available in February 1988. Highlights of the findings include:

- (1) Infant mortality has decreased to about 62 per 1000 live births. This is a 51% decrease over the last 18 years.
- (2) Levels of fertility appear not to have changed in the past three years. Honduran women can expect to have about 5.6 children (total fertility rate) during their reproductive years (3.8 in urban areas and 6.9 in rural areas).
- (3) Contraceptive prevalence has risen from 35% in 1984 to 40% in 1987. Most of this increase can be attributed to an increased reporting of rhythm and withdrawal. Levels of knowledge of these two methods have also increased. Whether or not these method-specific increases are attributable to increased promotion of the methods or is an artifact of interviewer techniques (greater explanation of the methods in 1987) is unclear.
- (4) ASHONPLAFA serves the majority of oral contraceptive users (56%), while the private sector accounts for 20% and the Ministry of Health, 16%. The Social Security Institute and

non-specified sources account for the remaining 8% of OC users. ASHONPLAFA also provides support for 72% of the voluntary female sterilizations.

A final report in English will be ready by December 31, 1988. The paper, "Changes in the Proximate Determinants of Fertility in Honduras 1981-87," will be presented at the 1988 APHA annual meeting. Findings about knowledge and attitudes towards STDs and AIDS will be presented by staff at the Honduran Ministry at the AIDS meeting in Ixtapa, Mexico, in October, 1988.

c) Honduras: Follow-up of Pregnant Women and Infants

The Honduras National Epidemiology and Family Health Survey just described was carried out in 1987. Of the 10,441 women of reproductive age who were interviewed, 2,845 were identified as either pregnant and/or has a child less than one year of age. These women will be contacted between September and December, 1988, in a follow-up survey to determine survival status of the infant and/or pregnancy outcome. The data will be useful in confirming (or refuting) the results of the 1987 survey which show infant mortality (IMR) to have dropped considerably from 71 per 1000 livebirths in 1981 to 61 per 1000 in 1985. Both of these estimates are based on indirect techniques on calculating infant mortality. According to direct estimates (the preferred technique if data are available), the 1985 IMR is about 48. Additional information will be collected on prenatal care, delivery

care and complications, and childcare practices. FHI is providing technical assistance to this study. The work will be supported through another buy-in to FHI.

#### d) Philippines: 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, an FHI consultant from Brown University. Analysis of fertility trends and decomposition of these trends in terms of the proximate determinants (e.g., breastfeeding, marriage patterns, contraceptive use) has been carried out by Dr. Casterline and UPPI colleagues. A draft of the project report was sent by Dr. Casterline to UPPI in June 1988; following in-country review, a final version will be available in early FY '89.

#### 4. Surveys of Young Adults

In many places, rapid urbanization has led to the breakdown of many of the traditional norms concerning sexuality, early marriage, and fertility, and premarital pregnancy among adolescents has become a serious national concern in many countries. Surveys of young adults are usually the first source of objective information on a group whose problems need to be recognized in order to design and implement

appropriate education and reproductive health programs. These data will also be useful in planning strategies to contain the spread of AIDS.

a) 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 years reported that they have had premarital sexual intercourse. The figures for males were 43% and 86%, respectively;
- (2) Of the unmarried respondents who were 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 was reported by 3% of these women and 12% of the men;

- (4) For unmarried men and women, the primary source of contraception was the private sector whereas for the married, the government was the primary source;
- (5) The preferred family size was two for both young men and women;
- (6) 78% of the women and 73% of the men had a sex education class in school; and
- (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 at national and international meetings. The final report in English was completed in March 1987 and the Spanish version is expected in October 1988.

b) 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 1,420 eligible female and 941 eligible male respondents ages 14-24.

Results show sexual relations are common before marriage, that a high proportion of the women interviewed got pregnant while they were in school, and most out-of-wedlock pregnancies are legitimized by marriage.

Knowledge of AIDS as well as syphilis and gonorrhoea was high. Seven percent of sexually active women and 12% of sexually active men reported that they had had a sexually transmitted disease. The correct percentage is likely higher, as some individuals probably had symptoms but did not seek treatment. In women, chlamydia infections may have gone unnoticed.

About a third of sexually active respondents (36% of women and 29% of men) said they had used a family planning method in the past four weeks. Among sexually active respondents using family planning, 10% of never married women, 3% of currently married women and 64% of never married men were currently using condoms.

A final report has been prepared and distributed to health policymakers in Zimbabwe; several papers on the implications of the study's findings are planned for FY '89.

c) 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 1,600 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, was 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.

Findings from the Reproductive Health Survey will be of considerable policy relevance to family planning officials in The Gambia. Analysis showed, for example, that more than one-fourth of single women and almost three-fourths of single men ages 14-24 in the sample were or had been sexually active. Among these single, sexually active young men

and women, the condom use was the best known and most used contraceptive method. Although more than half (56%) of sexually active single women ages 14-24 had contracepted, 51% of these women had been pregnant. Researchers concluded that young people in The Gambia had only limited access to modern family planning methods; sexually active young people themselves said that lack of knowledge about contraception or where to obtain it was the major reason for not contracepting.

In March 1988, a workshop was held in Banjul to present and discuss the findings of this survey with Gambian health care providers and researchers. Input from this meeting was used in the policy recommendations section of the Final Report for this project, completed in mid-1988. A paper on important findings from the study, including contraceptive use patterns and experience of young adults with STDs, was presented at the annual meeting of Population Association of America in April 1988.

d) Sri Lanka: Young Adults Reproductive Health Survey

A fuller understanding of the perceptions and attitudes of today's unmarried young adults is helpful for dealing with tomorrow's reproductive health issues and family planning needs. In 1986, the Sri Lanka's Family Planning Association, with FHI assistance, made an assessment of reproductive health problems, perceptions and attitude toward sex, timing of family formation, and contraception behavior. Interviews were conducted with 2,400 unmarried, young adults (both men and women) ages 16-24.

The first report was recently completed. A national level seminar for the dissemination of the results is planned for October 1988.. The Ministry of Health of the Government of Sri Lanka has expressed interest in utilizing the results of the seminars to design and implement programs for young adults in Sri Lanka.

## 5. Survey of Men

### a) Nigeria: Male Attitudes Study

In many countries, local and national family planning activities, 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 are as important in fertility control as in other areas of health care.

During the period covered by this report, a final report, based on interviews with 1,023 adult males (aged 18-60) residing in Benin City and 760 residents of several nearby rural villages in Bendel State, was prepared and distributed to health care providers and policymakers in Nigeria. Respondents were asked about their achieved and intended family size, attitudes toward child spacing in general, and knowledge and use of specific contraceptive methods. Data entry and preliminary tabulations for the study were accomplished at the University of Benin's Computer Centre, using software provided by FHI.

Results indicate that use of modern methods (oral contraceptives, IUDs, injectables, and condoms) is higher than indicated in the 1981 Nigerian Fertility Survey. Among those currently married, 16% of the urban and 5% of the rural respondents said they were using a modern method. Use among those who had never been married was even higher: 22% of those interviewed in Benin City and 10% of those in Udo. Most respondents agreed that family planning decisions should be made by both husband and wife, and the great majority of men--including nonusers--wish to become more informed about modern child-spacing methods.

The findings of this study and their implications are presently being used by the principal Nigerian investigator to design acceptable and effective information and service delivery system programs for men in Bendel State.

#### 6. Thailand: Macro and Micro-Economic Consequences of FP Use

The A.I.D. Administrator's Office, PPC, made funds available to FHI to support research on whether rapid fertility decline has resulted in economic benefits for Thai families and for the national economy. Two related studies are being supported under this buy-in and are being closely monitored.

The first is being 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 is assessing whether Thai families who have limited themselves to two children feel they have benefitted economically compared to families with four or more children. From February - June 1988, interviews were conducted in two provinces in rural Thailand gathering data on people's perceptions of the economic costs and benefits of smaller families. The qualitative component, using focus groups, will be done during the next reporting period.

The co-investigators are currently writing a report on the project. The second study is being conducted by the Thailand Development Research Institute (TDRI) and 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.

When the reports are completed, a workshop will be held to review the results of both studies and a full report will be given to the Administrator's office.

## 7. Informed Choice Projects

In September 1987, FHI received a buy-in from PPC/A.I.D. to initiate projects on informed choice. FHI is totally committed to A.I.D.'s policy of informed choice for voluntary family planning.

The project has three phases. The first phase was a review of the situation regarding informed choice of family planning methods in the U.S.A. A consultant, Dr. Susan Philliber, was engaged to prepare this paper. The paper was distributed to all the members of the Task Force on Informed Choice.

The second phase is to conduct a diagnostic study in a few countries which currently have a limited mix of methods due to policy, service, or user-related factors. The findings are to be utilized to design and implement appropriate intervention strategies to broaden the mix. The third phase will be a seminar to review and disseminate the results of phase two.

Site visits have been made to El Salvador, the Dominican Republic (DR) and Nepal. It was not feasible to do much work in El Salvador because of the political situation. Needs assessment in the Dominican Republic and Nepal have been completed. These countries were not suitable to implement intervention strategies (see below). Sri Lanka is under consideration as a site for an intervention project. FHI will do a site visit in September - October, 1988 for this purpose.

a) Dominican Republic

In July 1988, a FHI team visited the Dominican Republic (DR) to examine key programmatic and policy-related factors affecting the pattern of contraceptive use in the DR, to investigate whether the high prevalence of sterilization was due to lack of informed choice, and to assess the

appropriateness and feasibility of supporting an operations research project in improving contraceptive method mix in the (DR). The DR was selected as a possible site for the study because of the predominant use of a single method of contraception (female sterilization).

The high prevalence of sterilization in the DR did not appear to be due to a lack of informed choice. The knowledge of temporary methods of contraception is very high among women of reproductive ages. Eligible acceptors for sterilization are not given any compensation ("incentives") either in kind or in cash, but rather pay a small amount for the procedure (ranging from US \$3-7).

Dominican women typically refer to the process of making a decision to undergo sterilization as "Voy a prepararme" (I'm preparing myself) and may consider sterilization as a solution to their problems "arreglar el problema". The average desired birth-spacing is about two years. Most women have 2-3 children before age 30. In the Santiago PROFAMILIA clinic, which provided only temporary methods of family planning, counsellors commented that about one-fourth of the women already have a preconceived choice of method, and sought sterilization. In Santo Domingo clinics, this proportion was much higher.

The main factor related to the high demand for sterilization appears to be related to the timing of the initiation of childbearing. The typical pattern for a Dominican woman is to experience first birth before age 22 and have 2-3 children in rapid succession and then be sterilized while in their 20's. The use of contraception among

currently-in-union women with no children is less than 10%. Among women with one child, only one-in-three uses any type of contraception. The patterns of early age at first birth and non-use of contraception are more common among women in lower socioeconomic classes.

An analysis of the 1986 Demographic Health Survey for the DR has shown that an average of 25% of the Dominican women currently-in-union have an unmet need for reversible methods of contraception. The magnitude of this unmet need can be expected to be higher if potential needs of single women are included as well. Furthermore, the overall unmet need could be higher if women are properly educated and counselled about the availability and importance of using contraceptives. Temporary methods of contraception also may be increased by encouraging lower parity (one or two) women who do not desire to have any more children but are unable to obtain sterilization. In 1986, about 15% of the Dominican women under age 20 desired to stop childbearing, but did not have access to sterilization.

Over the last year and a half, several activities have been initiated in the DR which may have increased the prevalence of pills and condoms. The most important activity was the introduction of a new brand of a low-dose pill (Microgynon) by the contraceptive social marketing (CSM) program of PROFAMILIA. This pill has proved to be popular and sales have increased dramatically. The CSM also has developed TV commercials for condoms, which represents the first time that condoms have been advertised on TV in the DR. Furthermore, PROFAMILIA has continued to produce brochures on reproductive physiology and on various

contraceptives.

While it does not seem prudent to try to encourage those women who do not want any more children to use reversible methods of contraception, some improvement in the contraceptive method mix may be made by developing programs designed for specific population groups including women under age 25, particularly those who do not yet have a first child, and women in lower socioeconomic classes.

Methods of contraception for birth spacing may be promoted in several ways: (1) by providing refresher courses for promotoras and physicians; (2) by intensifying appropriate information and education materials through mass media, promotoras, and in waiting lounges of maternity hospitals; and (3) by implementing specialized family planning programs (with emphasis on spacing methods) in the sugar industry, free-trade zones, and other underserved communities.

b) Nepal: Needs Assessment on Predominance of Sterilization

Knowledge and use of family planning increased considerably during the decade mid-1976 - mid-1986 in Nepal. Significant improvements in availability of and accessibility to contraceptives were also made. However, a proportionately larger share of the achievements were made from 1976-1981 than in the 1981-86 period. The impact on fertility of contraceptive use during the decade was minimal. Because of the programs's continued strong emphasis on sterilization, both the knowledge and use of reversible methods of contraception have remained

very low. It is not clear if the welfare of couples who may be in need of contraception for spacing births, but not necessarily for terminating childbearing, is being adequately addressed by the national program. Several interrelated programmatic steps to improve the performance of the program and contraceptive method mix have been suggested, including a critical review of the program's overall direction and its current strategies for service delivery, implementation of training programs for family planning motivators and providers, and design of a more effective system for evaluating and monitoring the work performance of the program personnel.

The findings will be published in Studies in Family Planning.

Future Plans: Family Planning Evaluation

The goals of the Program Evaluation Department's work in reproductive health are being reordered. 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 as cost-effective as possible within the limited resources available. The Program Evaluation Division is pursuing the following themes in family planning evaluation:

## 1. Acceptability, Marketability and Use of New Contraceptives

Work will continue to explore acceptability of a variety of new contraceptive methods, including the plastic condom, stronger condoms, the transdermal patches, female condoms, NORPLANT, and, as they become available, NET injectables and NET implants. As with the current products, acceptability will be examined at all stages of development to insure that there is a market for any new methods and then to determine what that market is. An increasing emphasis will be placed on the marketability of new methods in developing countries, with studies including planners and providers as well as users.

FHI has completed one study of pill compliance and continuation in Colombia, will do another in Egypt in 1989, and is negotiating with other sites such as Guatemala and Kenya. A study in Thailand could also be considered. The studies will include 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.

In many areas of the world, women are put at increased risk of becoming pregnant and contracting STDs because their partners refuse to use barrier contraceptives. In response to this problem, FHI is planning

to evaluate the acceptability of a prototype female condom in a population of high risk women in Thailand. The female condom is a loose-fitting polyurethane sheath that can be inserted into the vagina well before intercourse, thus eliminating women's need to rely on their partners for protection against pregnancy and STDs.

## 2. India: Buy-In

The Program Evaluation Division has been requested by the USAID Mission/India to assist in the evaluation of the social marketing program in North India.

A preliminary site visit for development of the evaluation project was made in July 1988. This project is planned to be conducted in collaboration with the Population Services International/India. The scope of the activity, study design and the logistics for carrying out the study is being reviewed by FHI and A.I.D. Mission. FHI expects to undertake a follow-up visit in December 1988 and hopefully prepare the project subcontract.

Additional activities that are under consideration for India, as part of the buy-in money, include technical assistance to the National Institute of Health and Family Welfare, support for activities related to a study on maternal morbidity and support for a longitudinal study on lactation and amenorrhea. The study on lactation and amenorrhea is part of a multi-center study planned by WHO. Because of lack of funds, WHO requested FHI to consider funding the India site. The proposal was

sent to the A.I.D. Mission in India for review and concurrence. If expected, this study could start January 1, 1989.

### 3. Egypt: Oral Contraceptive Use

FHI will be conducting a study of how women take the pill and the effect of service delivery on that use in Egypt in 1989 using focus groups with providers and users throughout the country.

Also, in Egypt, as well as Botswana and Zimbabwe, a pill compliance module is being pretested as part of the National 1988 Demographic Health Survey.

### 4. Sri Lanka: Informed Choice

Female sterilization is the predominant method of contraception in Sri Lanka. The use of reversible, modern temporary methods of contraception has been very low. One of the major factors hindering higher use of the reversible methods has been identified to be based on an earlier study supported by FHI, the lack of accurate knowledge and correct perceptions of the pill or IUDs.

The Program Evaluation Division is conducting a trip in September 1988 to Sri Lanka to develop an operations research project. Dr. Sid Schuler of A.I.D./Washington is also participating in the development of this project.

The aim of this project would be to design I-E-C intervention materials on spacing methods, mainly the pill and IUD, and provide a refresher course on these methods to the clinic providers and community health workers. The study would investigate to what level the prevalence of these methods increases over time. The intervention would be carried out for about nine months when a post-intervention evaluation would be carried out.

## **B. AIDS Projects**

Program Evaluation is playing a major part in developing projects that support FHI programs in AIDS. Work under FHI's Cooperative Agreement with A.I.D.'s Office of Population includes: (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) development and use of an AIDS module in general-purpose surveys to ascertain knowledge of transmission of AIDS and whether concern about AIDS has influenced behavior, especially regarding use of condoms and spermicides.

### **1) Multi-country Acceptability of Spermicidally-Lubricated Condoms**

Laboratory studies suggest spermicidally lubricated condoms are more effective than untreated condoms in preventing the transmission of STDs. In order to determine whether A.I.D. should supplement its current procurement policy to include two types of spermicidally

lubricated condoms, FHI tested the initial acceptability of two such condoms: Prime (lubricated with 32 mg of Nonoxynol-9) and Double-S (with an additional 32 mg of Nonoxynol-9 suspended in an ointment in the tip).

The study was conducted in Bangladesh, Egypt, Ghana, Honduras and Mali. A total of 633 current users of condoms completed the study: 49% used the Prime and 51% the Double-S. Over 90% had been using brands of lubricated condoms distributed by A.I.D. Each man was asked to use only the study condoms during a one-month period.

The general acceptability of the Prime and Double-S condoms is clear. Given the choice of their usual condom or the test condom, 76% of the Double-S users and 85% of the Prime users said they would choose the test condom over their regular brand for future use. Most (83%) considered the spermicide a benefit and that protection against AIDS and other STDs would increase their interest in using them. However, 29% of the Double-S users did have some complaints, usually that there was too much lubrication or brief irritation.

A total of 248 partners were interviewed in Bangladesh, Ghana and Mali. Fifty percent of Double-S partners and 55% of Prime partners preferred them to the usual brand despite some reports of an unpleasant odor and irritation. Like the men, a high proportion of the partners (74%) said AIDS protection would increase their interest in using spermicidal condoms.

The Prime condom, with the single dose of spermicidal lubricant, was the most favorably received, with more Double-S users experiencing irritation and/or "wetness". Both of these problems with the Double-S were due to its extra dose of spermicide, which is expected to provide twice the protection of the Prime. The actual use-effectiveness of either condom against AIDS, other STDs and pregnancy, above and beyond that of a regular condom, could not be assessed in this acceptability trial.

Based in part on the results of this study, A.I.D. has added the Prime S-L condom to its inventory of contraceptives to distribute to developing countries. Countries requesting S-L condoms were asked to conduct research on the new condoms. FHI may be involved in some of this research in Thailand and elsewhere.

FHI has shared the results of the study through papers presented at the National Conference on International Health Regional Meeting and to the June 1988 IV International Conference on AIDS in Stockholm, Sweden. A paper will be prepared for publication in the coming months.

## 2) Brazil: AIDS Module for Young Adults

A survey of young adults was carried out in 1987 in Salvador, one of the largest cities in Brazil, with additional financial support from the Pathfinder Fund and technical assistance from the Centers for Disease Control. Since Brazil has begun an educational program to deal with AIDS, it was particularly appropriate to obtain information on

what is known about AIDS, what the perceptions of risk are and what kinds of protective behavior are prevalent. Young adults may be at risk because they often have multiple partners. The survey was carried out in the Fall of 1987. FHI will be responsible for analyzing the AIDS module. A paper was presented at the June 1988 AIDS meeting in Stockholm and another will be presented at the 1988 Annual APHA meeting.

### 3) Honduras: Impact of An Education Campaign on AIDS and STDs

A small number of very sexually active individuals have the potential to spread the HIV infection more rapidly than a larger number of only moderately sexually active individuals. Individuals with many partners are not only more likely to become infected but they can also spread AIDS to their partners and to rural communities when they return home. Therefore, educational campaigns are urgently needed for this high risk group.

At the request of the STD Program of the Honduran Ministry of Health, this project has these objectives: 1) the design and testing of educational materials for use at health centers for the high risk population; 2) the training of health care providers to use this material and to sensitize them to the need to educate the public about STDs and AIDS; 3) the promotion of the use of condoms among the high risk populations; 4) the evaluation of the impact of the educational materials, training and condom promotion on: knowledge of AIDS and STDs and attitudes towards them; and sexual practices, including the

use of condoms in the high risk populations.

The study design includes a health center in Tegucigalpa which routinely sees high risk populations. The intervention consists of educational materials for the client population and condom promotion. Pre- and post-tests based on interviews of the client population will be used to determine how attitudes and knowledge have changed. The pre- and post-test interviews will also take place at a health clinic in San Pedro Sula but no intervention will be carried out there; it will serve as a control site. In June and July 1988, Ministry and FHI staff participated in focus groups of high risk populations. Findings were used to develop the pre-intervention survey instruments which were pre-tested in Comayagua in August 1988. The first KAP survey will take place late September 1988 and the intervention period will extend for 10 weeks.

#### 4) HIV Transmission Through Breastfeeding

FHI staff prepared a paper on breastfeeding and HIV transmission that was presented as a poster at the IV International Conference on AIDS in Stockholm, June 12-16, 1988 and widely publicized on National Public Radio. WHO recommends that mothers in developing countries breastfeed regardless of HIV status, while CDC recommends that seropositive women not breastfeed. For this reason, the paper estimated the number of infant deaths (in areas like Africa) due to the breastfeeding transmission of the AIDS virus (plus all other causes of death to infants) and compared this to the number of deaths that would result if

breastfeeding were withheld. It was concluded that more infant deaths would probably occur due to not breastfeeding than to continuing to breastfeed despite positive serostatus. Since numerous requests for this paper have been received, publication is being pursued.

#### Future Plans: AIDS Projects

High priority activities for FHI in AIDS include intervention with high risk individuals; the protection value of barrier methods and spermicides; and information dissemination. Up to now, we have done little with family planning programs (public or private) in developing countries to see what more they could contribute to stopping the spread of AIDS. If funds are available, we would like to visit public and private FP organizations in developing countries to determine what they are doing, what more they could do with current resources, and what additional resources are needed. During the visit, limited technical assistance could be given including how to include HIV risk factors into contraceptive screening, sharing educational materials already available, advice on how to promote barrier methods more aggressively, and possibly some assistance in counselling. Before the visits, we will try to assess what assistance they would like and then identify appropriate staff or consultants to be on the team.

#### **C. 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 remain low among government priorities for health care. In such settings, FHI has conducted a variety of 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.

FHI has made available technical and financial assistance to three studies in sub-Saharan Africa designed to identify ways to improve the delivery of reproductive health care services. Similar in general concept and objectives, each was developed and implemented in response

to local conditions and priorities. The studies were conducted in Abidjan, Cote d'Ivoire, the Karawa Health Zone in northern Zaire, and in Kaolack Medical Region of Senegal.

During the current reporting period, a French-language version of the final report of the Abidjan study was distributed to health professionals and policymakers in Cote d'Ivoire, and data analysis was completed and reports drafted for the investigations in Zaire and Senegal.

Research findings from each of the country projects are being shared with government policymaking officials, health care providers, and international donor agencies. The broad goal of this series of studies has been 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 counselling and services for birth spacing.

a) Cote D'Ivoire: Pregnancy Care Surveillance in Abidjan

Field work for this study was conducted July 1984 to December 1985. The final report was distributed in 1987. Two seminars were conducted in Abidjan to present study results. The first seminar included Ivoirian staff who participated in the study (July 2-3, 1987). The second seminar was directed at key policy and decision makers in health

(May 12, 1988). A paper on maternal mortality will be presented at the XII World Congress of the International Federation of Gynecology and Obstetrics (FIGO) in October 1988.

Findings indicate that maternal mortality is still a problem of major proportion in Abidjan. Most women who died in hospitals were referred from health centers lacking facilities and equipment to manage complicated cases. These women often arrived at the hospital moribund and died shortly after admission.

Prenatal clinics are often crowded and understaffed, and there are no standardized criteria to identify women who should deliver in a hospital. To ensure uniform identification of women at risk, the prenatal screening process should be standardized. In addition, an IE&C campaign emphasizing the importance of starting prenatal care early and making regular visits should be established.

Improved family planning services are needed. Although only 7% of women reported having used a family planning method prior to this delivery, fully one-fourth reported that they wanted to use a clinical method following delivery. Currently, pharmacies are the main source of contraceptive supplies. To increase access to services, programs of information and referral should be combined with an increase in the number of service delivery sites.

b) Zaire: Traditional Birth Attendants (TBAs)

Data collection took place over a two-year period (July 1 1984 to June 30 1986) for two groups of women: those hospitalized for pregnancy-related care at the major referral hospital in Karawa Health Zone, and those attended by trained TBAs. In addition, the infants of women who delivered at home were followed-up for one year. The final report was distributed in July 1988. Translation into French is underway. Findings were presented through a series of in-service conferences in the Health Zone. A paper entitled "Causes of Infant Mortality and Sources of Treatment in Karawa Health Zone, Zaire" was presented at the APHA annual meeting in October 1987 and has been submitted for publication. A second paper entitled "Maternal Death in Zaire: Results of a Two-Year Pregnancy Care Monitoring Study in Karawa Health Zone" will be presented at the 1988 annual APHA meeting in November.

Much can be learned for the whole of Africa from the Karawa approach to implementation of a primary health care program. The innovative birth register system used in Karawa is a useful supervisory tool. To improve maternal survival, a dual emphasis on identification and referral of women at risk and expanding the number of sites that provide emergency obstetric services is necessary. Community members must be targeted in an information campaign about the danger signs of pregnancy and delivery. Risk identification and referral can succeed only if family and community members support the pregnant woman's right to adequate medical care.

Secondary analysis on referral practices of TBAs is ongoing through support from the International Center for Research on Women.

c) 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. Information was collected on 6,912 deliveries at a representative sample of twelve village level health huts, health posts, sub-regional health centers and the regional referral hospital.

Only a very small percentage of women in the first phase study had ever used modern contraceptive methods. Access to such methods appears to be very limited and an expansion of family planning services is urgently needed. Most women (83%) had had at least one prenatal visit. Since these women had significantly better perinatal outcomes than those with no prenatal visits, efforts to increase access of the women in remote rural areas to prenatal services appear warranted.

Additionally, the study highlighted a lack of resources at the referral hospital, including anesthetics and blood products, which are among the factors, along with inadequate family planning services, leading to the high maternal and perinatal mortality in the region.

A report has been prepared on principal findings of this study, and

will be distributed to researchers and policymakers in Senegal (French translation) and in the U.S..

The results 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.

## 2. Maternal Mortality Studies

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 in order to improve 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

Information was collected on all maternal deaths occurring in the Giza, Imbaba and Osim health sectors during a twelve month period beginning in 1986. The study objectives included 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.

Once maternal deaths were identified, trained social workers visited the household of the deceased and interviewed family members about the deceased's symptoms and the circumstances surrounding the maternal death. A medical panel then assessed the specific causes of death from the family interviews. A consultant obstetrician from Duke University reviewed all maternal death reports to provide a second opinion and to help create a special methodology showing temporally the contributing, underlying, and immediate causes of death.

One hundred fifty-six maternal deaths were identified out of 960 deaths to women of reproductive age. Information was also collected on over 6,500 hospital deliveries occurring in the Boulak el Dakroul Hospital during the study period, which included 17 maternal deaths. The data from Giza reaffirm that the majority of maternal deaths in this study

area could be prevented by improving prenatal care, by improving family planning and thus preventing high risk pregnancies (especially among older and higher parity women), by increasing the proportion of hospital deliveries, and by establishing a more effective referral system (including transport) for risky pregnancies and complications identified by TBA's and health workers.

The final report of this project is under review. A meeting will be held in Giza in February 1989 to share findings with Egyptian physicians, researchers and policymakers. This project has already helped to improve the health service statistics system through the design of a uniform reporting system for maternal deaths in Giza. Information will be used to design public health measures that will reduce the frequency of maternal deaths occurring in the home and in hospital settings throughout Egypt.

b) Egypt: Daya Maternal Mortality Study

This project follows up on the Maternal Mortality in Giza study. It examines the practices of traditional birth attendants (dayas) and the outcomes for the mothers whose babies they deliver. Focus groups with the dayas were conducted in February 1988 in the Governorate of Giza. During the summer of 1988, 273 dayas were interviewed to further explore their knowledge and practices and experience in dealing with pregnancy complications and maternal deaths. Forty-three of them reported maternal deaths among their clients in the past five years.

Historically, dayas in Egypt focus only on the actual delivery of the baby. Prenatal care and the mother's condition before or after birth are not of concern. If problems develop, they are seen as "God's will." Two hundred and seventy-one dayas were interviewed, only **eight percent** of whom had ever received any formal training. Hygienic practices were found to be minimal, with only a third using any antiseptic during delivery and one in eight washing the mother's perineum. However, three out of four referred their last problem delivery, usually for abnormal positioning, failure to dilate with contractions or postpartum hemorrhage. Thirty-nine of the dayas reported a maternal death in the past five years, most often due to hemorrhage. Information from this study can be used to develop training programs for the dayas to help them provide better care for women. This study is being funded through a USAID/Cairo buy-in.

### 3. Infant Health

During the past several years, FHI has provided technical and financial support to investigating 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.

a) Brazil: Infant Follow-up by Parteiras in the Northeast

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.

In May 1984, and for one year subsequently, questionnaires on home and hospital deliveries were completed for all residents of the county of Trairi, located in a rural area of the State of Ceara.

Of the 1,198 women initially attended by TBAs, 13% were referred to medical centers. Referral was higher for women 35 or older, for primiparous women and for women with at least three years of education. Referral was also higher for women who had antenatal care, some antenatal pathology or a suspected malpresentation. 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. There were no maternal deaths. 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. Recent focus of analysis has been on infant mortality which is estimated at 64/1000 live births, considerably lower than the estimate of 142 per 1000 for the Northeast Region as a whole. Diarrheal disease, the principal cause of death, claimed the lives of more than a third of the infants. Highly correlated to diarrhea as a cause of

death were early infant feeding practices, such as early supplementation with powdered milks and unhygienic preparation.

The training and use of TBAs in conjunction with a medically-oriented system of maternity care and the review of causes of infant deaths is an innovative accomplishment that will attract study and attention as an example for other parts of the world.

Several papers based on this study have been presented: "Delivery and Pregnancy Outcomes in a Rural Community in Northeast Brazil", at the 1986 APHA meeting and "Obstetric Care and Perinatal Mortality in Rural Northeast Brazil" at the 1987 meeting. A paper examining the determinants of infant mortality and causes of death will be presented at the 1988 APHA meeting. A paper on the impact of TBA training in rural Northeast Brazil "TBAs in Rural Northeast Brazil: Referral Patterns and Perinatal Mortality" has been published by the journal Health Policy and Planning In Development. The paper on perinatal mortality will be presented at the International FIGO meeting to be held in Brazil in October 1988.

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

The Ministry of Public Health in Thailand requested information to design programs to reduce infant and early child mortality. Data on babies born in Sukhothai Province, in North Central Thailand, were collected at 1, 3, 6, 9, 12 and 18 months after delivery.

An admission record was collected for 1,529 births during the one-year period (April 1985-March 1986). There are questions about the ratio of home-to-hospital deliveries. Under-reporting of home deliveries is evident.

Follow-ups were collected for 1, 3, 6, 9, 12 and 18 months. Initial analyses indicated that there was under-reporting of mortality and, although the follow-up rate was good, there was considerable missing information for important variables. Efforts were made to identify additional deaths in hospitals and to clarify reasons for missing data on follow-ups. During the period covered by this report, additional data were collected and all follow-ups were merged at FHI. These data were returned to TFRA for analysis and preparation of the final report.

Future Plans: Maternal and Child Health

As noted in the introduction, Program Evaluation has experienced a shortfall of funds, especially in the important area of MCH. Despite many needs and opportunities, the only project in this area we have been able to initiate in the past year is a Prospective Study of Pregnant Women and Infants Identified in 1987 MCH/FP Survey in Honduras, supported by bilateral funds. This survey will measure perinatal and neonatal mortality prospectively and also collect data on maternal morbidity, infant feeding and postpartum family planning. The results can be compared with rates obtained retrospectively in the 1987 Maternal and Child Health and Family Planning Survey. Field work for this study began in June 1988.

Should more funds become available, our first priority will be to conduct in-depth analysis leading to the publication of scientific papers from the three major pregnancy monitoring studies (Zaire, Cote d'Ivoire, and Senegal), including at least one comparative paper. Final reports have been completed for each of these studies and many excellent papers could be produced. For example, an examination could be made of all cases of maternal death identified in the course of each of the studies, with a focus on strategies to reduce preventable causes of maternal mortality.

A set of proposals on maternal mortality has been prepared for a U.S. foundation and await funding. Included, for example, are evaluations of the impact of mass media programs to communicate very simple messages designed to help women know the warning signs of when they should seek emergency care, which we think could reduce maternal deaths.

Referral of high risk women is a very important part of a good MCH program. More research is needed on how referral systems can be improved including referral by traditional birth attendants.

#### **D. Natural Family Planning**

The goal of current work is to complete 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.

The vaginal aspiration technique developed by Dr. Gebhard Schumacher, of the University of Chicago's Department of Obstetrics/Gynecology, and initially supported by FHI continues to be tested by other groups. FHI supported the development of Home Assay Kits with Dr. James Brown of the Royal Women's Hospital in Melbourne, Australia. 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 A.I.D. funded NFP project at Georgetown University, Washington, DC.

#### 1. Research to Improve NFP Methods

##### a) Multicenter: Study of NFP use by Breastfeeding Women in Canada, England, and Australia

FHI is conducting a multi-center study of NFP use among breastfeeding women with SERENA, Canada, Birmingham Maternity Hospital, England and Westmead Hospital, Australia; the latter two are being done with financial 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 main objective of the study is to evaluate the contraceptive effectiveness of the symptothermal method of NFP used during lactation. The data analysis will also 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 completed at all sites (25 women per location) and all centers are in the follow-up data collection phase. Follow-up is expected to end in Fiscal Year 1989 and the termination criterion is for the women to experience two normal cycles post partum.

## 2. Evaluation of NFP Service Programs

### a) Implementation and Evaluation of an NFP Program in Lima, Peru

A lengthy narrative report has been submitted by ATLF (Association Trabajo Laico Familiar) in Lima, documenting the history of the NFP project. The English translation has been edited and will be available for distribution upon the concurrence of ATLF. A report of the data collected by FHI will be available in fiscal year 1989.

b) 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. Details of the study were presented in the semi-annual report.

Preliminary study results were presented at the Ottawa IFFLP Congress in June 1986. A paper entitled "Ovulation Method (OM) of NFP in Developing Countries: Efficacy and Research Needs" was prepared by Drs. Miriam Labbok and Hanna Klaus and presented at the 1987 APHA annual meeting. The paper has been published in Studies in Family Planning. It found that NFP users in the four countries came from a diversity of religious and social backgrounds. The study has also shown the following: 1) many acceptors attend instruction sessions alone in all programs; 2) acceptors come from a variety of socioeconomic backgrounds and previous family planning experience; and 3) the percent of couples who have discussed family size is not, apparently, influenced by prior family planning experience. A second paper entitled "Factors Related to Ovulation Method Efficacy in Three Programs: Bangladesh, Kenya, and Korea" was published in the June 1988 issue of Contraception.

c) 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. The second project was 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. A total of about 1,250 ever-users of NFP were interviewed. The final report for both projects is currently under review. The KCS is planning to publish the report as a monograph.

d) 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, and use-effectiveness phases of three NFP methods: 1) the ovulation method, 2) the modified mucus method and 3) a mix of the two methods. The project is being carried out in five locations (Cilacap, Ruteng, Maumere, Kupang, and Atambua) in Indonesia where there are ongoing NFP programs. The implementing agency is

PERDHAKI (Voluntary Health Services Association of Indonesia).

A total of 912 acceptors were recruited. The mean age of all the acceptors was 28 and they had been married for an average of eight years. The average number of additional children wanted by the acceptors was 1.6. The acceptors of the mixed method generally had a lower socio-economic status than the other two groups. Fear of or actual side effects of appliance methods of family planning was the primary reason for using NFP. A report based on the admissions records was prepared and was discussed at a project review meeting in August 1987.

The collection of the data from the use-effectiveness phase was completed in July 1988. The data are now being cleaned and analyzed. The National Family Planning Coordination Board (BKKBN) has requested that the findings be presented in its semi-annual meeting in March 1989 for consideration for policy making and program development. A visit to help the Indonesians with data analysis will take place in early October 1988.

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

#### a) Sri Lanka: Traditional Contraceptive Survey

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 original purpose was to

investigate the reasons for the widespread use of "non-program" methods. However, after discussions between Census Bureau staff and data users in Sri Lanka (Family Health Bureau; FPA) the Sri Lanka Census Bureau, in consultation with FHI, decided to broaden the scope of the survey to add traditional methods of contraception; to examine husbands' attitudes and reported experience with contraceptive use; and to examine other issues such as method-specific side effects, and husband and wife communication and decision-making in family planning matters. 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 and a publication in Studies in Family Planning resulted. The findings of the first phase were utilized to develop the survey questionnaire.

More than 2,300 women of reproductive age and 577 of their husbands were interviewed for this study. A seminar to highlight preliminary findings of the study was held in Colombo in May 1986. The Final 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. It is currently being printed in Sri Lanka.

b) Sri Lanka: Trends and Determinants of Natural Family Planning Use

The 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 as well as more recently. FHI supported a project with the Carolina Population Center of the University of North Carolina at Chapel Hill, N.C. 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 has been 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) 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 was presented at the annual meeting of the Population Association of America in April 1987. A revised version of this paper is under review for publication.

In September 1987, FHI contracted with CPC to carry out more comprehensive analysis on contraceptive method choice in Sri Lanka, including data from the 1979 Sri Lanka Fertility Survey. A paper on method switching will be presented at the 1988 P.A.A. meeting.

These papers have been accepted for publication in Contraceptive Use Dynamics, a special supplement of Journal of Biosocial Science. They are expected to appear in March 1989.

FHI has also been invited to present a methodological paper based on the Sri Lanka study in an Expert Group Seminar on Contraceptive Use Effectiveness to be sponsored by the United Nations Population Division in New York in December 1988.

c) Sri Lanka: Use-effectiveness of Contraceptives

The 'clinical effectiveness' of various contraceptive methods is well known. However, very little is known about 'use effectiveness' (which refers to both technical failure of a method and the failure to use a method properly in the actual life conditions), especially in non-clinical populations in developing countries. Further, the use-effectiveness of non-program methods of family planning (such as the calendar rhythm or withdrawal) and use of such methods in combination with other program methods of family planning have rarely been studied. Yet such data are necessary for accurately assessing the impact of contraceptive use on fertility at the aggregate level and for evaluating the efficacy of the methods in regulating fertility at the individual level.

In 1986, FHI, in collaboration with the Family Planning Association of Sri Lanka, fielded a survey designed to investigate the

use-effectiveness of program and non-program methods of contraceptives as well as combined use of the methods in Sri Lanka. The methodology was similar to the one proposed by John Laing in the Philippines.

The preliminary results showed that there is a large variation in continuation rates for temporary methods of family planning. For program methods (pill, IUD, injectables, and condom), the annual continuation rates ranged from 83% (IUD) to 32% (condom). In contrast, the annual continuation rates for non-program methods (safe period which refers to calendar rhythm, withdrawal, abstinence, and other traditional) ranged from 38% to 50%. More importantly, the continuation rate for safe period and withdrawal was 57%, nearly as high as that of injectables.

The Pearl Pregnancy Rate expressed in terms of 100 women years of experience was nearly 8, while it was 13 for condoms. Safe period and withdrawal had PPR's of 32% and 34%, respectively. In contrast, when safe period was practiced in combination with condoms, the rate was only 8. Similarly, the combined use of safe period and withdrawal had considerably lower failure rates than when these methods were used individually.

Although the failure rates for the use of safe period and withdrawal, were higher than for other program methods, the annual continuation rates were high. This implies that the impact of non-program methods on fertility in the long-run is probably more substantial than

previously realized. Furthermore, since combined methods have a remarkably high use-effectiveness, family planning programs may do well to promote the use of reversible methods such as condoms in combination with calendar rhythm. A study of the Fertility Awareness Method (safe period plus condoms) to be conducted in Sri Lanka may be funded by the World Health Organization.

#### **E. Breastfeeding Studies**

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 in some developing countries, 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.

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.

1) Multi-Center Longitudinal Study of Breastfeeding and Return to Fertility in Four Developing Countries

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

The results of this study have been described in previous reports. The major findings from Mexico were published in Fertility and Sterility. The results from Thailand and Egypt have been submitted for publication. The results from Pakistan will be evaluated in Fiscal Year 1989. In this center the recovery of amenorrhea or pregnancy will be evaluated, and not the return of ovulation.

Three milestones easily observed by the mother, namely the first vaginal bleeding episode, the introduction of supplements and the child's 6-month birthday, were found to warn women of the recovery of ovulation. Before the occurrence of any one of those milestones, 88%, 96% and 100% of the volunteers in Thailand, Mexico and Egypt respectively were still anovular. This suggests that family planning outreach can be scheduled for the baby's 6-month birthday, and mothers instructed to seek family planning sooner if they bleed or supplement. The findings from these studies as well as the work of other investigators inspired a conference on the use of lactational amenorrhea for family planning. (See E.h. "Consensus Conference on

Lactation Infertility").

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

FHI supported a prospective study with Silliman University in Dumaguete, Philippines, in which pregnant women were taught guidelines for maximizing the nutritional and contraceptive benefits of breastfeeding. A control group of mothers not exposed to such teaching was also monitored. The duration of postpartum amenorrhea and patterns of infant feeding were compared between a group receiving the educational program and a control group. Mothers in the education group refrained from bottle use and delayed supplementation longer than the controls, but the duration of amenorrhea was the **same** in both groups. It is hypothesized that the similar frequencies and durations of breastfeeding in the groups was responsible for the similarity in amenorrhea. Education group babies had fewer illnesses, especially gastrointestinal, but growth was comparable between the two groups.

The final report of this project has been completed and a paper containing the major findings has been submitted for publication. Additional papers are being prepared on the health and growth of the infants on the patterns and perceptions of bleeding and a hazards model approach to analysis of the data.

3) 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 in 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. This study is similar to the aforementioned one in Dumaguete, although the education program was modified for the urban population.

In February and March 1988, Ms. Gail Savina, the Project Coordinator in the Dumaguete Study was contracted as a consultant by FHI to visit the PGH project to assess general operations and the education program. She provided some suggestions for making the health education sessions more interactive and more goal oriented while commending the health educators for their sensitivity and rapport with the mothers.

An FHI monitor also visited the study in May 1988 and found, as did the consultant, that coordination of tasks among project staff to be well defined. Administratively, financial arrangements for the study have been inordinately time-consuming (e.g. bank wire transfers have occasionally taken months to clear) but the project staff have persevered throughout. At the time of the visit, 49 of the 100 mothers in the experimental group were still breastfeeding and being given health education.

Originally scheduled for completion in March 1989, an extension of about six months will be sought in order to complete final follow-up and provide sufficient time for data analysis.

#### 4) Indonesia: Breastfeeding and Health Professionals

A paper has been prepared which analyzes data based on an FHI-supported study in Indonesia. The paper presents findings on knowledge, attitudes, and practices regarding breastfeeding management in the modern health sector in Indonesia. The study was carried out in teaching hospitals in major cities throughout Indonesia. The methodology applied was a standard survey questionnaire and an observation checklist of several elements of hospital practices.

The results showed that although the perinatal health care providers' attitudes toward breastfeeding were very positive, there were many areas in which knowledge was incomplete. A wide variation existed in advice given to breastfeeding mothers. The content of advice on breastfeeding was not always sound. Many thought that many different illnesses were a contraindication to breastfeeding, and almost one third felt breastfeeding should follow a fixed schedule rather than the baby's needs. Most of the providers did not seem to have the knowledge to cope with the common problem of insufficient breastmilk supply syndrome. Similarly, although support for the concept of rooming-in was strong, about a third of respondents did not think the mother and infant should be together for the full 24 hours implied by true rooming-in. Fears about the possibility of increased risk of infection with rooming-in were expressed. These and other misconceptions about rooming-in imply that a consistent, well-designed training program needs to be carried out nationally which will provide the necessary

information to health care providers about this important aspect of early infant care.

The results of the study were utilized in designing a series of training workshops on breastfeeding in Indonesia. The paper has been accepted for publication in Social Science and Medicine.

5) 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 concisely summarizes research on the effectiveness of breastfeeding, compared with other methods used in the postpartum period. Using a question and answer format, it suggests rough 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, to be produced by WHO, will be ready for production by late 1988. If funds are available, FHI will support an Arabic version of the pamphlet for distribution in the Middle East.

6) Breastfeeding, Birth Spacing and Child Survival

Using data from 29 developing countries, an analysis 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 could translate into a 12% rise in fertility, while halving the duration of breastfeeding could 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 also 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.

This paper has been published in Nature and was selected for coverage by the London Times.

7) Nepal: Breastfeeding (Secondary Data Analysis)

(a) This paper shows that, in Nepal, breastfeeding almost completely explains the effects of following birth interval on childhood mortality during the first 18 months of age, and partially explains the effects of following birth interval on childhood mortality between 18 and 60 months of age.

Breastfeeding does not explain the effect of preceding birth interval on childhood mortality. The analysis is based on application of hazard models to data from the Nepal Fertility Survey. This paper has been accepted for publication in Demography.

(b) Another paper investigates the effects of ethnicity on early childhood mortality in Nepal. The approach is through a series of hazard models, which incorporate ethnicity, year of birth, mother's literacy, father's literacy, rural-urban residence, region, sex, maternal age, survivorship of previous birth, previous birth interval, and breastfeeding as covariates. The analysis indicates that ethnic differentials in early childhood mortality are not explained by the other covariates. An implication is that future studies of ethnic differentials need to collect more detailed information on circumstances of childbirth and childrearing practices relating to health. A byproduct of the analysis is an improved specification of breastfeeding as an age-varying covariate that indicates that breastfeeding (relative to not breastfeeding) reduces age-specific mortality risks during the first two years of life by about 75%. This paper has been accepted for the Journal of Biosocial Science for publication.

#### 8) Bellagic Consensus Conference on Lactational Infertility

With support from the Rockefeller Foundation, WHO and A.I.D., the Bellagio Conference Center in Northern Italy was the venue for a small expert meeting from August 22-26, 1988 to discuss recent research in lactational infertility. Unlike most scientific meetings that are built around the presentation of formal papers, the researchers at the meeting presented original ideas and data in a discussion rather than

didactic setting, in order to generate new hypotheses and to test the notion that current data are sufficient to give at least preliminary guidelines for the use of breastfeeding as a family planning method.

The 25 participants achieved consensus in their discussions of the following questions:

- (a) Based on our current knowledge, what should breastfeeding women be told about the time to initiate family planning methods?
  
- (b) What studies are needed to advance our understanding of lactational infertility or to improve upon the advice that can be offered to breastfeeding mothers about their degree of protection from breastfeeding?

A consensus statement on the use of breastfeeding for family planning was prepared. This summary will be published by Lancet in the November 5, 1988 issue. The larger statement plus a report on the research priorities identified by the group will be published in early 1989.

Future Plans: Breastfeeding

1. Evaluation of Program to Promote Breastfeeding

We will be developing new projects on breastfeeding--particularly on breastfeeding promotion. Projects will be developed for Honduras and

the Philippines and possibly elsewhere. FHI will also participate in meetings planned on breastfeeding promotion.

a) Honduras

Since 1982, the Project to Promote Breastfeeding (PROALMA - Proyecto de Apoyo a la Lactancia Materna) has been promoting breastfeeding in the major urban hospitals and clinics of the Honduras Social Security Institute and the Ministry of Public Health in Tegucigalpa and San Pedro Sula. PROALMA activities have been directed at health care personnel in those hospitals who counsel women about breastfeeding at the time of delivery. In 1986, activities were extended to Ministry hospitals in all eight health regions of the country.

To evaluate the impact of Phase I and II activities, baseline and follow-up surveys were conducted in 1982 and 1985, and again in 1986 and 1988. Copies of the data tapes of those community level data will be analyzed at the Carolina Population Center by Dr. Barry Popkin. Examination of breastfeeding trends at a national level will be carried out at FHI using the nationally representative surveys of 1981 (Encuesta Nacional de Prevalencia de Anticonceptivos - ENPA), 1984 (Maternal-Child Health and Family Planning Survey - MCH/FP), and 1987 (Epidemiology and Family Health Survey - EFHS).

Both descriptive analyses and multivariate techniques will be used to determine if there is a correlation between breastfeeding practices, such as ever or never breastfeed, mean duration of breastfeeding, age

at supplementation, and place of birth.

b) Philippines

During a July 1988 site visit to the Philippines, project ideas on breastfeeding promotion were received from about 30 local organizations. Among the inexpensive proposals of particular interest to FHI were: (1) Follow up of women after discharge from hospitals which have initiated rooming-in and BF promotion programs; (2) continued monitoring of BF trends, in particular, replication of previous analyses of BF trends and patterns by urban/rural and education for 1988 data; (3) analysis of the costs and savings associated with rooming-in which will give a 15-year series of data on BF; and (4) integration of counselling on BF into family planning programs. Consideration of more expensive proposals will need to await development of a buy-in for BF promotion in the Philippines.

A briefing in Washington is planned for mid-October 1988 to discuss the Philippines projects identified and funding possibilities.

## **V. FIELD DEVELOPMENT AND TRAINING**

The Field Development and Training Division (FDT) has as its primary objectives the development of strong research organizations 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. 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 negotiations process through local governments and USAID Missions, study monitoring as needed, and coordination of international travel.

Activities during this reporting period cover the following areas: institutional development; training; support for conferences, seminars, and expert meetings; transfer of contraceptive technology; and information dissemination.

### **A. Institutional Development**

#### **1. Support to Family Health Research Centers (FHRCs)**

Support to five maturing Family Health Research Centers (FHRCs) and

several newer organizations remains the major activity sponsored by FDT. The FHRCs vary in focus, structure, and level of development depending on the socio-political environment in each country, and on the duration of FHI involvement with these programs. FDT's goal for each of these programs is to develop competent, well-managed and securely funded institutions capable of designing and implementing high quality research to meet a variety of needs in their own countries.

A third FHRC Directors Conference was held at FHI Headquarters, November 2-6, 1987. The purpose of this conference was to consult and exchange views on a wide range of topics of mutual interest, including research directions, financial management systems, training, and protection of human subjects. These periodic meetings (every 18-24 months) have proved extremely valuable to both FHI and the FHRCs. A fourth FHRC Directors Conference is tentatively planned for March 1989, in Egypt, hosted by the Egyptian Fertility Care Society.

The following sections describe each program and the development activities underway with FHI support through core subagreements, and summarizes other FHI contract activities being carried out by the FHRCs.

a. Bangladesh Fertility Research Programme (BFRP)

The Bangladesh Fertility Research Programme (BFRP) has an extensive network of centers and clinical investigators in Bangladesh. It has historically been the primary coordinator of clinical trials research

in Bangladesh, and by virtue of its recent efforts, has been recognized by the Ministry of Health and Family Planning as the organization through which new contraceptives are introduced into the country. Although FHI, with central and bilateral A.I.D. support, is its primary funding source, it also receives support from several other organizations.

The BFRP was established in 1976 as a quasi-governmental research organization funded by FHI. It operates under the guidance of an Executive Council chaired by the Secretary of the Ministry of Health and Family Planning. The BFRP coordinates a large network of hospitals, clinics, and researchers, and has a core administrative staff responsible for planning, implementing, and monitoring research.

The beginning of the year was marked by a number of strikes preceding the local elections held at the beginning of March 1988. These disturbances, which closed the office for many days over a four-month period, made it very difficult for the BFRP to function at normal efficiency. However, studies were continued at 12 different centers. Studies supported by FHI included three 200-case pre-introductory NORPLANT contraceptive implant trials, and a comparative study of Triquilar and Marvelon. A study of oral contraceptives with versus without iron which began in April 1987 was terminated in December 1987 because of difficulty in recruitment, and a shortage of resources.

With FHI assistance, the BFRP developed a protocol for a new study of prophylactic antibiotics with female sterilization cases, which was

initiated in September 1987 at eight centers. The purpose of the study is to compare post-operative infection rates after use of tetracycline, ampicillin, or a placebo. Data collection is now complete, and the data are being analyzed at the BFRP on its new computer. It is an important study relevant to both the safety and the cost of Bangladesh's family planning program.

The most ambitious undertaking of the year was the initiation of an expanded NORPLANT contraceptive implants program. This program has several components, including: development of IE&C materials and a training curriculum; establishment of a training center, training of physicians and support staff, initiation of expanded clinical trial caseloads at the three existing centers; and establishment of three new centers outside of Dhaka. In addition, a surveillance/registry system was devised and implemented during this period to keep track of acceptors who leave the immediate study area.

Each of the experienced centers is recruiting 250 clients/year over three years. The new centers are recruiting 200 clients/year over two years. All of the experienced and new centers have taken part in the training programs for this initiative, and new study management materials, developed by the BFRP, have been installed in each center to assure quality and maximum follow-up. The BFRP has also hired two new staff to monitor the centers on a regular basis.

In June 1988 the BFRP held the First National Conference on NORPLANT in Dhaka, with funding from Leiras Medica, the pharmaceutical firm that

manufactures NORPLANT. FHI supported the BFRP at the conference through the presence of a staff member who reviewed papers before the conference, presented a paper on NORPLANT, and participated in the general discussions. It is essential that the acceptability and relevance of NORPLANT to the all-important, government family planning program be established as soon as possible.

Two BFRP staff members attended an FHI-sponsored Data Analysis Workshop in Indonesia in January 1988. This 1-week workshop gave training in data analysis skills to staff from all the FHRCs. (See also discussion of the FHRC Data Analysis Workshop under Training section).

The BFRP has developed a six-week course in research methods, using their own staff as well as local experts. The first such course was held in 1987 and a second, attended by 20 participants from 12 local organizations, was held in January-February 1988.

Efforts to install the TI-352 microcomputer in November 1987 were frustrated because the microcomputer had been damaged during the shipping or in the custody of Bangladesh customs. FHI staff have worked in the U.S.A. and in Bangladesh to get the computer functioning again, but another visit is necessary before the BFRP can begin to really use the computer in a meaningful way. In the meantime, FHI helped the BFRP purchase (using Mission buy-in funds) an IBM PS-2 system, which is fully operational. The BFRP has also purchased an IBM XT clone, which is also being used for data and word processing.

With the help of consultants from Deloitte, Huskins and Sells, (DH&S) an international accounting and financial management firm, a new double-entry accounting system was installed during the previous fiscal year to assist the BFRP in tracking multiple projects and assigning overhead costs appropriately. The current fiscal year is the first complete year the system has been in operation. It seems to have been well accepted and understood by both BFRP accounting staff and administration, but has not yet reached its full potential as a management tool.

In fulfillment of the long-term goals agreed to by FHI and the BFRP, a stronger accounting system has helped the BFRP obtain funds from other donors. During the reporting period, the BFRP has conducted a study of contraceptive use dynamics (funded by WHO) and long term IUD follow-up (funded by University Research Corporation). The BFRP has also been awarded funds from the Ford Foundation for a maternal morbidity project and for institutional development.

During this period, the BFRP shifted its offices to more spacious facilities nearby. The new office accommodates an increased number of staff members hired for other FHI (funded by buy-ins and discussed elsewhere in this document) and non-FHI projects.

b. Egyptian Fertility Care Society (EFCS)

The Egyptian Fertility Care Society (EFCS) is a voluntary organization affiliated with the Egyptian Medical Association. Founded in 1974 with

a membership of over 260 medical specialists, the EFCS works closely with the Egyptian Ministry of Health (MOH), the National Population Council (NPC), the Egyptian Society of Obstetrics/Gynecology and the Egyptian Family Planning Association.

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

FHI began support for the EFCS in October 1980. The purpose of this support was to develop an independent research institution through training and research assistance. As of January 1, 1988 USAID/Egypt assumed funding for field costs in the EFCS core support/institutional development subgrant through a buy-in to FHI's Cooperative Agreement. FHI continues to provide technical assistance and considerable other support not included by the buy-in.

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 of

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 follow-up training under the current subagreement.

The clearest indicator of the success of EFCS occurred in August 1986 when it was designated by the National Population Council as the research agency to manage and coordinate a three year bilaterally funded NORPLANT project in Egypt (see Section on Transfer of Contraceptive Technology). This project gives national recognition to the EFCS and broadens EFCS's experience for coordinating a large multicenter 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. The large multi-center NORPLANT study includes provision for an additional computer through bilateral funds.

Training activities during FY 1988 are described below:

The EFCS Data Analyst, under a joint FHI/Population Council agreement, received extended training in biostatistics and analytic techniques at the University of North Carolina at Chapel Hill and at FHI Headquarters.

Two EFCS staff members in the Research Division attended the FHI sponsored Data Analysis Workshop in Indonesia. The objective of this

workshop was to establish standard methods of analysis of contraceptive clinical trials data for the five FHI supported Family Health Research Centers in Egypt, Thailand, Sri Lanka, Bangladesh and Indonesia.

A four-week session of financial management training was conducted by a Senior Consultant from Deloitte Haskins and Sells. Training included automation of the EFCS accounting system, installation and operation of the Solomon III software package and overall program financial management. EFCS continues to develop their financial management capabilities through a separate agreement with the financial accounting and management firm of Price Waterhouse. This international firm has offices in Egypt.

FHI's Director of Development spent one week at EFCS to assist staff to develop their skills in fund-raising and long range financial planning. A preliminary fund-raising strategy was developed during this site visit.

The FHI Information Coordinator provided assistance with bibliographic database management software and CD-ROM equipment and databases.

In the area of research:

A longitudinal study of the ML 250 IUD is being conducted to follow up an earlier EFCS 3-Way IUD study (TCu 200 versus ML 250 versus Lippes Loop). This study evaluates the long term usage of this IUD.

A multicenter maternity care monitoring study continues with the expansion of this program to two MOH hospitals in 1988 and three MOH hospitals in 1989.

A comparative study of the oral contraceptives Triovlar versus Ovril versus Nordette involving 2,100 cases randomly assigned and divided among ten centers continued. Recruitment was completed for this study in December 1987. Funds under this subagreement will cover patient follow-up during 1988 and analysis and report preparation in 1989.

Also in FY 1988 under a separate subcontract the EFCS initiated the management and implementation of \$2.2 million, three-year multicenter NORPLANT<sup>®</sup> research project mentioned above in the general description of EFCS activities.

In the area of information dissemination:

The EFCS conducted an Annual Investigators Meeting on July 14, 1988 at the National Population Council (NPC) offices in Cairo, Egypt. This meeting afforded EFCS investigators an opportunity to discuss their research projects.

A Clinical Trials Workshop was conducted from July 16 - 21, 1988 at the NPC offices in Cairo, Egypt. Sixteen physicians from the Ministry of Health Teaching Hospitals were trained in the design and implementation of clinical trials.

The EFCS published several issues of "Fertility Care Bulletin."

During 1989 the following activities are planned:

- Continuation and expansion of the MCM study;
- Conducting a Clinical Trials workshop;
- Long-term follow-up of the three-way IUD study;
- Follow-up of the Comparative Three-Way Oral Contraceptive Study (Triovlar versus Ovral versus Nordette);
- Local training for the Technical Officer on computer hardware maintenance and system diagnostics;
- Hiring of a Communications Officer and IE&C training at FHI;
- Initiation of a retrospective study using previously collected Egyptian clinical research data provided by FHI.

As with BFRP, the EFCS is diversifying its funding. On February 24-26, 1988, together with the Egyptian Society of Gynecology and Obstetrics and with funding from the Ford Foundation, the EFCS organized a Safe Motherhood Meeting in Ismailia, Egypt. The opening ceremony was attended by the First Lady of Egypt, Mrs. Mubarak, and the Minister of Health, Dr. Ragheb Dwidar. The meeting was attended by over 100 Egyptian professional representing all major governmental agencies and served to focus attention on maternal mortality in Egypt.

The EFCS has become a research institute of national prominence. Now with this greater diversification of funding and strengthened ability in financial management/planning, the EFCS is

moving towards financial independence and institutional autonomy.

c. Indonesian 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 member centers that are Government University teaching hospital departments of OB/GYN. The BKS PENFIN was established to serve primarily 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 and is attracting funding from a variety of sources.

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 core support funding from FHI has declined over 50 percent since 1985, and will end entirely upon the completion of their current subagreement on December 31, 1988. FHI will continue to contract with the BKS PENFIN to conduct other specific activities on a fixed cost or cost reimbursement basis. As core support funding is phased out, FHI (and all other BKS PENFIN funding sources) will be asked to pay a fair share of the BKS PENFIN's

overhead operational costs. FHI has contracted with the accounting firm Deloitte, Haskins and Sells to provide technical assistance to the BKS PENFIN (and other FHRCs as mentioned in this report) in establishing the systems necessary to manage multiple contracts with full direct and indirect cost allocation and recovery. These basic systems have been implemented, and further DH&S assistance is planned to automate their accounting and reporting through use of the PC and commercially available software.

As both the capacity of the BKS PENFIN centers to do clinical research and the capacity of the Secretariat at Bandung to coordinate and administer such research (including data processing, analysis and computer skills and budgeting and accounting 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. (The TI-1 Microcomputer provided in 1982 has been transferred to BKS PENFIN's center in Yogyakarta.) They have also acquired IBM-compatible PCs for administrative text processing and data analysis applications through use of commercially available software.

BKS PENFIN is currently conducting two multi-center clinical trials under contract with FHI: A 3,000 case evaluation of the TCu 380A and a 300-case study of the Filshie Clip versus Tubal Ring (via laparoscopy).

BKS PENFIN has recently attracted funding from WHO, IDRC, and the Indonesian Ministry of Health for a major new study of Maternal and

Perinatal Mortality in Central Java, scheduled to begin soon. Other studies, funded by non-FHI sources, are also continuing, and new ones are being planned or proposed. BKS PENFIN is trying to maintain a diversified program of research including both contraceptive and reproductive health components, with a correspondingly diversified range of funding sources. Also, BKS PENFIN makes its data processing facilities available under subcontract or a fee for services mechanism to other organizations, including PERDHAKI (which is conducting an FHI study of three NFP approaches) and the West Java Provincial Health Department.

The first local workshop in clinical trials research methods was conducted by the BKS PENFIN in October 1987, to strengthen the skills of five selected BKS PENFIN centers. Another clinical trials methods workshop, under contract to the National Family Planning Coordinating Board (BKKBN), was carried out by the BKS PENFIN (with limited assistance by FHI staff biostatisticians) during the week of January 18-23, 1988. The BKS PENFIN has submitted a funding proposal to FHI to support another workshop of this nature for additional BKS PENFIN Centers which did not participate in the October 1987 training. This capacity for training is a direct result of BKS PENFIN's participation in a regional training workshop sponsored by FHI in Singapore in May 1987. BKS PENFIN hopes to continue marketing this and other training activities for both the private and government sectors in Indonesia.

Planning is underway by BKS PENFIN and FHI to jointly conduct a training workshop on research and other applications of PCs for

personnel from all 14 BKS PENFIN centers. It is hoped that this type of training may also be replicated later by the BKS PENFIN alone for interested individuals or organizations in Indonesia on a fee for service or cost reimbursement basis. Other projects under consideration for FHI support in 1989 include an expanded program of information dissemination, an assessment of five year recall of NORPLANT acceptors, and the BKS PENFIN's annual meeting.

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

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

During this fiscal year, activity centered on continued clinical trial research, network development and planning for future initiatives in terms of increasing the FPA's ability to analyze and write up their own research results.

Subcontract clinical trials of NORPLANT in both Colombo and Kandy continued, with all FHI-sponsored studies now in the follow-up stage. Partly as a result of their significant role in the introductory trials of NORPLANT in Sri Lanka, the FPA was asked to participate in a pilot post-marketing research study and to coordinate a 1000-case post

marketing surveillance study being organized by the World Health Organization. Data from the FHI-sponsored NORPLANT studies at the FPA/SL, was also studied by the Ministry of Health's Formulary Committee, the local agency that decides on the use of new drugs. The data were an important factor in the committee's decision to approve NORPLANT for use in Sri Lanka late in 1987.

Two other subcontract studies were recently completed: a 300-case comparative study of the oral contraceptives Triquilar versus Lo-Femenal, and a 300-case comparative IUD study of the TCU 380A versus the Multiload Cu250. During a visit by FHI staff to Sri Lanka in July 1988, plans were made to pursue the idea of providing the two physicians most involved with these studies with an opportunity to receive training at FHI so that they can write up their own results and prepare a professional presentation.

A second study of the TCU 380A and the Multiload Cu250, being conducted by a physician with the Faculty of Medicine in Galle, was also recently completed. This physician has been encouraged to present the results from his study at the Annual Sri Lankan Medical Meeting.

A comparative vasectomy study (the standard incision technique vs. the Li puncture technique) got underway during this reporting period and has almost reached the halfway mark in terms of recruitment of the proposed 300 volunteers. This contract study is being supervised by the FPA and conducted by Dr. Beligawatte of the Sri Lankan Association

of Voluntary Surgical Contraception (SLAVSC). The FPA will review the study forms for accuracy prior to their being sent to FHI, just as they did for the IUD study in Galle.

In addition to the contract clinical trials studies mentioned above, the FPA/SL has completed field work on the Sri Lankan Young Adults Reproductive Health Survey. This is an expansion of a pilot study of Colombo youth completed in 1986. Data analysis has begun on the new study which has a larger and more nationally representative population and asks reproductive health and family planning questions which will be useful for programmatic purposes. A preliminary report of this survey will be presented at a seminar to be held in Sri Lanka early in FY '89.

A report written by Dr. Sriani Basnayake, Medical Director of FPA, in conjunction with FHI staff Shyam Thapa and Sandor Balogh, entitled "Evaluation of Safety, Efficacy and Acceptability of NORPLANT Implants in Sri Lanka," was published in the January/February 1988 issue of Studies in Family Planning. Dr. Basnayake has also written an article entitled "NORPLANT, a Boon to Women" which was published in the Sri Lankan newspaper The Island.

During this fiscal year, two FPA staff members attended a week-long data analysis workshop sponsored by FHI and BKS PENFIN in Bandung, Indonesia. The purpose of the workshop was to provide more detailed data analysis techniques to FHRC staff members closely involved in preparing tables and analyzing data in reproductive epidemiology

studies. One attendee was a senior staff member in the FPA's Evaluation and Research section; the other was the FPA's computer programmer.

In 1984, FHI donated a Texas Instruments WD 500 computer to the FPA and since that time their capability in computer processing and their computer equipment has increased significantly. While this has expanded the organization's capabilities, it has also increased the need of their medical staff to know more about computers. Plans are, therefore, underway for FHI to sponsor a "computer literacy" workshop specifically for Sri Lankan physicians.

e. Thailand Fertility Research Association (TFRA)

The TFRA was established with FHI assistance in 1979 to serve as a national center for research in support of the National Family Planning Program (NFPP) of Thailand. The TFRA is a private, non-profit organization that operates within the administrative structure of the Ministry of Public Health (MOPH) in Bangkok and, therefore, enjoys a close two-way relationship with the NFPP. As such, it is uniquely situated to enlist and coordinate capable researchers from both the private and public sectors--including centers serving small towns and rural populations. The TFRA's network consists of physician researchers from each of the country's medical schools and from numerous MOPH hospitals and MCH centers all over Thailand. The TFRA's close association with the MOPH also assures that research findings will reach relevant policymakers.

Successive FHI subagreements 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 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.

During this reporting period, follow-up work continued on two studies initiated under the previous core support subagreement:

- Comparative interval female sterilization study: Filshie clip vs tubal ring via laparoscopy, and
  
- Comparative interval female sterilization study: Filshie clip vs modified Pomeroy technique via minilaparotomy.

A study of OC pill compliance, designed by FHI staff, was funded during this reporting period by USAID/Thailand. In addition, under a contract with FHI, the TFRA initiated a crossover OC study in Haadyai, comparing the side-effects and acceptability of two OCs currently available through the National Family Planning Program.

The TFRA has conducted several studies under separate contracts with FHI and other funding sources. Field work is complete for these three studies funded by FHI and report writing is underway:

1. Infant health follow-up in Sukhothai;
2. Postpartum sterilization by nurses; and
3. Progestogen-only pills for lactating women.

Three other studies have been funded by FHI and other sources:

1. Analysis of NORPLANT acceptability survey data (MOPH)
2. KAP study of populations at high risk of AIDS (FHI)
3. OC pill compliance study (USAID)

The Seventh Annual Scientific Meeting of the Thailand Fertility Research Association (TFRA) was held in September 1988 in Pattaya, Thailand. It was attended by 150 physicians, government officials, medical students, and donor representatives. This annual event has gained in prestige as its scientific value has increased over the years. Now it is the only such conference in the country, and as such, is the only opportunity for scientists and researchers to gather and discuss recent study findings in the area of reproductive health. This year FHI funded the conference through a grant to the TFRA. Some costs were also borne by pharmaceutical companies.

f. Technical Assistance from Deloitte, Haskins and Sells (DH&S) to the Family Health Research Centers (FHRCs)

Several years ago, FHI embarked on a program to reduce the reliance of the FHRCs on FHI core funding and encourage them to develop a wider range of funding sources. A plan was developed to phase out core funding to the more mature FHRCs over a five-year period, while simultaneously strengthening them through the provision of technical assistance. The technical assistance was of several varieties: assistance in identification of alternative funding sources, strengthening the planning and monitoring of projects, and improving their financial management capabilities. Even after phasing out core support funding, FHI intends to sustain its support of the FHRCs through continued provision of technical assistance, separate research contracts with other divisions of FHI, and funding of special activities, e.g. annual scientific conferences. The five major FHRCs (Indonesia, Thailand, Sri Lanka, Bangladesh and Egypt) have all had their core funding reduced over the past three to four years. All have begun to seek support for their activities through research contracts with other donor agencies, their own governments, and pharmaceutical companies.

An integral part of this transition is being able to recover the overhead costs which had been covered by FHI core support from new contractual research projects. This requires the FHRCs to strengthen their overall financial management capabilities. They must be able to plan for future needs, obtain financial support to carry out their

program, have a workable system to recover costs from research contracts, and be able to demonstrate fiscal accountability to prospective donors.

FHI, through its contract with DH&S, has concentrated its technical assistance in financial management to three FHRCs: BFRP, EFCS, and BKS PENFIN. Phase I of this project assessed needs and planned the technical assistance. The second phase included the development of a generic FHRC accounting system model, the design of customized manuals for each FHRC, and site visits to train FHRC staff and implement the new system. This phase was extended through April 30, 1988, and also covered the development and implementation of an automated accounting and reporting system through use of a PC and commercially available software on a pilot basis at one FHRC (EFCS). An overall assessment of this and other aspects of the DH&S assistance to date and their proposals for additional work will be made in the next six months in order to determine how best to continue the strengthening of the FHRCs' financial management capacity.

Continued technical assistance in this area, by DH&S or others, will be incorporated into FHI's ongoing support to the respective FHRC's, rather than as a separate project under a single subcontract.

#### g. Other Technical Assistance and Development Activities

As resources permit and as local interest and absorptive capacities allow, FDT has initiated small institutional development programs in

other countries, currently in Mali, Niger, and Mexico. Core support for a similar program in Brazil (ABEPF), ended in November 1986, although activities with ABEPF have continued. Through buy-ins with USAID Missions, major institutional strengthening programs are underway in Egypt with the National Population Council, and planned in Kenya with the Department of Obstetrics and Gynecology at the University of Nairobi. FDT has also continued support for developing data processing capabilities within the FHRCs and other programs. Progress in these programs during this reporting period is described below.

(1) Technical Assistance to the AMPPF/Mali

FHI technical assistance to the Malian Family Planning Association (AMPPF) began in 1981. Broad-based assistance is continuing with the current two-year subagreement.

Acceptability and accessibility of contraceptive services are key issues which the AMPPF seeks to address. The AMPPF is interested in encouraging a more diversified contraceptive method mix and in expanding the family planning program to non-clinic settings. These steps are urgent and essential if meaningful services are ever to come to Mali. Since health professionals greatly influence client decisions, a KAP study (Knowledge, Attitudes and Practices) of health professionals to determine attitudes towards different contraceptive methods and towards different types of service delivery, i.e., community based distribution and social marketing, is being prepared. Physicians and midwives in Bamako and in each of the seven regions of

the country will be interviewed, and results will indicate the degree of support health professionals will give to proposed service delivery mechanisms.

At the beginning of 1988, a second surveillance study of IUD users was initiated to determine if expulsions and side effects, which were found previously to be high, have decreased after retraining of the midwives and better counseling of IUD users.

Monitoring of ongoing clinical trials of Ovrette in two MCH centers in Bamako continued. The quality of the data received has improved, now that the forms are reviewed and corrected by AMPPF staff before coming to FHI.

An activity being funded under the bilateral agreement between USAID and the Malian MOH is the construction of the new headquarters for the AMPPF. FHI is complementing this and other infrastructure development efforts by providing computer hardware, software and appropriate training to strengthen the AMPPF's capabilities in data processing, analysis and management. All of the above activities undertaken by FHI in Mali are aimed at generally strengthening the capacity of the AMPPF to carry out essential programmatic research, to influence attitudes and policies in Mali, and to develop and manage an effective and vital family planning services delivery program which is so urgently needed at present.

During 1987, FHI staff collaborated with the Sahel Institute, the Malian Family Planning Association (AMPPF), and the Family Health Division of the Ministry of Health to collect baseline data on: nutritional surveillance, vaccinations, oral rehydration and family planning.

Site visits were made in May 1987 to the fifteen participating Maternal and Child Health centers to gather information on present activities and the organization of the centers. AMPPF did a retrospective study of family planning clinic records (1985-86) to describe the characteristics of family planning acceptors, and the Sahel Institute gathered community-based data from the target area as part of the Demographic Health Services (DHS) survey. Data analysis was completed and a final report presented to USAID/Mali and the Malian Ministry of Health.

(2) Niger: Technical Assistance to the CNSF

The Centre National de Sante Familiale (CNSF) is the principal government agency providing family planning services in Niger. The Niger Ministry of Public Health and Social Affairs has requested FHI's technical assistance to the CNSF to strengthen its capacity to plan, manage and evaluate the national family health and family planning program in Niger.

The Family Planning Program in Niger is in a period of rapid expansion with services being extended to PMI's and maternities throughout Niamey

and in several departments around the country. It is important to the future of the program that new users get a positive impression of family planning services, and are not quickly discouraged. The CNSF is the model center for the Family Planning Program in Niger. A close examination of the problems in continuation of contraceptive use at the CNSF will provide important information for these new sites as well as for the CNSF.

The CNSF, in collaboration with FHI, has completed data collection on a surveillance study of the two most commonly prescribed pills in Niger, (Stediril and Minidril), to determine their side effects and continuation rates. One hundred fifty women in the study were followed up for 12 months or until they stopped taking the pill, whichever came first. The major finding was that discontinuation is very high, with over half of the women not returning for continued follow-up and supplies beyond six months. To find out the reasons for this discontinuation a study of all new acceptors of old methods is being planned for 1989.

Also in collaboration with FHI, the CNSF has carried out a Research Methodology Workshop which is detailed elsewhere in this report. Six research proposals were generated during the workshop, and the Ministry of Health has selected two studies for implementation with bilateral USAID funds and FHI assistance. The first project to be implemented with the Directorate of Family Planning in Niger at the CNSF is a study of contraceptive continuation/discontinuation in Niamey, Niger. The study will determine users' characteristics, their perceptions of

services offered by the CNSF, patterns of use of methods, constraints to continuation rates, rates of discontinuation over a six months period, and reasons for discontinuation. This research is aimed directly at developing IEC and other activities which will increase acceptability and continuation of family planning by couples in Niger.

The second project (to be implemented in FY '90) would expand the survey of new contraceptive users (Vanguard Acceptors Study of 1985 in Niamey) to one or two departments such as Zinder and/or Maradi.

(3) GIMIESAR: Mexico

As an outgrowth of the FHI supported epidemiologic training program at the Institute of Scientific Investigation of the University of Juarez, Durango, Mexico, the Mexican Inter-University 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 Methods Workshop. Currently there are six GIMIESAR affiliates.

FHI has provided core support to GIMIESAR during this fiscal year. The support provided 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. In particular, GIMIESAR developed a

five-year institutional development plan that will be forwarded to WHO and other sources of funding. FHI support will help GIMIESAR begin their development as a major epidemiologic research organization.

FHI has also 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 and GIMIESAR expects to further develop and expand their microcomputer capabilities, providing data analysis and processing support to the affiliates.

As the only inter-university epidemiologic research organization working in Mexico, GIMIESAR has attracted a great deal of attention from national health authorities. They are currently working with the national health ministry to address some of the more pressing epidemiologic concerns facing the Mexican maternal child health care program. Among the areas of focus for GIMIESAR is the provision of epidemiologic research methods training. During this reporting period FHI supported another Epidemiologic Research Methods Workshop in Durango, in which representatives from the GIMIESAR affiliates, other Mexican research centers and Central American scientists attended. This activity is reported elsewhere in this document.

#### (4) Egypt: Institutional Development Project (IDP/E)

The Institutional Development Project's major focus is to increase the family planning research coordination and information dissemination

capabilities of the Egyptian National Population Council. This project received USAID funding approval for a buy-in to FHI's Cooperative Agreement in June 1988. Multiple site visits were conducted by FHI staff and consultants in FY '88 to prepare for the initiation of this project. Specific purposes of the site visits were to identify the type and the amount of professional assistance needed for this program, assess staffing requirements for the NPC, estimate the regional level of effort and travel for FHI staff/consultants, finalize budget requirements, as well as discuss the various research projects included in this activity. In addition, FHI's Information Coordinator provided assistance and recommendations concerning the NPC library development, bibliographic data base management software and CD-ROM equipment and databases.

FHI will provide technical assistance for a period of three years to the NPC in the form of (a) management assistance, (b) training, (c) research planning, and (d) information dissemination and public relations. The focus of this activity will be to strengthen the NPC's capabilities to plan, coordinate, monitor and evaluate all population and family planning research activities by donor organizations and implementing agencies. A major emphasis will be the implementation of research activities as the project incorporates the development of twelve operations research projects and twenty other research projects over the three-year life of the program. This program includes a subcontract with E. Petrick & Associates for technical assistance to the NPC in research management.

(5) Egypt: Technical Assistance to Strengthen Egyptian Population Institutes

The focus of this project was to provide technical assistance, over a three year period, in assessing research and program needs of three major Egyptian family planning institutes and to provide guidance to develop policies, plans and programs with potential impacts on fertility reduction. A consultant was contracted to provide direct assistance to the National Population Council, the Egyptian Family Planning Association (EFPA) and the Family of the Future (FOF).

The consultant conducted site visits to the EFPA and FOF field offices in Port Said and Alexandria, concentrating on long/short range planning activities for EFPA and the coordination of the delivery of contraceptive methods in the private sector for the FOF. This project was terminated upon the completion of the consultant's contract on January 31, 1988.

(6) Egypt: Technical Assistance to the Ministry of Public Health

Through a USAID/Egypt buy-in, FHI subcontracted with the Sevin Group to provide technical assistance on research management to the Egyptian Ministry of Public Health. Due to personnel changes within the subcontracting organization, it was not possible to fulfill the terms of the agreement, and FHI terminated the subcontract early.

(7) Kenya: Reproductive Health Research/Institutional Development  
Project (RHR/IDP)

A three-year institutional development project will be initiated in October 1988 with the Department of Ob/Gyn, University of Nairobi, under a buy-in from USAID/Kenya to FHI's cooperative agreement. At USAID/Kenya's request, site visits were made by senior FHI staff during FY '88 to develop/finalize a project proposal and implementation plan. This plan includes the scope of work, University of Nairobi staff and equipment requirements, and administrative/management details.

The RHR/IDP was conceptualized in 1985, with the aim to develop the family planning research capabilities of the University of Nairobi's Department of Ob/Gyn. The RHR/IDP will initiate a series of workshops, seminars and training sessions to develop appropriate Kenyan family planning research projects. The planning, development, initiation and coordination of these research projects will be used to improve the department's research capabilities. A site visit to assess needs in microcomputer technology was also made by FHI's Scientific Support Services staff. This visit is discussed in more detail in the following section.

h. Microcomputer Development and Training

(1) New Microcomputer Installations

Trips were made to the Bangladesh Fertility Research Programme (BFRP)

in November 1987 and February 1988. BFRP staff were trained on the PS/2 in basic computer concepts, the DOS operating system, word processing and data analysis skills. In-house data entry and analysis will now be possible for the first time and the BFRP will be much less dependent on FHI for data processing and analysis. This visit was followed shortly by another FHI staff visit at which time more training was carried out in a range of computer-related activities, including coding and editing of forms, developing a code book, and generating tables.

A trip was made to the Department of Obstetrics and Gynaecology, University of Nairobi, Kenya, in August 1988. The purpose of this trip was to conduct a needs assessment of the data processing and data management needs of the Department to support its reproductive health program. The needs assessment included a review of existing computer technology and skills within the Department and a determination of locally available hardware, software, maintenance and training from computer firms in Nairobi.

## (2) Follow-up visits to Existing Microcomputer Sites

Follow-up visits were made to Bandung, Indonesia and Bangkok, Thailand. A follow-up visit was made to the BKS PENFIN in Bandung, Indonesia, in January 1988. Technical assistance was provided to the computer staff in preparation for the Clinical Trials Analysis workshop for FHRC data analysts in January 1988. The BKS PENFIN has acquired two personal computers, one of which was linked with the TI BS 352 to provide a

fifth terminal for the workshop. In addition, sample programs for the data analysis skills being taught in the workshop were prepared for use on both the TI and the PCs.

A follow-up visit was made to the Thai Fertility Research Association in March 1988. Further training in the use of their newly acquired personal computer was provided, with concentration on the areas of data analysis and communication with the TI system. Specifics of the DOS operating system were also reviewed.

A follow-up visit to the Egyptian Fertility Care Society (EFCS) in Cairo was made in May 1988. Technical assistance was provided to the quantitative staff of the EFCS in the use of their existing computer hardware and software systems. Several hardware components were installed on existing equipment to upgrade current capacity. An assessment of future computer needs was also conducted.

### (3) In-house Microcomputer Related Training

Ms. Maninaz El-Helw of the Egyptian Fertility Care Society received in-house microcomputer training at FHI from September to December 1987, while also taking biostatistics courses at the University of North Carolina, Chapel Hill. Using study data that Ms. El Helw brought with her, she received training in data analysis skills appropriate for the several computers available at the EFCS.

Mr. Prihandoko Achwandi, BKS PENFIN System Analyst, will visit FHI in October 1988 for consultation, program planning and training in computer skills and data analysis. During his stay, the BKS PENFIN's computing capacity and needs will also be discussed, as will plans for the proposed PC workshop for BKS PENFIN centers to be held in Bandung next year.

#### (4) Software Modifications

Field visits by Clinical Trials staff brought to light some discrepancies in the coding of the IUD Patient Summary Tables. Review of the program code and pertinent specifications revealed that the specifications do not accurately reflect the behavior of the code. These inconsistencies are currently being reviewed by Clinical Trials for determination of any modifications that might be desired.

## **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. Development of Reproductive Epidemiology Manual

FHI is collaborating with CDC and WHO to produce an epidemiology training curriculum entitled The Application of Epidemiologic Methods to Studies of Reproductive Health: An Eleven Part Series. Based on the earlier epidemiology training materials developed by FHI and CDC for use in Durango, Mexico, FHI has completed its initial phase of the project and has forwarded the draft manual to CDC for editing and revision. The materials should be ready for field testing, with support from WHO, in the Spring of 1989. Following final revisions, WHO will publish the series as a joint publication of the three agencies involved.

b. 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 and Portuguese. A French version is currently being produced for a future French language workshop. FHI has been pleased to receive several third party requests to use the material. For example, the BKKBN in Indonesia has reproduced the modules locally. Using these curricula, FHRCs in Egypt, Sri Lanka, and Indonesia are now able to carry out clinical trials workshops, with minimal technical assistance from FHI.

c. FHRC Clinical Trials Data Analysis Workshop

During this reporting period, FHI completed preparation of standardized training materials for the analysis of data from clinical trials of contraceptive methods. The materials are designed for use in a one-week course, intended mainly for current or potential researchers and/or their research assistants who are interested in doing their own analysis. Investigators who desire a more complete understanding of the analysis process would also be appropriate students. The format of this training involves a combination of lectures, self-instructional modules, and exercises designed to provide step-by-step instructions for analysis of data from contraceptive clinical trials.

FHI implemented this new curriculum for the first time in a one-week workshop for data analysts and other appropriate staff from the five major FHI-supported Family Health Research Centers (FHRCs). The Workshop was hosted by the BKS PENFIN in Bandung, Indonesia, January 25-29, 1988, and was conducted primarily by two FHI biostatisticians. The assessment of both instructors and the twelve participants was extremely positive. A final version of the training modules, incorporating significant revisions has been completed.

d. Brazil: Clinical Trials Workshop

A workshop on Clinical Trials Methodology for Contraceptive Research was carried out in collaboration with the University of Parana (F.U.Pr.) in Curitiba, Brazil, April 18-22, 1988.

The development and implementation of this workshop in Brazil marks an important step for FHI's Latin American program. It is anticipated that this project will greatly improve the Brazilian ability to conduct policy relevant clinical research. The affiliation with the F.U.Pr., and the participation of the Brazilian Society of Human Reproduction and other private sector family planning and research organizations, is expected to facilitate the evaluation of new contraceptive technologies through official government channels.

The workshop curriculum is based on the standardized curriculum developed prior to the Singapore workshop in May 1987. Modifications have been made according to suggestions made by trainers of previous workshops. FHI plans to run a second Brazil program in FY '89 using the core training staff, and expects that the team of highly-qualified trainers and researchers who participate in these workshops will be able to conduct similar workshops in the future with reduced direct FHI involvement. Professor Rosires Pereira de Andrade, local workshop coordinator, has expressed an interest in continuing to disseminate this technical training to other interested health care professionals in Brazil as an important way to strengthen the national capacity to conduct policy relevant research in Maternal Child Health Care.

- 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 want data that are specific to their region and conditions. However, interested professionals often have insufficient research background 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 two-week workshop on Applied Research Methods in Reproductive Health was held in Niamey, Niger in September 1987. This workshop gathered eight interested professionals (social scientists and health professionals) from the country. Workshop participants learned basic research skills and how to develop a research project. Teaching methods emphasized "learning by doing" with each participant involved in the project development. Mission funds are available to fund two research projects resulting from the workshop. The Ministry of Health has reviewed the list of proposed projects and chosen two that would contribute most to more effective family planning activities. Proposed projects are detailed above.

f. Zimbabwe: Anglophone Clinical Trials Workshop

A Clinical Trials workshop for Anglophone Africa was held July 10-16, 1988 in Harare, Zimbabwe. Sponsored by the Medical School of the

University of Zimbabwe, and using FHI facilitators, the workshop provided researchers with the skills necessary to carry out valid and reliable clinical trials. The course focus was the FHI self-instructional clinical trial modules: Introduction to Randomized Clinical Trials, Design Methodology for Randomized Clinical Trials, Methods of Analysis, and Practical Examples for Study Implementation. In addition a notebook on FHI study procedures, exercises and examples of case report forms and protocols were provided. The workshop combined didactic instruction, individual reading, group exercises and general discussion sessions. A session on new contraceptive technologies was also included. Twenty-one researchers from Zimbabwe, Nigeria, Ghana, Kenya and Cameroon participated in the workshop. Technical assistance was provided by FHI staff and a representative from A.I.D./Washington.

g. Mexico: Epidemiology Training

During this reporting period FHI provided support to GIMIESAR to conduct an Epidemiologic Research Methods course. The workshop, which ran from August 1-19, 1988, was attended by sixteen health professionals from throughout the Mexican Republic. Scientists from the GIMIESAR affiliates in Monterey, San Luis Potosi, Zacatecas, Durango and representatives from the University of Guadalajara, and the Hospital General de Veracruz attended the workshop. In addition, staff from PROFAMILIA in the Dominican Republic and from the Ministry of Health in Guatemala attended the workshop.

The two-week workshop was another in a series of similar training activities carried out by the core staff of GIMIESAR. The course covered the theoretical basis of epidemiologic methods, including research design, inferential statistics and data analysis and processing. In addition, all participants develop a research protocol on a topic of interest during the later half of the workshop.

The workshop was developed as part of GIMIESAR's plan to further strengthen the research capacity of their affiliates and to solidify the institution's ability to conduct similar workshops on a fee-for-services basis. The success of this workshop will help determine the economic feasibility of conducting future training activities.

#### h. Sharon Camp Fellowship

The Sharon Camp Fellowship Program was established in 1984, to enable a collaborating researcher each year to spend approximately six months in residence at FHI working on a project of mutual relevance and interest. To date, two fellows have participated in the program. Unfortunately, due to shortage of funds, no Sharon Camp Fellow was in residence during the reporting period.

### C. Support for Conferences, Seminars and Expert Meetings

FHI believes that international meetings, conferences and seminars, if carefully and appropriately chosen, are an important 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. Guatemala FLASOG

FHI provided partial support for the XII Latin American Congress of Obstetrics and Gynecology (FLASOG), which took place in Guatemala City on October 25-30, 1987. The special position that Latin America enjoys in the field of contraceptive development and this long-standing work with us made this a particularly important event for FHI. Latin America has provided the world with some of the most important advances in the field of health and contraceptive development and 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. Scientists from Latin America have contributed to the development of the copper bearing IUD, the sustained release of low dose progestogens, and non-surgical alternatives to tubal occlusion.

The FLASOG meeting offered an excellent opportunity to participate along with our Latin American colleagues in the scientific discussions

that took place at this bi-annual event. FHI participated in the pre-congress course, "The Past, Present and Future of Contraception", and participated in a round table discussion on "Advances in Contraception."

## 2. Mexico: AIBIR/ALIRH Conference

FHI provided support to the Mexican Academy of Research in Reproductive Biology (AIBIR) for their Thirteenth Annual Meeting held May 21-25, 1988. On this occasion, the meeting was jointly organized with the XI Biannual meeting of the Latin American Association of Research in Human Reproduction (ALIRH). In addition to the core support, FHI organized and conducted a symposium on "Biodegradable Microspheres as a Long Acting Delivery System for Hormonal Contraception".

## 3. Conference Travel (Non-FHI Staff)

FDT provided support for many of our international colleagues to attend and participate in ten international meetings and conferences. A list of FHI sponsored participants by the meetings they attended follows:

- a. "Better Health for Mothers and Children Through Family Planning" Conference, Nairobi, Kenya, October 5-9, 1987.

-Professor Roger V. Short, Melbourne, Australia.

b. American Public Health Association Annual Meeting, New Orleans,  
Louisiana, October 18-22, 1987.

-Ms. Elena Prada Salas, Magdalena, Colombia.

c. XII Latin American Congress of Obstetrics and Gynecology (FLASOG),  
Guatemala City, Guatemala, October 25-30, 1987.

-Dr. Jorge Lasso de la Vega, Panama City, Panama.

-Dr. Eduardo Israel Ardití, Valdivia, Chile.

-Professor Rosires Pereira de Andrade, Curitiba, Brazil.

-Dra. Rea Nunes, Porto Alegre, Brazil.

-Lic. Zandra Castaneda de Lastra, Magdalena, Colombia.

d. Pre-Congress Seminar of the XIth AFOG Congress, Bangkok, Thailand,  
December 1-4, 1987.

-Dr. Mahendra K. Chhetri, Kathmandu, Nepal.

-Prof. Hyun Mo Kwak, Seoul, Korea

-Dr. H. Prastowo Mardjikoén, Yogyakarta, Indonesia.

-Prof. R. S. Samil, Jakarta, Indonesia.

-Dr. Gulardi H. Wiknjosastro, Jakarta, Indonesia.

-Dr. Sumarti Sudomo, Jakarta, Indonesia.

e. Safe Motherhood Conference, Cairo, Egypt, February 21-27, 1988.

-Dr. Arthur Christakos, Durham, N.C., USA.

f. XIII Annual Meeting of the Mexican Academy for Research in Human Reproduction (AIBIR), Puerto Vallarta, Mexico, May 21-25, 1988.

-Dr. Rosires Pereira de Andrade, Curitiba, Brazil

-Dr. Rene Guzman Serani, Valdivia, Chile

g. CIOMS Conference (Council for International Organizations of Medical Sciences under the auspices of WHO/UNESCO) on "Ethics and Human Values in Family Planning", Bangkok, Thailand, June 19-24, 1988.

-Mr. Daya Abeywickrema, Colombo, Sri Lanka

-Dr. Halida Akhter, Dhaka, Bangladesh

h. First Italian-Arab Conference on Family Planning, Rome, Italy, June 1988.

-Dr. Abdel El-Kady, Cairo, Egypt (partial support)

i. Zimbabwe National Family Planning Council Donor's Workshop, Victoria Falls, Zimbabwe, July 25-29, 1988.

-Sister Lyntette Malianga, Harare, Zimbabwe

j. FHI/GIMIESAR Epidemiology Research Methods Course, Durango, Mexico, August 1-19, 1988.

-Dr. Elvira Jimenez, Santo Domingo, Dominican Republic

-Dr. Hector Montero, Santo Domingo, Dominican Republic

-Dr. Mario Santiso, Guatemala

-Dr. Raul Rosenberg, Guatemala

#### **D. Contraceptive Technology Transfer**

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

##### **1. Involvement of Private Sector Physicians in Voluntary Surgical Contraception in Mexico**

This project 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 were 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 AVSC 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 have been analyzed and the final report was completed during this reporting period. Plans are currently underway to publish the data in an appropriate Mexican scientific journal.

These data suggest that such short-term courses, directed at a carefully selected portion of the private medical community can increase the number of physicians providing surgical contraceptive services. The data demonstrate that short-term intensive training courses can be used to increase the number of physicians providing safe and effective services in the private sector.

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, completely voluntary.

## 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 direction 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 requested that the Egyptian Fertility Care Society (EFCS) be responsible for direct administrative control over the NORPLANT project. The decision to shift this project to the EFCS offices was made in July 1986, and the EFCS began to implement the project in the spring of 1987.

The project has several components: a large scale program of training and introduction designed to assess the performance of NORPLANT implants across a broad spectrum of providers; a detailed program of clinical research aimed at providing guidance to physicians and regulatory agencies regarding appropriate clinical management; a large-scale prospective cohort study to evaluate the relationship between NORPLANT implants and potential sources of morbidity and mortality; a program of small acceptability studies designed to indicate patterns of acceptability in various sectors; post-marketing surveillance scheme to monitor rare adverse events; and, the development of informational materials for both acceptors and counselors.

The initiation of this project was delayed due to a need to shift from using the NORPLANT two capsule system to the NORPLANT six capsule system.

At present, approval has been received by the appropriate government offices and 1,600 NORPLANT sets have arrived in Egypt.

### 3. PIO/T Senegal: Coordination and Management

The preintroductory NORPLANT clinical trial is being funded under a Senegal USAID PIO/T. The 50 women programmed for the first phase have been recruited into the study and are now being followed up. Negotiations are underway to expand the case load to 250. Another activity planned under the PIO/T is a study of continuation of contraceptive use and reasons for discontinuation. Both these projects are also reported on in the Clinical Trials and Program Evaluation sections of this report.

### 4. PIO/T Bangladesh: Coordination and Management

In 1986, the AID/Dhaka Mission added US \$556,000 to FHI's Cooperative Agreement to fund a variety of activities, most of which related to an expansion of NORPLANT activities in Bangladesh. Most of the projects involve coordination with the Bangladesh Fertility Research Programme (BFRP), through a series of subcontracts. Buy-in funds were used in 1988 to purchase an IBM Personal System 2 computer for the BFRP, and this computer is being used for in-house word processing and data analysis of projects.

Several studies are underway using these buy-in funds. The projects are described in more detail in other sections of this report.

Included are a four-phase NORPLANT Removal, Motivation, and Acceptability study, and a five-part expansion of NORPLANT clinical trials, including training, educational materials, a registry/surveillance system, and the trials themselves.

Some of the activities originally proposed for the buy-in were dropped during this fiscal year (e.g. a use effectiveness study of male and female sterilization). The remaining buy-in money will be used for a variety of study and institutional development purposes, a list of which has been submitted to the Dhaka Mission for approval. Included were the development of clinical guidelines for contraceptive use, training programs for BFRP staff, and technical assistance to the BFRP by FHI and consultant staff.

##### 5. Gambia: Contraceptive Continuation Rates and Reasons for Discontinuation

FHI will provide technical assistance to the Gambian Family Planning Association (GFPA) in developing a protocol, questionnaire, and data analysis plan for a prospective study on contraceptive continuation rates and reasons for discontinuation at four GFPA clinics. Field costs will be provided by the International Development Research Center (IDRC).

This study will collect information on why acceptors or potential acceptors become "inactive". Of particular interest are those factors that can be influenced by the nature of the service delivery program:

counseling, both for new clients and for continuing users; laboratory tests required before certain methods are provided; clinic hours of operation; and the frequency with which acceptors are required to return for resupply.

The study protocol and questionnaires have been finalized and data collection will be initiated in all four centers on October 1, 1988.

#### 6. El Salvador: Postpartum IUD Introduction and Evaluation

Family Health International, through a PIO/T with USAID/El Salvador, is providing technical assistance to the Salvadoran Demographic Association for the introduction and evaluation of a postpartum IUD program. FHI has been one of the leading organizations in evaluating the efficacy and safety of the postpartum IUD in many countries around the world, and Salvadoran family planning officials are interested in working with us to evaluate this technology in El Salvador.

The program has four components: information dissemination, training, clinical research, and a final evaluation. Each of the components was developed in accordance with the stated interest of the Salvadoran family planning program. The program is intended to provide a complete understanding of the strategy and techniques to be employed in the introduction and evaluation of this technology in El Salvador.

The program goal is to increase the use of the IUD in El Salvador by implementing a postpartum IUD insertion campaign in the hospitals of

the Ministry of Health (MOH) and the Salvadorean Social Security Institute (ISSS).

The specific objectives are:

- a. To inform the Salvadorean family planning community about the programmatic utility of a postpartum IUD program;
- b. To train physicians from the Ministry of Health and the Social Security System in the proper techniques for successfully inserting an IUD in the postpartum period;
- c. To implement a 400 case non-comparative clinical trial of post partum IUD insertion in El Salvador; cases will be divided evenly between the Ministry of Health and the Social Security System; and
- d. To perform an evaluation of the program which measures the impact of the introduction of the postpartum IUD on contraceptive choice and method satisfaction.

During this reporting period a series of meetings were held in El Salvador in preparation for the initiation of the project; training has been carried out and the initiation of the clinical trial and the early phases of the evaluation component begun.

## E. Information Dissemination

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 translation, production and dissemination of country-specific and topic-specific informational materials. These materials are designed to make scientific literature and contraceptive research more accessible and therefore usable by policymakers and health care providers and family planners.

### 1. International Journal of Gynecology & Obstetrics

This year 300 subscriptions to the International Journal of Gynecology & Obstetrics were provided to research collaborators who depend on the medical information the Journal contains to update their knowledge of the latest contraceptive methods and techniques.

Elsevier Scientific Publishers, Ireland, has changed the Journal to standard journal size and began using the American A4 format. In an effort to increase the amount of current information available to its readers, the publisher also doubled the number of pages per issue with only a slight increase in cost. Readers using the Journal to teach students or as a medical reference now have a major source of current knowledge.

## 2. Indonesia MCH Monograph

Work progressed in collaboration with the BKS PENFIN on a monograph on their large maternal care monitoring (MCM) data set and possibly other related Indonesian data such as RAMOS. The monograph will document, with Indonesian data, the relationship between various obstetric and contraceptive variables and maternal and child health.

FHI has produced a draft set of graphs from the data for review and expansion by the Indonesian authors. They are working on the narrative text (which FHI will help edit) and on collecting photographs suitable for inclusion in the monograph. The monograph will be reviewed before publication.

## 3. network

Themes addressed in network in 1988 included long-acting steroids, post-marketing surveillance of contraceptives, maternal mortality and the evaluation of social marketing programs. Each was distributed to over 4,000 subscribers. Network continues to be used as a teaching reference by many institutions and universities.

## 4. network in SPANISH

Readership of network en espanol, FHI's three-year-old Spanish-language newsletter, has increased to 2,500, including the addition of key contacts with the National AIDS Commissions throughout Latin America.

Volume 3 of network en espanol on IUDs was distributed in April 1988.

5. network in FRENCH

The third volume of FHI's newsletter in French, a 20-page issue on maternal morbidity, male involvement in family planning and AIDS, was published and distributed in September 1988 to approximately 800 subscribers.

6. Other Dissemination Activities

FHI is an important source of information on reproductive health and contraception. A program of information dissemination to the public media is actively maintained.

FHI's program to report research findings and accurate information on contraception to the media, policymakers, and IEC personnel in family planning organizations around the world continues to expand.

a. African Journalists Workshop

A two-week workshop on journalism skills and population and reproductive health issues for Francophone African health journalists was held in September 1988, in Dakar, Senegal. There were sixteen participants from nine countries -- Mali, Niger, Burkina Faso, Cote d'Ivoire, Cameroon, Zaire, Togo, Benin and Senegal. Participants visited hospitals, family planning clinics and an STD clinic and wrote

articles on contraceptive methods, AIDS, family planning services and the impact of sexually transmitted diseases on health. The group formed an African health journalists committee and planned ways to regularly collect and distribute articles on family health issues. One of the main objectives of the workshop, co-sponsored by Projet Sante Familiale et Population of Senegal, was to create a network of knowledgeable African health writers. The committee formed during the workshop plans to organize a meeting in Cotonou, Benin in March/April 1989 to enlarge the scope of the network to health journalists trained by the Pan African News Agency (PANA), the West African News Agency for Development (WANAD), the PANOS Institute (London) and FHI.

b. Information Packets

Customized information packets are routinely assembled for special events, investigators, conferences, and visitors. Since April 1988, FHI has also distributed 2,000 packets on AIDS to USAID Missions, organizations, and individuals in the medical profession. AIDS information packets continue to be distributed on a bi-monthly basis.

c. IUD Monograph

A monograph entitled Long-Term IUD Use in Ljubljana, Yugoslavia containing fifteen years of data was published in July 1988. The monograph was disseminated to approximately 500 individuals and organizations. Requests were received from the Egyptian Fertility Care Society and the Zimbabwe National Family Planning Council for an

additional 120 copies for use by professors, university centers and other institutions.

d. Translation Program

Funds have been set aside to translate selected articles that are of interest for Africa and the Latin American region. This activity is an important new component of our information dissemination activities.

e. Information Management

The FHI library was transferred to the Field Development and Training Division and combined with the other information dissemination operations in order to improve coordination and develop an integrated system for information management. The first result of this merger has been the AIDS bibliographic information database which provides the articles for the bimonthly AIDS packet mailing, as well as serving as a resource for the FHI staff. The automated database began in February 1988 and now includes over 1500 documents, including many in French and Spanish.

## VI. MANAGEMENT

### PROTECTION OF HUMAN SUBJECTS COMMITTEE

Four meetings of the Protection of Human Subjects (PHSC) were held at FHI to review 68 research proposals, inclusive of amendments and those for expedited review: November 6, 1987; March 4, 1988; May 20, 1988 and August 31, 1988.

Two committee members rotated off at the end of the 1987 calendar year: Mrs. Thelma Battle and Dr. Josefina Tiryakian (social scientists).

Reappointed to the committee to serve another three-year term as the clergy representative was:

Dennis M. Campbell, PhD, BD; Dean of the Divinity School and Professor of Theology at Duke University, Durham, NC. He is a United Methodist minister, a Danforth Fellow, an Elder in the North Carolina Conference of the United Methodist Church, and a member of the Board of Ordained Ministry and its Executive Committee.

Two new committee members were appointed for three-year terms:

Vanessa P. Haygood, MD, an Assistant Chief of the Obstetrical/Gynecological Teaching Service, The Moses H. Cone Memorial Hospital in Greensboro, NC and the Medical Director of Maternity and Family Planning Services of the Guilford County Health Department.

David B. Pryor, MD, an Assistant Professor of Medicine (Cardiology) and Director, Section Clinical Epidemiology & Biostatistics, Duke University, Durham, NC. Since 1981, he has served as a cardiology consultant to the Veterans Administration Hospital in Fayetteville, NC. Dr. Pryor is the author and/or co-author of numerous scientific publications.

Dr. John Shelton Reed, Jr. continues to serve as Chairman of the Committee and Dr. Dennis M. Campbell was appointed as Vice Chairman, effective January 1, 1988.

Karen Denny, formerly of the Clinical Trials Division and Paul Feldblum of the Reproductive Epidemiology/Sexually Transmitted Diseases Division represented FHI at the NIH/FDA Regional Workshop on the Protection of Human Subjects, held May 12-13, 1988 in Baltimore, Maryland. A new Public Health Service (PHS) policy for AIDS activities was distributed

at the workshop: Policy on Informing those Tested about HIV Serostatus. The new PHS policy, which applies to both domestic/foreign research and service activities, mandates when HIV testing is conducted or supported by PHS that individuals whose test results are associated with personal identifiers must be informed of their own test results and provided with the opportunity to receive appropriate counseling.

The Chairman of FHI's PHSC, Dr. John Shelton Reed, accompanied Mr. Mark Robbins of the Field Development & Training Division on a monitoring trip to Jakarta and Bandung, Indonesia, July 10-18, 1988, to appraise the Institutional Review Board process, protocol compliance, and the informed consent procedures/documentation for safeguarding the welfare of voluntary human subjects enrolled in FHI's research studies.

#### TECHNICAL ADVISORY COMMITTEE

The Technical Advisory Committee (TAC) held its annual meeting at FHI on Thursday, June 30, 1988. All eight of the committee members attended, including the two new appointees who will be serving three-year terms (1987-90):

Deborah J. Anderson, PhD - Director, Fearing Research Laboratory  
and Associate Professor of Obstetrics, Gynecology and  
Reproductive Biology, Harvard Medical School, Boston, Mass;

Jorge Martinez Manautou, MD - President, Academia Mexicana de Investigacion y Demografia Medica, AC, and Head, Family Planning Services Division, Mexican Institute of Social Security (IMSS), Mexico.

Three observers attended the 1988 TAC meeting:

Dr. Jose Barzelatto, Director, Special Programme of Research Development and Research Training in Human Reproduction, World Health Organization;

Dr. Philip Corfman, Supervisory Medical Office for Fertility and Maternal Health Drugs, US/Food & Drug Administration;

Dr. Rosemarie Thau, Director of Contraceptive Development, The Population Council.

Drs. Michael JK Harper and Rochelle N. Shain and Ms. Judith P. Rooks have been reappointed to the Committee for three-year terms (1988-91).

BOARD OF DIRECTORS

The Board of Directors held two meetings:

Spring meeting, April 22-24, 1988; London, England;

Annual meeting, September 25-26, 1988; FHI's new headquarters office.

Four new Directors were elected for a three-year term:

King K. Holmes, MD, PhD - Professor/Vice-Chairman, Department of Medicine, University of Washington and Chief of Medicine, Harborview Medical Center, Seattle, WA;

Luella V. Klein, MD - Professor/Chair, Department of Gynecology/Obstetrics, Emory University School of Medicine and Chief of Obstetrical Service, Grady Memorial Hospital, Atlanta, GA;

Halfdan T. Mahler, MD - Recently retired Director-General of the World Health Organization, Versoix, Switzerland;

Donald R. Seawell, JD - Chairman of the Board, The Denver Center  
for the Performing Arts, Denver, CO.

Three incumbent Directors were re-elected for three-year terms:

Arthur C. Christakos, MD - Professor of Obstetrics/Gynecology,  
Duke University Medical Center, Durham, NC;

Malcolm Potts, MB, BChir, PhD - President of Family Health  
International;

Pramilla Senanayake, MBBS, DTPH, PhD - Assistant Secretary  
General, International Planned Parenthood Federation, London,  
England.

Appointed as Corporate Officers were the following:

Dr. Roger Short, Chairperson

Dr. Torrey Brown, Vice Chairperson

Dr. Malcolm Potts, President/COO

Mr. William Schellstede, Senior Vice President

Mr. Robert Hughes, Vice President of Administration &  
Controller/Assistant Treasurer

Mrs. JoAnn H. Lewis, Vice President of Programs

Mr. Alfredo Perez, Vice President of Health

Gen. Alexander Andrews, Secretary

Mrs. Marie F. Porter, Assistant Secretary

Mr. Peyton Woodson, III, Treasurer

The following Directors were appointed as observers (1988/89) to FHI's  
external advisory committees:

Dr. Torrey Brown - Protection of Human Subjects Committee

Drs. Arthur Christakos & Pramilla Senanayake - Technical  
Advisory Committee

Dr. King Holmes - Technical Advisory Group

Dr. Sharon Camp - Latin America Advisory Committee

**APPENDIX A**

Publications List

Family Health International  
Annual Publications Listing  
October 1, 1987 - September 30, 1988

Published

- M Potts. Preparing for the Battle. People 14(4):3, 1987. (87-25)
- I Chi, LR Wilkens, AJ Siemens, M Potts. Rare Events Occurring at Insertion of an Intrauterine Device--A Review of an International Experience. Adv Contracept 3:39, 1987. (87-26)
- JA Fortney, S Gadalla, S Saleh, I Susanti, M Potts, SM Rogers. Causes of Death to Women of Reproductive Age in Two Developing Countries. Popul Res and Policy Rev 6:137, 1987. (87-27)
- MJG Farthing, PMG Inge, RM Pearson. Effect of D-propranolol on Growth and Motility of Flagellate Protozoa. J Antimicrob Chem 20:519, 1987. (87-28)
- AS Zavala, M Perez-Gonzalez, PC Miller, M Welsh, LR Wilkens, M Potts. Reproductive Risks in a Community-Based Program of Oral Contraceptives, Matamoros, Mexico. Stud Fam Plann 18(5):284, 1987. (87-29)
- Smoking and Reproductive Health, MJ Rosenberg, Ed. (Littleton, MA: PSG Publishing, 1987). (87-30)
- MJ Rosenberg, DW Cramer, PJ Feldblum. Reply to STDs, IVF, and Barrier Contraception (letter). JAMA 258(13):1729, 1987. (87-31)
- M Potts, DA Grimes. STDs, IVF and Barrier Contraception (letter). JAMA 258(13):1729, 1987. (87-32)
- S Thapa, D Abeywickrema, LR Wilkens. Effects of Compensatory Payments on Vasectomy Acceptance in Urban Sri Lanka: A Comparison of Two Economic Groups. Stud Fam Plann 18(6):352, 1987. (87-33)
- S Thapa, M Salgado, JA Fortney, GS Grubb, V de Silva. Women's Perceptions of the Pill's Potential Health Risks in Sri Lanka. Asia-Pacific Pop J 2(3):39, 1987. (87-34)
- J Zipper, LP Cole, M Rivera, E Brown, RG Wheeler. Efficacy of two insertions of 100-minute releasing quinacrine hydrochloride pellets for non-surgical female sterilization. Adv Contracept 3:255, 1987. (87-35)
- NE Williamson. Breastfeeding Women and Family Planning Programs: Special Needs and Opportunities. Asian Pacific Pop Forum 1(5):1, 1987. (87-36)
- I Chi, CB Champion, LR Wilkens. Cervical Dilatation in Interval Insertion of an IUD: Who Requires It and Does It Lead to a High Expulsion Rate? Contracept 36(4):403, 1987. (87-37)

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- BA Gross. Natural Family Planning Indicators of Ovulation. Clin Reprod Fertil 5:91, 1987. (87-38)
- S Sidney. Vasectomy and the Risk of Prostatic Cancer and Benign Prostatic Hypertrophy. J Urol 138:795, 1987. (87-39)
- I Chi, SC Smith, E Borko, T Sun, SF Begum, WL Hunt, LR Wilkens. Clinical Acceptability, Use-patterns and Use-effectiveness of the Vaginal Contraceptive Sponge and Neo Sampooon Tablets--An International Multi-center Randomized Clinical Trial. Contraception 36(5):499, 1987. (87-40)
- B Behlilovic, AJ Rowan. A Comparative Study of Norinyl 1/35 Versus Norinyl 1/50. Contraception 36(5):515, 1987. (87-41)
- B Janowitz, F Bailey, J Ochoa, M Suazo. Contraceptive Use and Fertility in Honduras, 1981-84. Stud Fam Plann 18(5):291, 1987. (87-42)
- M Potts. The Most Presumptuous Pox--AIDS and Contraception. Brit J Fam Plann 13(4):144, 1987. (87-43)
- M Potts. The Most Presumptuous Pox--AIDS and Contraception. Brit J Fam Plann 13(4):144, 1987. (87-44)
- JA Fortney. Causes of Death to Menoufia Women of Reproductive Age: An Overview. In: Maternal Mortality in Menoufia: A Study of Reproductive Age Mortality, S Morsy, Ed. (Cairo: Social Research Center, American University in Cairo, 1987), p. 10. (87-45)
- S Saleh, S Gadalla, JA Fortney. Maternal Mortality in Menoufia: A Study of Reproductive Age Mortality, S Morsy, Ed. (Cairo: Social Research Center, American University in Cairo, 1987). (87-46)
- G Ahmed, WP Schellstede, NE Williamson. Underreporting of Contraceptive Use in Bangladesh. Int Fam Plann Perspect 13(4):136, 1987. (87-47)
- MM Shaaban, GH Sayed, SA Ghaneimah. The Recovery of Ovarian Function During Breast-feeding. J Steroid Biochem 27(4-6):1043, 1987. (87-48)
- R Rivera, G Alvarado, S Aldaba, C Flores, A Hernandez. Esteroides Microencapsulados como una Alternativa en Anticoncepcion de Accion Prolongada. In: Avances Recientes en Regulacion de la Fertilidad, V. 1, Metodos Anticonceptivos de Accion Prolongada, G Perez-Palacios, J Garza-Flores, PE Hall, Eds. (Geneva: World Health Organization, 1987), p. 149. (87-49)
- M Potts. Acquired Immunodeficiency Syndrome (AIDS): A Commentary on the International Aspects of the Disease. Int J Gynecol Obstet 26(1):1, 1988. (88-01)

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NE Williamson. The Potential Contribution of Family Planning Programs to AIDS Prevention in Developing Countries. In: *Selected Proceedings of Southern Regional Conference on International Health in the 1990s: Directions in Research and Development*, Chapel Hill, North Carolina, October 29-31, 1987 (Washington, DC: National Council for International Health, 1988), p. 97. (88-12)

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26

- R Rivera, KI Kennedy, E Ortiz, M Barrera, P Bhiwandiwalla. Breast-feeding and the Return to Ovulation in Durango, Mexico. *Fertil Steril* 49(5):780, 1988. (88-14)
- PJ Feldblum, E Bernardik, MJ Rosenberg. Spermicide Use and Sexually Transmitted Disease. *JAMA* 259(19):2851, 1988. (88-15)
- SM Rosenthal. Recent Declines in Reproductive Mortality in England and Wales. *Brit J Fam Plann* 14(2):46, 1988. (88-16)
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- L Andolsek, M Kozuh-Novak, SA Balogh, C Waszak. Long-Term IUD Use in Ljubljana, Yugoslavia. Research Triangle Park, NC, Family Health International. (88-20)
- RE Roddy. Genital Herpes. *Phy Assist* 12(7):21, 1988. (88-21)
- K Henry. Mopping Up a Lingering Threat. *South* 94:113, 1988. (88-22)
- L Potter, S Wright, D Berrio, P Suarez, R Pinedo, Z Castaneda. Oral Contraceptive Compliance in Rural Colombia: Knowledge of Users and Providers. *Int Fam Plann Perspect* 14(1):27, 1988. (88-23)
- B Janowitz, P Bailey, RC Dominik, L Araujo. TBAs in Rural Northeast Brazil: Referral Patterns and Perinatal Mortality. *Health Pol Plann* 3(1):48, 1988. (88-24)
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201

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**APPENDIX B**

Consultant Reports

Completed Consultant Reports (CRs)

October 1987 - September 1988

| <u>Title</u>   | <u>Prepared for</u>                     | <u>Center</u>        | <u>Study</u> |
|--|---|----------------------|--------------|
| Evaluation of the Safety, Effectiveness and Acceptability of Propranolol Tablets for Vaginal Contraception   | Jamie Zipper                            | 0088                 | 7790<br>7791 |
| A Comparative Study of the Filshie Clip & Wolf Clip Methods of Tubal Occlusion   | J. Lasso de la Vega                     | 0832                 | 6266         |
| A Comparative Study of the Filshie Clip & Tubal Ring Methods of Tubal Occlusion  | J. Contreras                            | 0083                 | 6264         |
| A Comparative Study of the Filshie Clip & Yoon Ring Methods of Tubal Occlusion   | Jose M. Moreno Arosemena                | 0081                 | 6265         |
| Surveillance Study of Female Sterilization at Three Centers in Mexico  | Rodolfo Quinones                        | Multi                | 6906         |
| Evaluation of the Safety, Effectiveness, & Acceptability of Ortho Contraceptive Foaming Vaginal Tablets Containing Nonoxynol-9 vs. Ortho Contraceptive Foaming Vaginal Tablets Containing Menfegol at Three U.S. Sites         | Gary Ruoff<br>Nona Niland<br>John Halki | 0220<br>0930<br>0909 | 7799         |
| Evaluation of the Safety, Effectiveness, & Acceptability of Ortho Contraceptive Foaming Vaginal Tablets Containing Nonoxynol-9 vs. Ortho Contraceptive Foaming Vaginal Tablets Containing Menfegol at a Clinic in Accra, Ghana | C. Klufio                               | 0044                 | 7798         |
| A Study of a Progestogen-Only Oral Contraceptive for Lactating Women in Curitiba   | Rosires P. de Andrade                   | 8058                 | 8875         |
| A Comparative Clinical Trial of NeoSampooon Vaginal Tablets & Emko Vaginal Foam in Ljubljana, Yugoslavia   | Lidija Andolsek                         | 20                   | 785          |
| A Study of a Progestogen-Only Oral Contraceptive for Lactating Women in Ciudad Juarez, Mexico  | Rebecca Ramos                           | 840                  | 8875         |

| <u>Title</u>  | <u>Prepared for</u> | <u>Center</u> | <u>Study</u> |
|---|---------------------|---------------|--------------|
| Evaluation of the Safety, Effectiveness & Acceptability of Ortho Contraceptive Foaming Vaginal Tablets Containing Nonoxynol-9 versus Ortho Contraceptive Foaming Tablets Containing Menfegol in Bangkok, Thailand | S. Chompootaweeep   | 0773          | 7798         |
| Effectiveness of Tioconazole in Preventing Vaginal Infections   | O. Jarmillo         | 8062          | 7800         |
| A Study of a Progestogen-Only Oral Contraceptive for Lactating Women in Accra, Ghana  | C. Gardiner         | 0043          | 8876         |

**APPENDIX C**

**Study Status Lists**

STUDY STATUS LIST  
FEMALE STERILIZATION STUDY

GATES/ROSMAN

OCTOBER 1988

DESCRIPTION OF STUDY: RETROSPECTIVE FILSHIE CLIP

STUDY NUMBER: 6240

TOTAL NUMBER OF CASES: 800

TOTAL NUMBER OF STUDIES: 1

| CENTER | INVESTIGATOR/<br>COUNTRY | INDEX<br>NUMBER | DATE<br>INITIATED | DATE<br>ACTIVE | EXPIRATION<br>DATE | PROPOSED<br>NO. OF<br>CASES | FORMS PROCESSED |     |     |      | DATE<br>LAST<br>SHIPMENT | DATE<br>LAST<br>SITE VISIT | STATUS/<br>COMMENTS |
|--------|--------------------------|-----------------|-------------------|----------------|--------------------|-----------------------------|-----------------|-----|-----|------|--------------------------|----------------------------|---------------------|
|        |                          |                 |                   |                |                    |                             | ADP             | FU  | FU  | LIEU |                          |                            |                     |
| 747    | ARSHAT/<br>MALAYSIA      | FS 36/009       | 9/86              | 1/87           | 6/88               | 800                         | 441             | 130 | 342 | *193 | 9/28/88                  | 9/88 DG                    | ACTIVE              |

\*FORMS RECEIVED/NOT PROCESSED

STUDY STATUS LIST  
FEMALE STERILIZATION

OCTOBER 1988

DESCRIPTION OF STUDY: LAPAROSCOPY - FILSHIE CLIP

STUDY NUMBER: 6249

TOTAL NUMBER OF CASES: 1795

TOTAL NUMBER OF STUDIES: 11

| CENTER | INVESTIGATOR/<br>COUNTRY | INDEX<br>NUMBER | DATE<br>INITIATED | DATE<br>ACTIVE | DATE LAST<br>ADM. | PROPOSED<br>NO. OF<br>CASES | EOPMS PROCESSED |           |           |            | DATE<br>LAST<br>SHIPMENT | DATE<br>LAST<br>SITE VISIT | STATUS/<br>COMMENTS |            |
|--------|--------------------------|-----------------|-------------------|----------------|-------------------|-----------------------------|-----------------|-----------|-----------|------------|--------------------------|----------------------------|---------------------|------------|
|        |                          |                 |                   |                |                   |                             | ADM             | 1MO<br>FU | 6MO<br>FU | 12MO<br>FU |                          |                            |                     | 24MO<br>FU |
| 284    | YUZPE/CANADA             | FS 85/007       | 6/85              | 7/85           | 5/24/88           | 250                         | *213            | *156      | *150      | *108       | *18                      | 9/26/88                    | 9/88 KK             | FU ONLY    |
| 285    | O'BRIEN/<br>ENGLAND      | FS 85/020       | 10/85             | 1/86           | 1/06/88           | 100                         | 77              | 66        | 43        | 26         | X                        | 5/19/88                    | 4/88 DG             | FU ONLY    |
| 224    | COMBIE/<br>ENGLAND       | SUBCONTRACT     | 10/85             | 8/87           | 9/21/87           | 50                          | 10              | 9         | 6         | *5         |                          | 9/23/88                    | 4/88 DG             | FU ONLY    |
| 286    | NEWTON/<br>ENGLAND       | SUBCONTRACT     | 10/85             | 4/86           | 4/29/88           | 250                         | *276            | *245      | *198      | *148       | *45                      | 9/23/88                    | 4/88 DG             | FU ONL     |
| 293    | POSHORE/<br>ENGLAND      | SUBCONTRACT     | 10/85             | 10/86          | 4/20/88           | 150                         | *64             | 49        | *37       | 26         | *6                       | 9/23/88                    | 4/88 DG             | FU ONL     |
| 201    | CAMPBELL/<br>ENGLAND     | FS 86/006       | 04/86             | 8/86           | 4/27/88           | 200                         | 216             | 161       | 112       | 54         | X                        | 5/23/88                    | 4/88 DG             | FU ONL     |
| 200    | DAIRD/<br>SCOTLAND       | FS 86/007       | 04/86             | 7/86           | 10/28/87          | 220                         | 220             | 158       | 191       | 111        | X                        | 9/19/88                    | 4/88 DG             | FU ONL     |
| 283    | GOMEL/CANADA             | FS 85/009       | 2/86              | 7/86           | 12/17/87          | 75                          | 80              | 47        | 34        | 26         | X                        | 8/12/88                    | 3/88 SMC            | FU ONL     |
| 274    | MILNE/CANADA             | FS 86/005       | 5/86              | 12/86          | 2/01/87           | 200                         | *54             | *50       | *37       | *24        | X                        | 9/26/88                    | 9/88 KK             | FU ONL     |
| 263    | FILSHIE/CANADA           | FS 87/005       | 1/87              | 5/87           | 6/14/88           | 200                         | *143            | *113      | *79       | *28        | X                        | 9/26/88                    | 9/88 KK             | FU ONL     |
| 284    | FILSHIE/CANADA           | FS 87/009       | 11/87             | 2/88           | 6/03/88           | 100                         | 103             | 107       |           |            | X                        | 7/07/88                    | 5/88 CEC            | FU ONL     |

2/88

APPLICABLE TO ALL PROCESSED

STUDY STATUS LIST  
FEMALE STERILIZATION

OCTOBER 1989

DESCRIPTION OF STUDY: MINILAPARTOMY - FILSHIE CLIP VS. SECUCLIP (ADMISSIONS CLOSED)

STUDY NUMBER: 6258

TOTAL NUMBER OF CASES: 200

TOTAL NUMBER OF STUDIES: 2

| CENTER | INVESTIGATOR/<br>COUNTRY | INDEX<br>NUMBER | DATE<br>INITIATED | DATE<br>ACTIVE | DATE LAST<br>ADM. | PROPOSED<br>NO. OF<br>CASES | ADM | FORMS PROCESSED |           |            |            | DATE<br>LAST<br>SHIPMENT | DATE<br>LAST<br>SITE VISIT | STATU<br>COMMEN |
|--------|--------------------------|-----------------|-------------------|----------------|-------------------|-----------------------------|-----|-----------------|-----------|------------|------------|--------------------------|----------------------------|-----------------|
|        |                          |                 |                   |                |                   |                             |     | 1MO<br>FU       | 6MO<br>FU | 12MO<br>FU | 24MO<br>FU |                          |                            |                 |
| 865    | BUSSEMEYER/<br>BRAZIL    | FS 84/004       | 8/84              | 8/84           | 7/25/85           | 100                         | 93  | 69              | 80        | 70         | 44         | 01/04/83                 | 3/87 DB                    | CLOSI           |
| 836    | NAGAHATA/<br>PERU        | FS 84/005       | 8/84              | 8/84           | 4/28/84           | 100                         | 75  | 75              | 74        | 73         | 70         | 08/28/85                 | 10/87 DB                   | CLOSE           |

112

STUDY STATUS LIST  
FEMALE STERILIZATION

OCTOBER 1988

DESCRIPTION OF STUDY: MINILAPAROTOMY - FILSHIE CLIP VS POMEROY

STUDY NUMBER: 6260

TOTAL NUMBER OF CASES: 1400

TOTAL NUMBER OF STUDIES: 4

| CENTER | INVESTIGATOR/<br>COUNTRY    | INDEX<br>NUMBER | DATE<br>INITIATED | DATE<br>ACTIVE | DATE LAST<br>ADM | PROPOSED<br>NO. OF<br>CASES | ADM | FORMS PROCESSED |           |            |             | DATE<br>LAST<br>SHIPMENT | DATE<br>LAST<br>SITE VISIT | STATUS<br>COMMENT |
|--------|-----------------------------|-----------------|-------------------|----------------|------------------|-----------------------------|-----|-----------------|-----------|------------|-------------|--------------------------|----------------------------|-------------------|
|        |                             |                 |                   |                |                  |                             |     | 1MO<br>FU       | 6MO<br>FU | 12MO<br>FU | 24+MO<br>FU |                          |                            |                   |
| 075    | SUPORN/<br>THAILAND         | FS 85/017       | 9/85              | 12/85          | 11/12/86         | 300                         | 300 | 312             | 138       | 150        | *124        | 9/23/88                  | 9/88 DG                    | FU ON             |
| 600    | APELO/<br>PHILIPPINES       | FS 83/009       | 4/84              | 4/84           | 12/06/84         | 300                         | 300 | 214             | 140       | 148        | 243         | 5/24/88                  | 5/88 SMC                   | CR IN<br>PROGR    |
| 781    | YAH/<br>TAIWAN              | FS 84/003       | 4/84              | 4/84           | 6/20/86          | 200                         | 200 | 130             | 186       | 161        | 141         | 8/03/88                  | 9/88 DG                    | CLOSI             |
| 832    | LASSO OF-<br>LA VEGA/PANAMA | FS 84/007       | 2/84              | 2/84           | 9/14/84          | 300                         | 300 | 297             | 291       | 288        | 267         | 3/16/87                  | 6/87 CEC                   | CLOSE             |
|        |                             |                 |                   | 12/86          | 9/11/87          | 300                         | 300 | 273             | 267       | 248        | 2           | 7/13/88                  | 2/88 CEC                   | FU ON             |

FORMS RECEIVED/NOT PROCESSED

273

STUDY STATUS LIST  
FEMALE STERILIZATION

OCTOBER 1988

DESCRIPTION OF STUDY: MINILAPAROTOMY - FILSHIE CLIP VS. TUBAL PING

STUDY NUMBER: 8264

TOTAL NUMBER OF CASES: 1240

TOTAL NUMBER OF STUDIES: 6

| CENTER | INVESTIGATOR/<br>COUNTRY | INDEX<br>NUMBER | DATE<br>INITIATED | DATE<br>ACTIVE | DATE LAST<br>ADM | PROPOSED<br>NO. OF<br>CASES | ADM | EDBMS PROCESSED |           |            |            | DATE<br>LAST<br>SHIPMENT | DATE<br>LAST<br>SITE VISIT | STATUS/<br>COMMENTS |                 |
|--------|--------------------------|-----------------|-------------------|----------------|------------------|-----------------------------|-----|-----------------|-----------|------------|------------|--------------------------|----------------------------|---------------------|-----------------|
|        |                          |                 |                   |                |                  |                             |     | 1MO<br>FU       | 6MO<br>FU | 12MO<br>FU | 24MO<br>FU |                          |                            |                     |                 |
| 083    | CONTRERAS/<br>PANAMA     | FS 84/019       | 7/84              | 10/84          | 11/29/85         | 300                         | 300 | 284             | 283       | 299        | 17         | 03/26/87                 | 7/86                       | CEC                 | CLOSED          |
| 451    | GITHIARI/<br>KENYA       | FS 85/004       | 2/86              | 10/86          | 10/21/87         | 140                         | 112 | 89              | 73        | 43         | 18         | 07/07/88                 | 10/88                      | PG                  | FU ONLY         |
| 635    | SAGAHATA/<br>PERU        | FS 84/011       | 12/84             | 3/85           | 3/25/86          | 200                         | 200 | 200             | 166       | 167        | 1          | 09/23/87                 | 9/87                       | DB                  | CP IN<br>REVIEW |
| 865    | ROSSEFFER/<br>BRAZIL     | FS 84/022       | 2/85              | 11/85          | 5/13/86          | 100                         | 100 | 66              | 60        | 37         | 19         | 02/25/88                 | 3/87                       | DB                  | CLOSING         |
| 8594   | PEPEZ-PALACIOS<br>MEXICO | FS 87/007       | 3/87              | 12/87          | 3/30/88          | 200                         | 156 | 123             | 19        |            | X          | 09/06/88                 | 5/88                       | CEC                 | FU ONLY         |

#FUS IS RECEIVED/NOT PROCESSED

STUDY STATUS LIST  
FEMALE STERILIZATION

OCTOBER 1988

DESCRIPTION OF STUDY: LAPAROSCOPY - FILSHIE CLIP VS. TUBAL RING

STUDY NUMBER: 6265

TOTAL NUMBER OF CASES: 2120

TOTAL NUMBER OF STUDIES: 5

| CENTER | INVESTIGATOR/<br>COUNTRY       | INDEX<br>NUMBER       | DATE<br>INITIATED | DATE<br>ACTIVE | DATE LAST<br>ADM | PROPOSED<br>NO. OF<br>CASES | FORMS PROCESSED |           |           |            | DATE<br>LAST<br>SHIPMENT | DATE<br>LAST<br>SITE VISIT | STATUS/<br>COMMENTS |            |
|--------|--------------------------------|-----------------------|-------------------|----------------|------------------|-----------------------------|-----------------|-----------|-----------|------------|--------------------------|----------------------------|---------------------|------------|
|        |                                |                       |                   |                |                  |                             | ADM             | 1MO<br>FU | 6MO<br>FU | 12MO<br>FU |                          |                            |                     | 24MO<br>FU |
| 075    | SUPORN/<br>THAILAND            | FS 84/015<br>SUBGRANT | 10/84             | 10/84          | 3/24/86          | 300                         | 301             | 299       | 269       | 235        | 21                       | 5/18/88                    | 9/88 DG             | CLOSING    |
| 081    | MORENO/<br>PANAMA              | FS 85/002             | 2/85              | 3/85           | 9/02/85          | 300                         | 300             | 223       | 405       | 227        | 302                      | 9/16/87                    | 6/87 CEC            | CLOSED     |
| 739    | THOUW/<br>INDONESIA            | FS 85/018             | 11/85             | 6/86           | 11/11/87         | 150                         | 150             | 140       | *138      | *113       | *23                      | 10/03/88                   | 9/88 DG             | FU ONLY    |
| 741    | KORCHIIT/<br>THAILAND          | FS 84/023<br>SUBGRANT | 6/85              | 8/85           | 10/27/86         | 300                         | 158             | 123       | 100       | 101        | X                        | 5/27/87                    | 9/88 DG             | FU ONLY    |
|        |                                |                       |                   | 4/86           | 02/26/88         | 300                         | 300             | 259       | *221      | *144       | X                        | 10/03/88                   | 9/88 DG             | FU ONLY    |
| 754    | MOELOEK/<br>INDONESIA          | FS 85/019             | 11/85             | 7/86           | 9/30/87          | 150                         | 144             | 115       | 97        | *113       | Y                        | 8/11/88                    | 9/88 DG             | FU ONLY    |
| 892    | ORTIZ-<br>MARIACHI/MEXICO      | FS 85/012             | 7/85              | 5/86           | 1/26/88          | 220                         | 216             | 183       | 120       | 96         | X                        | 9/16/88                    | 5/88 CEC            | FU ONLY    |
| 894    | CONDEMO/<br>GUATEMALA REPUBLIC | FS 85/011             | 3/85              | 3/87           | 2/10/88          | 300                         | 255             | 243       | 138       | 63         | X                        | 9/05/88                    | 8/88 CEC            | FU ONLY    |

\*FORMS RECEIVED/NOT PROCESSED

STUDY STATUS LIST  
FEMALE STERILIZATION

OCTOBER 1988

DESCRIPTION OF STUDY: MINILAPAROTOMY - FILSHIE CLIP VS. WOLF CLIP

STUDY NUMBER: 6266

TOTAL NUMBER OF CASES: 1150

TOTAL NUMBER OF STUDIES: 4

| CENTER | INVESTIGATOR/<br>COUNTRY       | INDEX<br>NUMBER | DATE<br>INITIATED | DATE<br>ACTIVE | DATE LAST<br>ADM | PROPOSED<br>NO. OF<br>CASES | ADM | FORMS PROCESSED |           |            | DATE<br>LAST<br>SHIPMENT | DATE<br>LAST<br>SITE VISIT | STATUS/<br>COMMENTS |
|--------|--------------------------------|-----------------|-------------------|----------------|------------------|-----------------------------|-----|-----------------|-----------|------------|--------------------------|----------------------------|---------------------|
|        |                                |                 |                   |                |                  |                             |     | 1MO<br>FU       | 6MO<br>FU | 12MO<br>FU |                          |                            |                     |
| 332    | LASSO DE-<br>LA VEGA/PANAMA    | FS 85/013       | 8/85              | 9/85           | 5/22/86          | 300                         | 300 | 289             | 238       | 279        | 5/18/87                  | 6/87 CEC                   | CLOSED              |
| 8044   | CORDERO/<br>DOMINICAN REPUBLIC | FS 85/014       | 8/85              | 10/85          | 2/25/87          | 300                         | 302 | 260             | 213       | 193        | 7/18/88                  | 8/88 CEC                   | FU ONLY             |
| 684    | THAMRU/<br>MALAYSIA            | FS 85/024       | 9/86              | 12/86          | 1/27/88          | 150                         | 106 | *76             | *95       | *33        | 9/28/88                  | 9/88 DG                    | FU ONLY             |
| 8593   | REMEZ/<br>MEXICO               | FS 87/008       | 8/87              | 9/87           | 5/12/88          | 300                         | 138 | 113             | 29        |            | 8/03/88                  | 12/87 HW                   | FU ONLY             |
| 685    | LIM/<br>MALAYSIA               | FS 85/024       | 9/86              | 12/86          | 12/01/86         | 100                         | 5   | 5               | 5         |            | 2/25/88                  | 10/87 DG                   | FU ONLY             |

\*FORMS RECEIVED BUT NOT PROCESSED

STUDY STATUS LIST  
FEMALE STERILIZATION

OCTOBER 1988

DESCRIPTION OF STUDY: LAPAROSCOPY - FILSHIE CLIP VS. WOLF CLIP

STUDY NUMBER: 6267

TOTAL NUMBER OF CASES: 1500

TOTAL NUMBER OF STUDIES: 4

| CENTER | INVESTIGATOR/<br>COUNTRY | INDEX<br>NUMBER | DATE<br>INITIATED | DATE<br>ACTIVE | DATE LAST<br>ADM | PROPOSED<br>NO. OF<br>CASES | FORMS PROCESSED |           |           |            | DATE<br>LAST<br>SHIPMENT | DATE<br>LAST<br>SITE VISIT | STATUS<br>COMMENTS |     |         |
|--------|--------------------------|-----------------|-------------------|----------------|------------------|-----------------------------|-----------------|-----------|-----------|------------|--------------------------|----------------------------|--------------------|-----|---------|
|        |                          |                 |                   |                |                  |                             | ADM             | 1MO<br>FU | 6MO<br>FU | 12MO<br>FU |                          |                            |                    |     |         |
| 841    | SANTISOL/<br>GUATEMALA   | FS 85/010       | 2/86              | 2/86           | 7/30/86          | 300                         | 238             | 236       | 234       | 121        | 22                       | 5/27/88                    | 11/87              | CEC | CLOSING |
| 8009   | LOUISSANTIN/<br>HAITI    | FS 85/016       | 9/85              | 9/85           | 9/30/86          | 300                         | 237             | 215       | 131       | 116        | X                        | 10/20/87                   | 4/87               | SB  | CLOSED  |
| 364    | URIBE/MEXICO             | FS 85/022       | 11/85             | 1/86           | 4/13/86          | 400                         | 400             | 343       | 257       | 215        | 42                       | 8/23/88                    | 5/88               | CEC | FU ONL  |
| 100    | ZICHELOIN/<br>VENEZUELA  | FS 86/001       | 12/85             | 1/86           | 5/22/87          | 300                         | 300             | 271       | 194       | 136        | 33                       | 9/21/88                    | 6/88               | CEC | FU ONL  |

\*FORMS RECEIVED/NOT PROCESSED

66  
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STUDY STATUS LIST  
FEMALE STERILIZATION STUDY

OCTOBER 1988

DESCRIPTION OF STUDY: BIPOLAR ELECTROCAUTERY VS. FILSHIE CLIP

STUDY NUMBER: 6269

TOTAL NUMBER OF CASES: 1075

TOTAL NUMBER OF STUDIES: 5

| CENTER | INVESTIGATOR/<br>COUNTRY | INDEX<br>NUMBER | DATE<br>INITIATED | DATE<br>ACTIVE | DATE LAST<br>ADM | PROPOSED<br>NO. OF<br>CASES | FORMS PROCESSED |           |           |            | DATE<br>LAST<br>SHIPMENT | DATE<br>LAST<br>SITE VISIT | STATUS/<br>COMMENTS |
|--------|--------------------------|-----------------|-------------------|----------------|------------------|-----------------------------|-----------------|-----------|-----------|------------|--------------------------|----------------------------|---------------------|
|        |                          |                 |                   |                |                  |                             | ADM             | 1MO<br>FU | 6MO<br>FU | 12MO<br>FU |                          |                            |                     |
| 029    | KAUPPILAINEN/<br>FINLAND | FS 87/002       | 12/86             | 2/87           | 1/28/88          | 200                         | 199             | 130       | 0         | 44         | 9/02/88                  | 4/88 DG                    | FU ONLY             |
| 750    | KWAK/KOREA               | FS 87/004       | 3/87              | 6/87           | 9/10/87          | 300                         | 300             | 269       | 298       | 1          | 9/12/88                  | 9/88 DG                    | FU ONLY             |
| 781    | YAN/TAIWAN               | FS 86/015       | 9/86              | 3/87           | 11/28/87         | 75                          | 75              | 64        | 38        |            | 12/30/87                 | 9/88 DG                    | FU ONLY             |
| 231    | LEODOLTER/<br>AUSTRIA    | FS 86/014       | 9/86              | 3/87           | 03/28/88         | 300                         | 200             | 124       | 106       | 17         | 8/12/88                  | 4/88 DG                    | FU ONLY             |
| 260    | LAGENFICHLER/<br>AUSTRIA | FS 87/001       | 12/86             | 6/87           | 11/26/87         | 200                         | 200             | 200       | 164       | 55         | 7/14/88                  | 4/88 DG                    | FU ONLY             |

FORMS RECEIVED NOT PROCESSED

STUDY STATUS LIST  
 FEMALE STERILIZATION STUDY

OCTOBER 1988

DESCRIPTION OF STUDY: MINILAPAROTOMY AND LAPAROSCOPY - FILSHIE CLIP

STUDY NUMBER: 6700

TOTAL NUMBER OF CASES: 200

TOTAL NUMBER OF STUDIES: 1

| CENTER | INVESTIGATOR/<br>COUNTRY | INDEX<br>NUMREF | DATE<br>INITIATED | DATE<br>ACTIVE | EXPIRATION<br>DATE | PROPOSED<br>NO. OF<br>CASES | FORMS PROCESSED |           |           |            |            | DATE<br>LAST<br>SHIPMENT | DATE<br>LAST<br>SITE VISIT | STATUS/<br>COMMENT |
|--------|--------------------------|-----------------|-------------------|----------------|--------------------|-----------------------------|-----------------|-----------|-----------|------------|------------|--------------------------|----------------------------|--------------------|
|        |                          |                 |                   |                |                    |                             | ADM             | 1MC<br>FU | 6MO<br>FU | 12MO<br>FU | 24MO<br>FU |                          |                            |                    |
| 8063   | ADGALA/<br>BRAZIL        | FS 35/015       | 6/85              | 7/85           | 3/87               | 200                         | 198             | 197       | 197       |            |            | 4/21/87                  | 4/26DB                     | CLOSED             |
|        |                          |                 |                   |                |                    | CORRECTED FORMS             | 200             | 140       | 145       | 150        | 10         |                          |                            |                    |

STUDY STATUS LIST  
 MALE STERILIZATION STUDY

OCTOBER - 1988

DESCRIPTION OF STUDY: STANDARD INCISION VS. PUNCTURE METHOD OF VASECTOMY

STUDY NUMBER: 764

TOTAL NUMBER OF CASES: 600

TOTAL NUMBER OF STUDIES: 4

| CENTER | INVESTIGATOR/<br>COUNTRY  | INDEX<br>NUMBER | DATE<br>INITIATED | DATE<br>ACTIVE | EXPIRATION<br>DATE | PROPOSED<br>NO. OF<br>CASES | FORMS PROCESSED |       |        | DATE<br>LAST<br>SHIPMENT | DATE<br>LAST<br>SITE VISIT | STATUS/<br>COMMENTS |
|--------|---------------------------|-----------------|-------------------|----------------|--------------------|-----------------------------|-----------------|-------|--------|--------------------------|----------------------------|---------------------|
|        |                           |                 |                   |                |                    |                             | ADM             | EARLY | 10 WKS |                          |                            |                     |
| 733    | RELIGASATTE/<br>SRI LANKA | MS88/002        | 3/88              | 8/88           | 8/88               | 300                         | 52              | 52    |        | 8/31/88                  | 7/88 MCI                   | ACTIVE              |
| 692    | APICHART/<br>THAILAND     | MS88/001        | 3/88              | 4/88           | 10/88              | 300                         | 300             | 196   | 28     | 9/09/88                  | 9/88 DG                    | FU ONLY             |

\*FORMS RECEIVED/NOT PROCESSED

STUDY STATUS LIST  
IUD

Cheryle Champion

October 1988

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/<br>COUNTRY | INDEX NUMBER | DATE INITIATED | EXPIRATION DATE | PROPOSED NO. OF CASES | FORMS PROCESSED |           |           |           |             | DATE LAST SHIPMENT | DATE LAST SITE VISIT | STATUS/<br>COMMENTS |
|---------------|--------------------------|--------------|----------------|-----------------|-----------------------|-----------------|-----------|-----------|-----------|-------------|--------------------|----------------------|---------------------|
|               |                          |              |                |                 |                       | ADM             | 1MO<br>FU | 3MO<br>FU | 6MO<br>FU | 12MO+<br>FU |                    |                      |                     |
| 020           | ANDOLSEK/YUGOSLAVIA      | 80/002       | 3/83           | 6/87            | 500                   | 499             | 436       | 424       | 444       | 463         | 6/12/87            | 4/87 JB              | CLOSED              |
| 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                   | 300             | 235       | 229       | 245       | 239         | 5/18/88            | 8/87 CEC             | CLOSED              |

Description of Study: Introduction of Postpartum IUD Insertion

Study Number: 574

Total Number of Cases: 400

Total Number of Studies: 2

FCO: 5583

| CENTER NUMBER | INVESTIGATOR/<br>COUNTRY | INDEX NUMBER | DATE INITIATED | EXPIRATION DATE | PROPOSED NO. OF CASES | FORMS PROCESSED |           |          |           |             | DATE LAST SHIPMENT | DATE LAST SITE VISIT | STATUS/<br>COMMENTS |
|---------------|--------------------------|--------------|----------------|-----------------|-----------------------|-----------------|-----------|----------|-----------|-------------|--------------------|----------------------|---------------------|
|               |                          |              |                |                 |                       | ADM             | 1MO<br>FU | 3M<br>FU | 6MO<br>FU | 12MO+<br>FU |                    |                      |                     |
| 823           | VASQUEZ/EL SALVADOR      | 88/002       | 5/88           | 7/90            | 200                   |                 |           |          |           |             |                    | 5/88 DC              | ACTIVE              |
| 824           | HERNANDEZ/EL SALVADOR    | 88/003       | 5/88           | 7/90            | 200                   |                 |           |          |           |             |                    | 5/88 DC              | ACTIVE              |

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

Study Number: 532

Total Number of Cases: 900

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+ |                    |                      |                 |
| 084           | DELGADO/MEXICO       | 85/008       | 7/85           | 6/87            | 300                   | 300             | 260    | 269    | 288    | 282      | 12/08/87           | 5/87 CEC             | CLOSED          |
| 060           | DAVID/PHILIPPINES    | 86/004       | 7/87           | 1/88            | 200                   | 198             | 135    | 104    | 77     | 16       | 7/08/88            | 5/88 SM              | ACTIVE          |
| 061           | ALFONSO/PHILIPPINES  | 86/006       | 7/87           | 5/88            | 200                   | 200             | 190    | 168    | 44     |          | 7/25/88            | 5/88 SM              | ACTIVE          |
| 066           | DACALOS/PHILIPPINES  | 86/007       | 7/87           | 5/88            | 200                   | 80              | 26     | 26     | 73     |          | 5/24/88            | 5/88 SM              | ACTIVE          |

STUDY STATUS LIST  
IUD

October 1988

Description of Study: TCu200 vs Adapted 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                   | 172             | 137    | 105    | 102    | 83                 | 7/19/88              | 2/88 JM         | ADMISSIONS<br>CLOSED FU ONLY |

STUDY STATUS LIST  
IUD

October 1988

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

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             | 1MO | 3MO | 6MO | 12MO+ |                    |                      |                 |
| 100           | ZIGHELBOIM/VENEZUELA | 85/006       | 6/85           | 9/87            | 300                   | 300             | 176 | 188 | 177 | 158   | 1/21/88            | 1/88 CEC             | CLOSED          |

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

Study Number: 550

Total Number of Cases: 3600

Total Number of Studies: 11

FCO: 3151

| CENTER NUMBER | INVESTIGATOR/COUNTRY | INDEX NUMBER         | DATE INITIATED | EXPIRATION DATE | PROPOSED NO. OF CASES | FORMS PROCESSED |     |     |     |       | DATE LAST SHIPMENT | DATE LAST SITE VISIT | STATUS/COMMENTS |
|---------------|----------------------|----------------------|----------------|-----------------|-----------------------|-----------------|-----|-----|-----|-------|--------------------|----------------------|-----------------|
|               |                      |                      |                |                 |                       | ADM             | 1MO | 3MO | 6MO | 12MO+ |                    |                      |                 |
| 342           | EFCS/EGYPT           | 86/008<br>SUB 3151-4 | 9/87           | 9/88            | 1000                  | 981             | 787 | 644 | 618 | 468   | N/A                | 1/88 CBC             | ACTIVE          |
| 363           | TOPPOZADA/EGYPT      | 85/005               | 6/85           | 6/87            | 200                   | 199             | 71  | 73  | 68  | 59    | 4/27/88            | 2/88 PG              | ACTIVE          |
| 401           | MUHKTAR/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 380 A vs. TCu 200

(cont'd)

Study Number: 550

Total Number of Cases: 3600

TOTAL NUMBER OF STUDIES: 11

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           | DOR/CAMEROON         | 86/012       | 6/86           | 6/88            | 300                   | 274             | 195    | 142    | 92     | 68       | 8/08/88            | 11/87 RD             | ACTIVE          |
| 680           | HUSAIN/PAKISTAN      | 85/15        | 3/86           | 11/87           | 300                   | 294             | 201    | 171    | 202    | 139      | 6/08/88            | 2/88 SB              | ACTIVE          |
| 821           | HENRIQUE EL SALVADOR | 85/17        | 1/86           | 11/87           | 300                   | 300             | 261    | 220    | 213    | 220      | 7/18/88            | 4/88 DC              | CLOSING         |
| 825           | ALVARADO/MEXICO      | 85/12        | 8/85           | 9/87            | 300                   | 300             | 257    | 253    | 245    | 237      | 9/ 8/87            | 5/87 CEC             | CLOSED          |
| 854           | BELTRAN/CHILE        | 86/009       | 6/86           | 1/88            | 300                   | 300             | 288    | 282    | 284    | 180      | 11/16/87           | 10/87 CEC            | CLOSED          |
| 8020          | AGUINAGA/BRAZIL      | 85/011       | 10/85          | 1/88            | 300                   | 300             | 217    | 163    | 142    | 92       | 4/12/88            | 11/87 DB             | ACTIVE          |
| 8052          | IHSS/HONDURAS        | 86/010       | 6/86           | 6/88            | 300                   | 295             | 236    | 177    | 130    | 312      | 8/29/88            | 1/88 DC              | ACTIVE          |
| 8065          | FERNANDEZ/COSTA RICA | 86/011       | 3/87           | 6/88            | 200                   | 74              | 65     | 55     | 11     | -        | 9/28/87            | 6/88 CEC             | ACTIVE          |

STUDY STATUS LIST  
IUD

October 1988

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

Study Number: 552

Total Number of Cases: 800

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                   | 300             | 260    | 210    | 197    | 135      | 7/27/88            | 7/88 SB              | ACTIVE          |
| 101           | ACOSTA/PERU          | 85/16        | 12/85          | 5/88            | 300                   | 291             | 236    | 224    | 232    | 231      | 9/02/88            | 6/88 CEC             | ACTIVE          |
| 304           | KISNISCI/TURKEY      | 85/002       | 7/86           | 6/87            | 200                   | 170             | 107    | 69     | 66     | 84       | 4/21/88            | 2/88 PG              | ACTIVE          |

Description of Study: Evaluation of TCu 380 A vs. MLCu250

Study Number: 553

Total Number of Cases: 2150

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                   | 300             | 299    | 288    | 276    | 267      | 5/18/88            | 2/88 SM              | ACTIVE          |
| 741           | DAMRONG/THAILAND      | 85/009<br>SUB 3151-1 | 5/85           | 9/88            | 1400                  | 1396            | 1260   | 1151   | 1093   | 1593     | 8/26/88            | 6/88 JM              | ACTIVE          |
| 779           | GUNASEKERA SRI LANKA  | 86/003               | 2/86           | 1/88            | 300                   | 300             | 273    | 264    | 264    | 259      | 7/25/88            | 7/88 SM              | ACTIVE          |
| 780           | CHOONG MALAYSIA       | 86/001               | 1/86           | 2/88            | 150                   | 148             | 139    | 122    | 119    | 85       | 8/16/88            | 7/88 SM              | ACTIVE          |

STUDY STATUS LIST  
IUD

October 1988

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           | 4/88            | 1800                  | 2418 | 2209            | 1275   |        |          | N/A                | 3/88 MW              | CLOSING         |
| 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<br>SUB 3156-1 | 7/86           | 6/88            | 1800                  | 1275 | 1144            | 1222   |        |          | 09/12/88           | 3/88 RD              | ACTIVE          |

STUDY STATUS LIST  
IUD

October 1988

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

Study Number: 5550

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             | FU 1MO | FU 3MO | FU 6MO |                    |                      |                 | FU 12MO+ |
| 079           | SHRESTHA/NEPAL       | 87/001       | 9/87           | 10/39           | 200                   | 13              | -      | -      | -      | -                  | 12/22/87             | 6/87 SB         | ACTIVE   |
| 875           | ARBOLEDA/COLOMBIA    | 87/C05       | 3/87           | 4/89            | 400                   | 89              | -      | -      | -      | -                  | 12/03/87             | 9/87 DB         | ACTIVE   |

STUDY STATUS LIST  
IUD

October 1988

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<br>PENFIN | INDONESIA            | 85/18<br>SUB 3151-3 | 5/86           | 9/88            | 3000                  | 2992            | 2960   | 2900   | 2849   | 2532               | N/A                  | 3/88 CBC         | ACTIVE   |

Description of Study: IUD Surveillance Using TCu200 and Lippes Loops

Study Number: 5339

Total Number of Cases: 300

Total Number of Studies: 1

FCO: 3581

| 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 |
| 441           | SANGARET/MALI        | 88/001       | 5/88           | 6/90            | 300                   | 56              | 36     |        |        |                    | 8/05/88              | 3/88 KJ          | ACTIVE  |

WBL

STUDY STATUS LIST  
 INVESTIGATOR NETWORK NEEDS  
 FCO 3114  
 ACTIVE STUDIES

CHERYLE CHAMPION

OCTOBER 1988

DESCRIPTION OF STUDY: TCU 380A VS TCU 200

STUDY NUMBER: 5550

TOTAL NUMBER OF CASES: 600

TOTAL NUMBER OF STUDIES: 2

| CENTER | INVESTIGATOR/<br>COUNTRY | INDEX<br>NUMBER | DATE<br>INITIATED/<br>DATE ACTIVE | EXPIRATION<br>DATE | PROPOSED<br>NO. OF<br>CASES | ADM | FORMS PROCESSED |            |            |             | DATE<br>LAST<br>SHIPMENT | DATE<br>LAST<br>SITE VISIT | STATUS/<br>COMMENTS |
|--------|--------------------------|-----------------|-----------------------------------|--------------------|-----------------------------|-----|-----------------|------------|------------|-------------|--------------------------|----------------------------|---------------------|
|        |                          |                 |                                   |                    |                             |     | 1 MO<br>FU      | 3 MO<br>FU | 6 MO<br>FU | 12 MO<br>FU |                          |                            |                     |
| 079    | SHRESTHA/NEPAL           | IUD<br>87/001   | 11/87                             | 2/89               | 200                         | 199 | 201             | 159        | 107        |             | 9/16/88                  | 2/88 JH                    | ACTIVE              |
| 875    | ARBOLEDA/COLOMBIA        | IUD<br>87/005   | 9/87                              | 4/89               | 400                         | 365 | 285             | 230        | 184        | 3           | 9/06/88                  | 9/87 DB                    | ACTIVE              |

5/88

STUDY STATUS LIST  
 INVESTIGATOR NETWORK NEEDS  
 FCO 3114  
 ACTIVE STUDIES

OCTOBER 1988

DESCRIPTION OF STUDY: FS SURVEILLANCE

STUDY NUMBER: 6900

TOTAL NUMBER OF CASES: 200

TOTAL NUMBER OF STUDIES: 1

| CENTER | INVESTIGATOR/<br>COUNTRY | INDEX<br>NUMBER | DATE<br>INITIATED/<br>DATE ACTIVE | EXPIRATION<br>DATE | PROPOSED<br>NO. OF<br>CASES | FORMS PROCESSED |            |            |            | DATE<br>LAST<br>SHIPMENT | DATE<br>LAST<br>SITE VISIT | STATUS/<br>COMMENTS |             |        |
|--------|--------------------------|-----------------|-----------------------------------|--------------------|-----------------------------|-----------------|------------|------------|------------|--------------------------|----------------------------|---------------------|-------------|--------|
|        |                          |                 |                                   |                    |                             | ADM             | 1 MO<br>FU | 3 MO<br>FU | 6 MO<br>FU |                          |                            |                     | 12 MO<br>FU |        |
| 040    | OTOLORIN/NIGERIA         | FS<br>86/003    | 6/86                              | 9/86               | 2/88                        | 200             | 190        | 176        | X          | 74                       | X                          | 8/88                | 8/88 RD     | ACTIVE |

DESCRIPTION OF STUDY: NONCOMPARATIVE STUDY OF LO-FEMENAL

STUDY NUMBER: 8822

TOTAL NUMBER OF CASES: 100

TOTAL NUMBER OF STUDIES: 1

| CENTER | INVESTIGATOR/<br>COUNTRY | INDEX<br>NUMBER | DATE<br>INITIATED/<br>DATE ACTIVE | EXPIRATION<br>DATE | PROPOSED<br>NO. OF<br>CASES | FORMS PROCESSED |            |            |            | DATE<br>LAST<br>SHIPMENT | DATE<br>LAST<br>SITE VISIT | STATUS/<br>COMMENTS |             |        |
|--------|--------------------------|-----------------|-----------------------------------|--------------------|-----------------------------|-----------------|------------|------------|------------|--------------------------|----------------------------|---------------------|-------------|--------|
|        |                          |                 |                                   |                    |                             | ADM             | 1 MO<br>FU | 4 MO<br>FU | 8 MO<br>FU |                          |                            |                     | 12 MO<br>FU |        |
| 683    | LUBIS/INDONESIA          | 86/016          | 9/87                              |                    | 12/89                       | 100             | 87         | 81         | 64         | 24                       |                            | 9/22/88             | 7/88 MR     | ACTIVE |

2/89

STUDY STATUS LIST  
 INVESTIGATOR NETWORK MEETS  
 FCO 3114  
 ACTIVE STUDIES

DESCRIPTION OF STUDY: TRIQUILAR VS LO-DVPAL

OCTOBER 1988

STUDY NUMBER: 8841

TOTAL NUMBER OF CASES: 400

TOTAL NUMBER OF STUDIES: 2

| CENTER | INVESTIGATOR/<br>COUNTRY | INDEX<br>NUMBER | DATE<br>INITIATED/<br>DATE ACTIVE | EXPIRATION<br>DATE | PROPOSED<br>NO. OF<br>CASES | EORYS PROCESSED |            |            |            |             | DATE<br>LAST<br>SHIPMENT | DATE<br>LAST<br>SITE VISIT | STATUS/<br>COMMENTS |
|--------|--------------------------|-----------------|-----------------------------------|--------------------|-----------------------------|-----------------|------------|------------|------------|-------------|--------------------------|----------------------------|---------------------|
|        |                          |                 |                                   |                    |                             | ADM             | 1 MO<br>FU | 4 MO<br>FU | 8 MO<br>FU | 12 MO<br>FU |                          |                            |                     |
| 613    | CRUZ/PHILLIPINES         | SYS<br>87/001   | 3/87                              | 3/89               | 200                         | 196             | 180        | 73         | 38         | 10          | 8/19/88                  | 5/88 SM                    | ACTIVE              |
| 6000   | VILLAMAR/<br>PHILIPPINES | SYS<br>87/002   | 3/87                              | 12/89              | 200                         | 92              | 79         | 32         | 9          |             | 5/25/88                  | 5/88 SM                    | ACTIVE              |

DESCRIPTION OF STUDY: TRIQUILAR VS HARVELON

STUDY NUMBER: 9830

TOTAL NUMBER OF CASES: 200

TOTAL NUMBER OF STUDIES: 1

| CENTER | INVESTIGATOR/<br>COUNTRY | INDEX<br>NUMBER | DATE<br>INITIATED/<br>DATE ACTIVE | EXPIRATION<br>DATE | PROPOSED<br>NO. OF<br>CASES | EORYS PROCESSED |            |            |            |             | DATE<br>LAST<br>SHIPMENT | DATE<br>LAST<br>SITE VISIT | STATUS/<br>COMMENTS |                             |
|--------|--------------------------|-----------------|-----------------------------------|--------------------|-----------------------------|-----------------|------------|------------|------------|-------------|--------------------------|----------------------------|---------------------|-----------------------------|
|        |                          |                 |                                   |                    |                             | ADM             | 1 MO<br>FU | 4 MO<br>FU | 8 MO<br>FU | 12 MO<br>FU |                          |                            |                     |                             |
| 7020   | ISMAL/MALAYSIA           | SYS<br>86/001   | 1/86                              | 4/88               | 200                         | 198             | 179        | 165        | 123        | 111         | 3                        | 1/28/88                    | 10/87 DG            | CLOSED<br>CR IN<br>PROGRESS |

2/88

STUDY STATUS LIST  
 INVESTIGATOR NETWORK NEEDS  
 FCO 3114  
 ACTIVE STUDIES

OCTOBER 1988

DESCRIPTION OF STUDY: MORIDAY VS. LO-FERENAL

STUDY NUMBER: 9850

TOTAL NUMBER OF CASES: 200

TOTAL NUMBER OF STUDIES: 1

| CENTER | INVESTIGATOR/<br>COUNTRY | INDEX<br>NUMBER | DATE<br>INITIATED/<br>DATE ACTIVE | EXPIRATION<br>DATE | PROPOSED<br>NO. OF<br>CASES | FOBMS PROCESSED |            |            |            |                | DATE<br>LAST<br>SHIPMENT | DATE<br>LAST<br>SITE VISIT | STATUS/<br>COMMENTS |                          |
|--------|--------------------------|-----------------|-----------------------------------|--------------------|-----------------------------|-----------------|------------|------------|------------|----------------|--------------------------|----------------------------|---------------------|--------------------------|
|        |                          |                 |                                   |                    |                             | ADM             | 1 MO<br>FU | 4 MO<br>FU | 8 MO<br>FU | 12 MO PC<br>FU |                          |                            |                     |                          |
| 440    | TRAORE/MALI              | SYS<br>83/032   | 9/84 / 9/84                       | 9/87               | 200                         | 200             | 165        | 140        | 96         | 84             | 1                        | 3/08/88                    | 2/88 KJ             | CLOSED<br>CR IN PROGRESS |

DESCRIPTION OF STUDY: OVRETTE VS. MICRONOVUM

STUDY NUMBER: 8877

TOTAL NUMBER OF CASES: 1400

TOTAL NUMBER OF STUDIES: 1

| CENTER | INVESTIGATOR/<br>COUNTRY | INDEX<br>NUMBER | DATE<br>INITIATED/<br>DATE ACTIVE | EXPIRATION<br>DATE | PROPOSED<br>NO. OF<br>CASES | FOBMS PROCESSED |            |            |            | DATE<br>LAST<br>SHIPMENT | DATE<br>LAST<br>SITE VISIT | STATUS/<br>COMMENTS |
|--------|--------------------------|-----------------|-----------------------------------|--------------------|-----------------------------|-----------------|------------|------------|------------|--------------------------|----------------------------|---------------------|
|        |                          |                 |                                   |                    |                             | ADM             | 1 MO<br>FU | 3 MO<br>FU | 6 MO<br>FU |                          |                            |                     |
| MULTI  | BERMENE/ZIMBABWE         | POC<br>85/004   | 10/85/10/85                       | 4/89               | 1400                        | 1146            | 696        | 727        | 513        | 9/13/88                  | 7/88 RD                    | ACTIVE              |

24

STUDY STATUS LIST  
 INVESTIGATOR NETWORK REEFS  
 FCO 3114  
 ACTIVE STUDIES

OCTOBER 1988

DESCRIPTION OF STUDY: LOW DOSE AND STANDARD DOSE SURVEILLANCE

STUDY NUMBER: 5890

TOTAL NUMBER OF CASES: 200

TOTAL NUMBER OF STUDIES: 1

| CENTER | INVESTIGATOR/<br>COUNTRY | INDEX<br>NUMBER | DATE<br>INITIATED/<br>DATE ACTIVL | EXPIRATION<br>DATE | PROPOSED<br>NO. OF<br>CASES | FORMS PROCESSED |            |            |            | DATE<br>LAST<br>SHIPMENT | DATE<br>LAST<br>SITE VISIT | STATUS/<br>COMMENTS |             |
|--------|--------------------------|-----------------|-----------------------------------|--------------------|-----------------------------|-----------------|------------|------------|------------|--------------------------|----------------------------|---------------------|-------------|
|        |                          |                 |                                   |                    |                             | ADM             | 1 MO<br>FU | 4 MO<br>FU | 8 MO<br>FU |                          |                            |                     | 12 MO<br>FU |
| 463    | MAIDOUKA/NIGER           | SYS<br>86/013   | 9/86                              | 6/88               | 200                         | 141             | 118        | 88         | 59         | 47                       | 7/19/88                    | 9/87RD              | ACTIVE      |

.ALSTAT(NLJ)

Gary Grubb- Project Manager

STUDY STATUS LIST  
NET MICROSPHERES

October 1988

Description of Study: Contraceptive Effectiveness of 100 mg NET Microspheres

Study Number: 851

Total Number of Cases: 800

Total Number of Studies: 8

| Center | Investigator/<br>City, Country | Sub-<br>Agreement<br>Number | PHSC-# | Date First<br>Injection | Contract<br>Expiration<br>Date | Proposed<br>Number of<br>Cases |     |    |    |    |    |    |    |    | Date<br>Last<br>Ship | Date<br>Last<br>Visit | Status/<br>Comments |
|--------|--------------------------------|-----------------------------|--------|-------------------------|--------------------------------|--------------------------------|-----|----|----|----|----|----|----|----|----------------------|-----------------------|---------------------|
|        |                                |                             |        |                         |                                |                                | ADM | 3  | 6  | 9  | 12 | 15 | 18 | 21 |                      |                       |                     |
| 0363   | Said/Alexandria, Egypt         | 3131-35                     |        |                         |                                | 100                            | 0   | 0  | 0  | 0  | 0  | 0  | 0  | 0  |                      |                       |                     |
| 0223   | Hanson/Minneapolis, MN         | 3131-16                     | 841-2  |                         | 5/91                           | 100                            | 0   | 0  | 0  | 0  | 0  | 0  | 0  | 0  |                      |                       |                     |
| 0225   | Poindexter/Houston, TX         | 3131-14                     | 841-2  | 8/88                    | 5/91                           | 100                            | 28  | 0  | 0  | 0  | 0  | 0  | 0  | 0  | 9/88                 |                       | Active              |
| 0226   | Yon/Seattle, WA                | 3131-27                     | 841-3  |                         | 5/91                           | 100                            | 0   | 0  | 0  | 0  | 0  | 0  | 0  | 0  |                      | 6/88                  |                     |
| 0798   | Ratnam/Singapore               | 3131-18                     | 841-1  | 4/88                    | 9/90                           | 100                            | 20  | 11 | 0  | 0  | 0  | 0  | 0  | 0  | 9/88                 | 7/88                  | Active              |
| 8067   | Alvarado/Durango, Mexico       | 3131-21                     | 841-1  | 1/88                    | 9/90                           | 100                            | 51  | 16 | 2  | 0  | 0  | 0  | 0  | 0  | 9/88                 | 5/88                  | Active              |
| 0850   | Guzman-Serani/Valdivia, Chile  | 3131-20                     | 841-1  | 11/87                   | 9/90                           | 100                            | 100 | 85 | 63 | 31 | 0  | 0  | 0  | 0  | 9/88                 | 4/88                  | Active              |
| 0920   | Darney/San Francisco, CA       | 3131-23                     | 841-2  |                         | 5/91                           | 100                            | 0   | 0  | 0  | 0  | 0  | 0  | 0  | 0  |                      | 6/88                  |                     |

Description of Study: Contraceptive Effectiveness of 65 mg NET Microsphere.

Study Number: 853

Total Number of Cases: 400

Total Number of Studies: 4

| Center | Investigator/<br>City, Country | Sub-<br>Agreement<br>Number | PHSC-# | Date First<br>Injection | Contract<br>Expirat<br>Date | Proposed<br>Number of<br>Cases |     |    |    |   |    | Date<br>Last<br>Ship | Date<br>Last<br>Visit | Status/<br>Comments |        |
|--------|--------------------------------|-----------------------------|--------|-------------------------|-----------------------------|--------------------------------|-----|----|----|---|----|----------------------|-----------------------|---------------------|--------|
|        |                                |                             |        |                         |                             |                                | ADM | 3  | 6  | 9 | 12 |                      |                       |                     |        |
| 0005   | Bassol/Torreón, Mexico         | 3131-24                     | 838-2  | 11/87                   | 10/89                       | 100                            | 54  | 35 | 21 | 5 | 0  |                      | 9/88                  | 5/88                | Active |
| 0923   | Pasquale/New Brunswick, NJ     | 3131-32                     | 839-5  |                         | 5/90                        | 100                            | 0   | 0  | 0  | 0 | 0  |                      |                       | 6/88                |        |
| 0025   | Boya/Charlotte, NC             | 3131-34                     | 838-4  | 8/88                    | 5/90                        | 100                            | 7   | 0  | 0  | 0 | 0  |                      | 9/88                  | 6/88                | Active |
| 0926   | Huggins/Baltimore, MD          |                             |        |                         | 5/90                        | 100                            | 0   | 0  | 0  | 0 | 0  |                      |                       | 8/88                |        |

STUDY STATUS LIST  
NET MICROSPHERES

October 1988

Description of Study: Comparative Evaluation of 65 mg and 100 mg NET Microspheres

Study Number: 852

Total Number of Cases: 500

Total Number of Studies: 5

| Center | Investigator/<br>City, Country | Sub-<br>Agreement<br>Number | PHSC-# | Date First<br>Injection | Contract<br>Expirat<br>Date | Proposed<br>Number of<br>Cases |     |    |    |   |    |    |    |    |    |   | Date<br>Last<br>Shipm | Date<br>Last<br>Visit | Status/<br>Comments |
|--------|--------------------------------|-----------------------------|--------|-------------------------|-----------------------------|--------------------------------|-----|----|----|---|----|----|----|----|----|---|-----------------------|-----------------------|---------------------|
|        |                                |                             |        |                         |                             |                                | ADM | 3  | 6  | 9 | 12 | 15 | 18 | 21 | 24 |   |                       |                       |                     |
| 0908   | Archer/Norfolk, VA             | 3131-33                     | 842-2  | 12/87                   | 9/90                        | 100                            | 100 | 66 | 38 | 0 | 0  | 0  | 0  | 0  | 0  | 0 | 9/88                  | 8/88                  | Active              |
| 0912   | Shoupe/Los Angeles, CA         | 3131-30                     | 842-5  |                         | 5/91                        | 100                            | 0   | 0  | 0  | 0 | 0  | 0  | 0  | 0  | 0  | 0 |                       |                       |                     |
| 0918   | Balmaceca/Garden Grove, CA     | 3131-31                     |        |                         | 5/91                        | 100                            | 0   | 0  | 0  | 0 | 0  | 0  | 0  | 0  | 0  | 0 |                       |                       |                     |
| 0952   | Singh, Saxena/New York, NY     | 3131-29                     | 842-3  | 8/88                    | 5/91                        | 100                            | 20  | 0  | 0  | 0 | 0  | 0  | 0  | 0  | 0  | 0 | 9/88                  |                       | Active              |
| 0961   | Groff/San Antonio, TX          | 3131-26                     | 842-4  |                         | 5/91                        | 100                            | 0   | 0  | 0  | 0 | 0  | 0  | 0  | 0  | 0  | 0 |                       |                       |                     |

Description of Study: Comparative Evaluation of 65 mg and 100 mg NET Microspheres

Study Number: 854

Total Number of Cases: 200

Total Number of Studies: 1

| Center | Investigator/<br>City, Country | Sub-<br>Agreement<br>Number | PHSC-# | Date First<br>Injection | Contract<br>Expirat<br>Date | Proposed<br>Number of<br>Cases |     |   |   |   |    |    |    |    |    |   | Date<br>Last<br>Shipm | Date<br>Last<br>Visit | Status/<br>Comments |
|--------|--------------------------------|-----------------------------|--------|-------------------------|-----------------------------|--------------------------------|-----|---|---|---|----|----|----|----|----|---|-----------------------|-----------------------|---------------------|
|        |                                |                             |        |                         |                             |                                | ADM | 3 | 6 | 9 | 12 | 15 | 18 | 21 | 24 |   |                       |                       |                     |
| 0075   | Suporn/Bangkok, Thailand       | 3131-28                     | 843-1  | 5/88                    | 9/90                        | 200                            | 8   | 0 | 0 | 0 | 0  | 0  | 0  | 0  | 0  | 0 | 9/88                  | 7/88                  | Active              |

Totals Across All Studies

|              | 65mg | 100mg | TOTAL |
|--------------|------|-------|-------|
| Admissions   | 124  | 264   | 388   |
| Women-months | 309  | 702   | 1011  |

Gary Grubb - Project Manager

STUDY STATUS LIST  
NET PELLET IMPLANT

October 1988

Description of Study: Evaluation of the Safety and Pharmacokinetics of Biodegradable Norethindrone Pellet Implants

Study Number: 880

Total Number of Cases: 35

Total Number of Studies: 1

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| Center | Investigator/<br>City, Country | PHSC-# | Date First<br>Insertion | Contract<br>Expiration<br>Date | Proposed<br>Number of<br>Cases | ADM | 3  | 6 | 9 | 12 | 15 | 18 | 21 | 24 | Date<br>Last<br>Shipment | Date<br>Last<br>Visit | Status/<br>Comments |
|--------|--------------------------------|--------|-------------------------|--------------------------------|--------------------------------|-----|----|---|---|----|----|----|----|----|--------------------------|-----------------------|---------------------|
| 0908   | Archer/Norfolk, Va.            | 844    | 3/88                    | 4/90                           | 35                             | 19  | 15 |   |   |    |    |    |    |    | 8/88                     | 8/88                  | Active              |

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13

STUDY STATUS LIST  
NORPLANT Implant Studies

DATE: OCTOBER 1988

Description of Study: NORPLANT IMPLANTS - Pre-introductory Clinical Trials

Project Manager: S. Balogh

Study Number: 866

Total Number of Admissions: 3785

Total Number of Studies: 36

| Center Number | Investigator/<br>Country | Index Number | Date Initiated | Expiration Date | Proposed No. of Cases | Forms Processed |         |         |         |         |         | Date Last Shipment | Date Last Monitor Visit |         |
|---------------|--------------------------|--------------|----------------|-----------------|-----------------------|-----------------|---------|---------|---------|---------|---------|--------------------|-------------------------|---------|
|               |                          |              |                |                 |                       | ADM             | FU Slot |                    |                         |         |
| 040           | O. LADIPO<br>NIGERIA     | NOR 85/014   | 10/11/85       | 2/89            | 120                   | 131             | 1       | 6       | 12      | 18      | 24      | 36                 | 9/12/88                 | 7/20/88 |
| 041           | A. COLLISON<br>GHANA     | NOR 85/012   | 10/16/85       | 8/87            | 100                   | 4               | 5       | 1       |         |         |         |                    | 3/18/87                 | 6/05/87 |
| 042           | C. EKWEMPU<br>NIGERIA    | NOR 85/013   | 10/10/85       | 2/89            | 105                   | 71              | 68      | 62      | 43      | 37      | 33      |                    | 7/27/88                 | 7/21/88 |
| 435           | O. FAKEYE<br>NIGERIA     | NOR 86/004   | 1/13/86        | 6/89            | 105                   | 101             | 88      | 75      | 77      | 39      | 35      |                    | 8/22/88                 | 7/19/88 |
| 437           | E. OKPERE<br>NIGERIA     | NOR 85/015   | 10/09/85       | 2/89            | 105                   | 94              | 89      | 77      | 48      | 29      | 23      |                    | 4/19/88                 | 7/26/88 |
| 453           | J. OTUBU<br>NIGERIA      | NOR 86/005   | 11/08/85       | 6/89            | 100                   | 96              | 84      | 79      | 50      | 43      | 38      |                    | 8/02/88                 | 7/22/88 |
| 468           | J. MARTEY<br>GHANA       | NOR 87/007   | 6/08/87        | 3/89            | 100                   | 93              | 61      | 11      | 8       |         |         |                    | 8/02/88                 | 6/08/87 |
| 482           | J-C. MOREAU<br>SENEGAL   | NOR 87/002   | 12/10/86       | 10/88           | 50                    | 56              | 52      | 50      | 38      | 13      |         |                    | 9/08/88                 | 7/27/88 |
| 600           | R. APELO<br>PHILIPPINES  | NOR 85/005   | 2/07/85        | 10/90           | 50                    | 50              | 48      | 51      | 41      | 11      | 47      | 23                 | 3/06/88                 | 5/12/88 |
| 600           | R. APELO<br>PHILIPPINES  | NOR 86/007   | 9/27/85        | 9/90            | 100                   | 100             | 81      | 88      | 75      | 57      | 33      | 2                  | 9/06/88                 | 5/12/88 |

601

| Center Number | Investigator/<br>Country      | Index Number | Date Initiated | Expiration Date | Proposed No. of Cases | Forms Processed |           |           |            |            |            | Date Last Shipment | Date Last Monitor Visit |            |
|---------------|-------------------------------|--------------|----------------|-----------------|-----------------------|-----------------|-----------|-----------|------------|------------|------------|--------------------|-------------------------|------------|
|               |                               |              |                |                 |                       | ADM             | FU Slot 1 | FU Slot 6 | FU Slot 12 | FU Slot 18 | FU Slot 24 |                    |                         | FU Slot 36 |
| 602           | N. PUERTOLLANO<br>PHILIPPINES | NOR 85/006   | 2/07/85        | 3/91            | 50                    | 50              | 44        | 59        | 58         | 36         | 34         | 23                 | 9/20/88                 | 5/06/88    |
| 602           | I. BENITEZ<br>PHILIPPINES     | NOR 86/008   | 6/27/86        | 6/90            | 100                   | 100             | 95        | 102       | 98         | 69         | 6          |                    | 9/29/88                 | 5/06/88    |
| 674           | R. I. QURESHI<br>PAKISTAN     | NOR 88/005   |                | 9/89            | 100                   |                 |           |           |            |            |            |                    |                         |            |
| 675           | M. SAEED<br>PAKISTAN          | NOR 88/006   |                | 9/89            | 100                   |                 |           |           |            |            |            |                    |                         |            |
| 676           | A. MUNIR<br>PAKISTAN          | NOR 88/007   |                | 9/89            | 100                   |                 |           |           |            |            |            |                    |                         |            |
| 677           | S. JANJUA<br>PAKISTAN         | NOR 88/008   |                | 9/89            | 100                   |                 |           |           |            |            |            |                    |                         |            |
| 678           | ZAKHAR-UN-NISA<br>PAKISTAN    | NOR 88/009   |                | 9/89            | 100                   |                 |           |           |            |            |            |                    |                         |            |
| 703           | S. BASNAYAKE<br>SRI LANKA     | NOR 85/010   | 5/14/85        | 1/91            | 275                   | 275             | 294       | 285       | 295        | 285        | 266        | 135                | 7/25/88                 | 7/25/88    |
| 704           | K. BEGUM<br>BANGLADESH        | NOR 85/001   | 2/17/85        | 5/91            | 200                   | 230             | 221       | 217       | 219        | 191        | 150        | 47                 | 8/12/88                 | 6/11/88    |
| 718           | T. CHOWDHURY<br>BANGLADESH    | NOR 85/002   | 2/20/85        | 5/91            | 200                   | 225             | 219       | 200       | 196        | 158        | 123        | 47                 | 8/12/88                 | 6/13/88    |
| 721           | S. RAHMAN<br>BANGLADESH       | NOR 85/003   | 2/19/85        | 5/91            | 200                   | 226             | 227       | 223       | 220        | 199        | 158        | 47                 | 8/12/88                 | 6/13/88    |
| 729           | H. LAMA<br>NEPAL              | NOR 85/004   | 2/14/85        | 9/91            | 300                   | 307             | 304       | 282       | 257        | 188        | 171        | 234                | 9/09/88                 | 11/15/87   |
| 731           | A. BHATTA<br>NEPAL            | NOR 85/008   | 5/09/85        | 9/91            | 100                   | 100             | 71        | 86        | 87         | 62         | 38         | 4                  | 8/23/88                 | 11/13/87   |

10/2

| Center Number | Investigator/<br>Country     | Index Number | Date Initiated | Expiration Date | Proposed No. of Cases | Forms Processed |           |           |            |            |            | Date Last Shipment | Date Last Monitor Visit |            |
|---------------|------------------------------|--------------|----------------|-----------------|-----------------------|-----------------|-----------|-----------|------------|------------|------------|--------------------|-------------------------|------------|
|               |                              |              |                |                 |                       | ADM             | FU Slot 1 | FU Slot 6 | FU Slot 12 | FU Slot 18 | FU Slot 24 |                    |                         | FU Slot 36 |
| 735           | M. CHHETRI<br>NEPAL          | NOR 87/003   | 2/18/87        | 9/92            | 200                   | 192             | 164       | 39        | 15         | 1          |            | 8/05/88            | 11/18/87                |            |
| 736           | H. SHARMA<br>NEPAL           | NOR 87/004   | 2/21/87        | 9/92            | 200                   | 92              | 84        | 53        | 20         |            |            | 7/18/88            | 11/17/87                |            |
| 742           | K. P. YADAV<br>NEPAL         | NOR 87/005   | 2/17/87        | 9/92            | 200                   | 126             | 119       | 86        | 51         |            |            | 8/05/88            | 11/19/87                |            |
| 749           | S. CHINNATAMBY<br>SRI LANKA  | NOR 85/009   | 5/16/85        | 9/91            | 200                   | 200             | 153       | 211       | 209        | 169        | 147        | 19                 | 9/22/88                 | 7/23/88    |
| 750           | I. VINITHARATNE<br>SRI LANKA | NOR 85/011   | 5/17/85        | 1/91            | 200                   | 200             | 200       | 193       | 194        | 183        | 149        | 14                 | 7/25/88                 | 7/26/88    |
| 798           | S. RATNAM<br>SINGAPORE       | NOR 85/007   | 2/04/85        | 3/91            | 100                   | 100             | 104       | 99        | 103        | 95         | 84         | 9                  | 9/14/88                 | 8/05/88    |
| 800           | M.A. SALAZAR<br>EL SALVADOR  | NOR 88/003   | 2/01/88        | 4/89            | 50                    | 20              | 14        | 1         |            |            |            |                    | 9/16/88                 | 5/03/88    |
| 821           | S. CASTRO<br>EL SALVADOR     | NOR 88/001   | 2/05/88        | 4/89            | 100                   | 41              | 35        | 3         |            |            |            |                    | 9/16/88                 | 5/02/88    |
| 823           | R. VASQUEZ<br>EL SALVADOR    | NOR 88/002   | 2/04/88        | 4/89            | 150                   | 67              | 49        | 5         |            |            |            |                    | 9/16/88                 | 5/03/88    |
| 824           | M. HERNANDEZ<br>EL SALVADOR  | NOR 88/004   | 2/04/88        | 4/89            | 100                   | 62              | 46        |           |            |            |            |                    | 9/16/88                 | 5/03/88    |
| 8017          | R. BOULOS<br>HAITI           | NOR 86/001   | 11/11/85       | 9/89            | 350                   | 175             | 160       | 147       | 119        | 78         | 74         |                    | 8/02/88                 | 10/19/87   |
| 8331          | G. THEODORE<br>HAITI         | NOR 86/003   | 11/14/85       | 9/89            | 350                   | 151             | 139       | 68        | 132        | 66         | 82         |                    | 6/08/88                 | 10/20/87   |
| 8332          | F. LOLAGNE<br>HAITI          | NOR 86/002   | 11/16/85       | 9/89            | 50                    | 50              | 50        | 36        | 40         | 31         | 19         |                    | 6/08/88                 | 10/21/87   |

206

STUDY STATUS LIST  
NORPLANT Expansion Studies

Description of Study: NORPLANT IMPLANTS - Expanded Clinical Trials

DATE: OCTOBER 1988

Project Manager: S. Balogh

Study Number: 1866

Total Number of Admissions: 410

Total Number of Studies: 9

| Center Number | Investigator/<br>Country     | Index Number | Date Initiated | Expiration Date | Proposed No. of Cases | Forms Processed |         |         |         |         |         | Date Last Shipment | Date Last Monitor Visit |          |
|---------------|------------------------------|--------------|----------------|-----------------|-----------------------|-----------------|---------|---------|---------|---------|---------|--------------------|-------------------------|----------|
|               |                              |              |                |                 |                       | ADM             | FU Slot |                    |                         |          |
| 166           | M.A. SATTAR<br>BANGLADESH    | NOR 88/015   | 6/05/88        | 9/90            | 200                   | 12              | 1       | 6       | 12      | 18      | 24      | 36                 | 8/12/88                 | 6/11/88  |
| 167           | M.L. RAHMAN<br>BANGLADESH    | NOR 88/016   |                | 9/90            | 200                   |                 |         |         |         |         |         |                    |                         |          |
| 703           | S. BASNAYAKE<br>SRI LANKA    | NOR 86/009   | 6/06/86        | 10/89           | 80                    | 80              | 81      | 82      | 73      | 70      | 45      | 11                 | 7/25/88                 | 7/25/88  |
| 704           | K. BEGUM<br>BANGLADESH       | NOR 88/010   | 4/13/88        | 9/90            | 250                   | 19              | 13      |         |         |         |         |                    | 8/12/88                 | 6/11/88  |
| 718           | T.A. CHOWDHURY<br>BANGLADESH | NOR 88/011   | 4/05/88        | 9/90            | 250                   | 24              | 7       |         |         |         |         |                    | 8/12/88                 | 6/13/88  |
| 721           | S. RAHMAN<br>BANGLADESH      | NOR 88/012   | 5/04/88        | 9/90            | 250                   | 41              | 34      |         |         |         |         |                    | 8/12/88                 | 6/13/88  |
| 722           | M.A. QUADER<br>BANGLADESH    | NOR 88/013   | 4/05/88        | 9/90            | 200                   | 27              |         |         |         |         |         |                    | 8/12/88                 | 6/13/88  |
| 729           | H. LAMA<br>NEPAL             | NOR 87/006   | 2/24/87        | 9/92            | 200                   | 200             | 191     | 167     | 157     | 11      |         |                    | 9/09/88                 | 11/15/87 |
| 766           | M. SADEQUE<br>BANGLADESH     | NOR 88/014   | 4/10/88        | 9/90            | 300                   |                 |         |         |         |         |         |                    | 8/12/88                 | 4/10/88  |

1/10

STUDY STATUS LIST  
NORPLANT-2 Implant Studies

DATE: OCTOBER 1988

Description of Study: NORPLANT-2 IMPLANTS - Pre-introductory Clinical Trial

Project Manager: S. Balogh

Study Number: 872

Total Number of Admissions: 12

Total Number of Studies: 1

| Center Number | Investigator/<br>Country  | Index Number | Date Initiated | Expiration Date | Proposed No. of Cases | Forms Processed |         |         |         |         |         | Date Last Shipment | Date Last Monitor Visit |         |         |
|---------------|---------------------------|--------------|----------------|-----------------|-----------------------|-----------------|---------|---------|---------|---------|---------|--------------------|-------------------------|---------|---------|
|               |                           |              |                |                 |                       | ADM             | FU Slot |                    |                         |         |         |
| 798           | S. S. RATNAM<br>SINGAPORE | NOR 86/010   | 6/01/87        | 9/90            | 100                   | 12              | 11      | 6       | 12      | 7       | 18      | 24                 | 36                      | 9/14/88 | 8/05/88 |

126

QUARTER 1988

Description of Study: OC's With vs Without Iron

Research Analyst: Amanda Rowan

Study Number: 8856 FCO: 3136

Strategy cancelled: 12/16/87

Total Number of Cases: 1280

Total Number of Studies: 5

| Center | Investigator/<br>Country                   | Index<br>Number | Date<br>Init | Date<br>Actv | Expiration<br>Date | Proposed<br>No. of<br>Cases | ADM/<br>LAB | Hours Processed |              |              | Date<br>Last<br>Shipment | Date<br>Last<br>Site Visit | Status/<br>Comments |
|--------|--|-----------------|--------------|--------------|--------------------|-----------------------------|-------------|-----------------|--------------|--------------|--------------------------|----------------------------|---------------------|
|        |  |                 |              |              |                    |                             |             | 6 wks<br>FU     | 14 wks<br>FU | 26 wks<br>FU |                          |                            |                     |
| 085    | Cassol/Torreón,<br>Mexico                  | 86/007          | 7/86         | 8/86         | 3/89               | 320                         | 43/<br>42   | 40/<br>36       | 39/<br>35    | 32/<br>30    | 8/23/88                  | 5/88CC                     | Cancelled           |
| 603    | Agp/POPOOM<br>Legaspi City,<br>Philippines | 86/022          | 9/86         |              | 7/88               | 320                         |             |                 |              |              |                          | 1/87SK                     | Cancelled           |
| 621    | BKS PENFIN/Soeprapti<br>Bandung, Indonesia | 86/006          | 11/85        | 2/87         | 4/88               | 320                         | 12/17       | 5               |              |              | 11/2/87                  | 3/87MR                     | Cancelled           |
| 704    | Barua/BFRP<br>Dhaka, Bangladesh            | 86/020          | 3/87         | 4/87         | 6/88               | 320                         | 70/141      |                 | 57           | 18           | 2/3/88                   | 9/87JM                     | Cancelled           |
| 869    | Oetina/Mexico<br>Merida/Yucatan            | 87/003          | 8/87         | 11/87        | 2/89               | 320                         | 12/12       |                 |              |              | 3/10/88                  | 11/87CC                    | Cancelled           |

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

178

STUDY STATUS LIST  
SYSTEMICS

OCTOBER 1988

Description of Study: Crossover - Norciday 1/50 to Lo-Ferenal; Lo-Ferenal to Norciday 1/50

Study Number: 8845 FOD: 3139

Total Number of Cases: 1200

Total Number of Studies: 4

| Center       | Investigator/<br>Country             | Index<br>Number | Date<br>Init | Date<br>Actv | Expiration<br>Date | Proposed<br>No. of<br>Cases | Forms Processed |            |            |            |            | Date<br>Last<br>Shipment | Date<br>Last<br>Site Visit | Status/<br>Comments |
|--------------|--------------------------------------|-----------------|--------------|--------------|--------------------|-----------------------------|-----------------|------------|------------|------------|------------|--------------------------|----------------------------|---------------------|
|              |                                      |                 |              |              |                    |                             | ADM             | 1 mo<br>FU | 3 mo<br>FU | 4 mo<br>FU | 6 mo<br>FU |                          |                            |                     |
| 023          | Breznik/Maribor,<br>Yugoslavia       | 85/008          | 6/85         | 11/85        | 12/86              | 300                         | 295             | 293        | 277        | 245        | 232        | 3/12/87                  | 4/87JB                     | CR604               |
| 112          | Kanchanasinith<br>TFRA/Thailand      | 88/002          | 3/88         |              | 5/90               | 300                         | 10              | 2          |            |            |            | 8/2/88                   | 3/88JM                     | EDI 4/88            |
| 602+         | Benitez/Metro Manila,<br>Philippines | 85/009          | 9/85         | 2/86         | 6/88               | 300                         | 293             | 270        | 246        | 227        | 205        | 10/16/87                 | 5/88SM                     | Closed              |
| 8593**<br>++ | Renes/Veracruz,<br>Mexico            | 86/019          | 9/86         | 10/86        | 11/88              | 300                         | 246             | 197        | 138        | 101        | 73         | 6/27/88                  | 1/88*H                     | Active              |

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

\*\*Nominest instead of Norciday. Ferenal instead of Lo-ferenal.

+Given the 2nd pill first, then crossed over to the other study pill for the entire study period (R.A. list backwards).

++Study to be closed at the end of '88 fiscal year, no further monitoring of this site.

All remaining active CC studies to be monitored only once a year.

261

STUDY STATUS LIST  
SYSTEMICS

CCICHR 1900

Description of Study: Triquilar vs Lo-Femeral

Study Number: 8840 FID: 3138

Total Number of Cases: 1500

Total Number of Studies: 6

| Center | Investigator/<br>Country                          | Index<br>Number | Date<br>Init | Date<br>Actv | Expiration<br>Date | Proposed<br>No. of<br>Cases | Forms Processed |            |            |             |     | Date<br>Last<br>Shipment | Date<br>Last<br>Site Visit | Status/<br>Comments                              |
|--------|---|-----------------|--------------|--------------|--------------------|-----------------------------|-----------------|------------|------------|-------------|-----|--------------------------|----------------------------|--|
|        |   |                 |              |              |                    |                             | 1 mo<br>AD14    | 4 mo<br>FU | 8 mo<br>FU | 12 mo<br>FU |     |                          |                            |  |
| 400+   | Gerais/Khartoum,<br>Sudan                         | 86/002          | 2/86         | 8/86         | 9/88               | 300                         | 299             | 276        | 253        | 232         | 39  | 2/3/88                   | 3/87PG                     | Active<br>(Adm. Closed)<br>(FU to Close 9/30/88) |
| 703    | Basnayake/Colombo,<br>Sri Lanka                   | 86/004          | 2/86         | 4/86         | 9/88               | 300                         | 299             | 273        | 263        | 239         | 223 | 7/25/88                  | 3/8894                     | Closed   |
| 850    | Guzman-Serani/<br>Valdivia, Chile                 | 86/005          | 3/86         | 4/86         | 3/88               | 300                         | 299             | 294        | 291        | 259         | 220 | 1/15/88                  | 10/870C                    | Closed   |
| 964+   | Agueyo/Quito,<br>Ecuador                          | 86/024          | 1/87         | 1/87         | 3/89               | 150                         | 94              | 52         | 30         | 13          | 9   | 9/7/88                   | 3/880C                     | Active<br>(Adm. to close 9/30/88)                |
| 8057+  | Calventi/<br>Santo Domingo,<br>Dominican Republic | 86/003          | 6/86         | 3/87         | 12/89              | 150                         | 93              | 35         | 13         | 3           |     | 9/7/88                   | 8/880C                     | Active   |
| 8058   | Andrade/Curitiba<br>Brazil                        | 86/018          |              | 4/90         | 12/89              | 150                         |                 |            |            |             |     |                          | 3/880B                     | EDI 8/86   |

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

\*Study to be closed at the end of '88 fiscal year, no further monitoring as of 6/88.

370

STUDY STATUS LIST  
SYSTMICS

OCTOBER 1988

Description of Study: Loestrin vs Lo-Femeral

Study Number: 8820 FOD: 3134

Total Number of Cases: 1500

Total Number of Studies: 5

| Center | Investigator/<br>Country               | Incls:<br>Number | Date<br>Init | Date<br>Adv | Expiration<br>Date | Proposed<br>No. of<br>Cases/<br>Site | Forms Processed |            |                    |                    |             | Date<br>Last<br>Shipment | Date<br>Last<br>Site Visit | Status/<br>Comments                |
|--------|--|------------------|--------------|-------------|--------------------|--------------------------------------|-----------------|------------|--------------------|--------------------|-------------|--------------------------|----------------------------|------------------------------------|
|        |  |                  |              |             |                    |                                      | ADM/<br>Lab     | 1 mo<br>FU | 4 mo<br>FU/<br>Lab | 8 mo<br>FU/<br>Lab | 12 mo<br>FU |                          |                            |                                    |
| 076    | Mukherjee/<br>Malaysia                 | 86/023           | 2/87         | 4/87        | 2/89               | 300                                  | 298             | 293        | 282                | 198                | 43          | 9/21/88                  | 7/88SM                     | Active                             |
| 314    | Suleh/Cairo,<br>Egypt                  | 86/014           | 7/86         | 10/86       | 6/88               | 300                                  | 300             | 297        | 267                | 221                | 155         | 9/2/88                   | 10/88PG                    | *Closed                            |
| 679    | Borawoj/Bangkok,<br>Thailand           | 87/004           | 11/87        | 12/87       | 11/89              | 300                                  | 88              | 51         | 24                 |                    |             | 8/18/88                  | 2/88JM                     | Active<br>(Adm. to close 11/30/88) |
| 633    | Lubis/Jakarta,<br>Indonesia            | 86/016           | 9/86         | 1/87        | 8/88               | 300                                  | 19              | 8          | 5                  |                    |             | 6/12/87                  | 3/87MR                     | Closed                             |
| 8594   | Perez-Palacios/<br>Mexico City, Mexico | 86/011           | 5/86         | 6/86        | 1/89               | 200/                                 | 144/            | 134        | 118/               | 97/                | 41          | 9/6/88                   | 5/88CC                     | Active                             |

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

\*Closed- Closure form not complete.

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

OCTOBER 1988

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

Study Number: 877, 878      EOC: 3133

Total Number of Cases: 800

Total Number of Studies: 3

| Center | Investigator/<br>Country          | Index<br>Number | Date<br>Init./Active | Expiration<br>Date | Proposed<br>No. of<br>Cases | Forms Processed |           |           |           |           |           |           | Date<br>Last<br>Shipment | Date<br>Last<br>Site Visit | Status/<br>Comments |
|--------|-----------------------------------|-----------------|----------------------|--------------------|-----------------------------|-----------------|-----------|-----------|-----------|-----------|-----------|-----------|--------------------------|----------------------------|---------------------|
|        |                                   |                 |                      |                    |                             | 1mo<br>ADM      | 2mo<br>FU | 3mo<br>FU | 4mo<br>FU | 5mo<br>FU | 6mo<br>FU | 7mo<br>FU |                          |                            |                     |
| 340    | Eltan/Mehalla-<br>Kubra, Egypt    | 85/005          | 6/86                 | 1/89               | 300                         | 247             | 190       | 192       | 195       | 192       | 190       | 181       | 2/25/88                  | 10/88PG                    | Active              |
| 871    | Moggia/Buenos<br>Aires, Argentina | 85/004          | 10/85 10/85          | 4/87               | 300                         | 300             | 250       | 210       | 231       | 219       | 220       | 246       | 3/9/87                   | 4/87CC                     | Closed              |
| 871    | Moggia/Buenos<br>Aires, Argentina | 86/001          | 8/86 11/86           | 4/88               | 200                         | 196             | 156       | 135       | 150       | 130       | 142       | 162       | 1/15/88                  | 10/87CC                    | Closed              |

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

1/16

STUDY STATUS LIST  
PROGESTOGEN-ONLY ORAL CONTRACEPTIVES

OCTOBER 1988

Description of Study: Progestogen-only Oral Contraceptives in Lactating Women

Study Number: 8875 FOC: 3142

Total Number of Cases: 4000

Total Number of Studies: 20

| Center | Investigator/<br>Country       | Index<br>Number | Date<br>Init./ | Date<br>Active | Expiration<br>Date | Proposed<br>No. of<br>Cases | Forms Processed |            |            |             |          | Date<br>Last<br>Shipment | Date<br>Last<br>Site Visit | Status/<br>Comments     |
|--------|--------------------------------|-----------------|----------------|----------------|--------------------|-----------------------------|-----------------|------------|------------|-------------|----------|--------------------------|----------------------------|-------------------------|
|        |                                |                 |                |                |                    |                             | ADM             | 2 mo<br>FU | 6 mo<br>FU | 12 mo<br>FU | PI<br>FU |                          |                            |                         |
| 084    | Dalgado/Mexico<br>Villahermosa | 84/034          |                | 11/84          | 11/87              | 200                         | 199             | 198        | 195        | 189         |          | 12/9/87                  | 5/87 CC                    | Closed                  |
| 102    | Guzman/Peru<br>Lima            | 84/018          |                | 7/84           | 11/87              | 200                         | 199             | 148        | 112        | 75          |          | 11/4/87                  | 1/87 CC                    | Closed                  |
| 110    | Negahata/Peru<br>Lima          | 84/014          |                | 3/84           | 9/87               | 200                         | 193             | 191        | 187        | 190         |          | 1/15/87                  | 1/87 CC                    | CR 597                  |
| 400    | Gerais/Sudan<br>Khartoum       | 85/002          |                | 2/85           | 2/87               | 200                         | 200             | 200        | 186        | 174         |          | 5/21/86                  | 3/87 PG                    | CR 596                  |
| 422    | Broquet/Rwanda<br>Gisenyi      | 84/004          |                | 6/85           | 3/87               | 200                         | 18              | 11         | 1          |             |          | 5/20/86                  | 5/86 FD                    | Closed                  |
| 452    | Doh/Cameroon<br>Yaounde        | 84/030          |                | 12/84          | 1/87               | 200                         | 228             | 128        | 98         | 91          |          | 1/6/87                   | 2/87 FD                    | CR 587                  |
| 453    | Wright/Nigeria<br>Jos          | 84/035          |                | 3/86           | 7/88               | 100                         | 101             | 82         | 58         | 42          |          | 6/28/88                  | 6/87 SB                    | Active<br>(Adm. Closed) |
| 483    | Ndiaye/Senegal<br>Dakar        | 84/004          |                | 11/84          | 10/88              | 200                         | 139             | 115        | 79         | 59          |          | 4/05/88                  | 9/87/FD                    | Active<br>(Adm. Closed) |
| 831    | Aranda/Costa Rica<br>San Jose  | 84/019          |                | 9/84           | 9/86               | 200                         | 169             | 115        | 71         | 53          |          | 2/19/86                  | 1/86 CC                    | CR 578                  |
| 840    | FERN/Mexico<br>Ciudad Juarez   | 84/029          |                | 10/84          | 9/86               | 200                         | 200             | 164        | 134        | 59          | 63       | 5/1/86                   | 12/85 CC                   | CR 620                  |
| 841    | Santana/Quatemala              | 84/031          |                | 12/84          | 10/86              | 200                         | 199             | 192        | 162        | 148         |          | 11/11/86                 | 3/87 CC                    | CR 606                  |

2/2

OCTOBER 1988

| Center | Investigator/<br>Country         | Index<br>Number | Date<br>Init./ | Date<br>Active | Expiration<br>Date | Proposed<br>No. of<br>Cases | Forms Processed |            |            |             |          | Date<br>Last<br>Shipment | Date<br>Last<br>Site Visit | Status/<br>Comments      |
|--------|----------------------------------|-----------------|----------------|----------------|--------------------|-----------------------------|-----------------|------------|------------|-------------|----------|--------------------------|----------------------------|--------------------------|
|        |                                  |                 |                |                |                    |                             | NM              | 2 mo<br>FU | 6 mo<br>FU | 12 mo<br>FU | PT<br>FU |                          |                            |                          |
| 843    | Bonfim/Brazil<br>Fortaleza       | 84/036          |                | 12/84          | 4/87               | 200                         | 196             | 160        | 112        | 67          | 72       | 5/18/87                  | 4/87 DB                    | Closed<br>CR in progress |
| 865    | Bartosa/Brazil<br>Santa Maria    | 84/038          |                | 2/85           | 7/88               | 200                         | 197             | 132        | 82         | 44          | 25       | 3/08/88                  | 4/87 DB                    | Closed                   |
| 869    | Culina/Mexico<br>Merida          | 84/015          |                | 7/84           | 6/86               | 200                         | 200             | 185        | 146        | 93          |          | 6/11/86                  | 12/85 CC                   | CR 568                   |
| 871    | Mogyia/Argentina<br>Buenos Aires | 84/020          |                | 8/84           | 9/86               | 200                         | 200             | 162        | 1          | 130         |          | 4/21/86                  | 4/86 CC                    | CR 579                   |
| 893    | Czeresnia/Brazil<br>Sao Paulo    | 84/037          |                | 2/85           | 12/87              | 200                         | 147             | 130        | 75         | 35          | 48       | 7/14/87                  | 4/87 DB                    | Closed<br>CR in Progress |
| 8014   | Iecoin/Haiti<br>Port-au-Prince   | 84/016          |                | 8/84           | 6/86               | 200                         | 199             | 170        | 109        | 79          |          | 2/28/86                  | 9/85 KJ                    | CR 575                   |
| 8056   | Oliveira/Brazil<br>Londrina      | 84/039          |                | 2/85           | 4/87               | 200                         | 196             | 155        | 91         | 43          | 16       | 4/14/87                  | 8/86 DB                    | Closed<br>CR in Progress |
| 8058   | Andrade/Brazil<br>Curitiba       | 84/041          |                | 5/85           | 4/87               | 200                         | 205             | 158        | 97         | 44          | 54       | 5/5/87                   | 4/87 DB                    | CR 618                   |
| 8059   | Nunes/Brazil<br>Porto Alegre     | 84/040          |                | 2/85           | 4/87               | 200                         | 200             | 195        | 177        | 126         | 43       | 1/20/87                  | 4/87 NN                    | CR 609                   |

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

Closed\*- Closure form not complete.

File

STUDY STATUS LIST  
EXPANDED PROGESTOGEN-ONLY OC

OCTOBER 1988

Description of Study: Expanded Strategy for Progestogen-only pills (either several centers per country or through CED programs)

Study Number: 8876 FCD: 3142

Total Number of Cases: 10,000

Total Number of Studies:

| Center | Investigator/<br>Country         | Index<br>Number | Date<br>Init./Active | Date<br>Expiration<br>Date | Proposed<br>No. of<br>Cases | ADM | Forms Processed |            |             | PT<br>FU | Date<br>Last<br>Shipment | Date<br>Last<br>Site Visit | Status/<br>Comments      |
|--------|----------------------------------|-----------------|----------------------|----------------------------|-----------------------------|-----|-----------------|------------|-------------|----------|--------------------------|----------------------------|--------------------------|
|        |                                  |                 |                      |                            |                             |     | 2 mo<br>FU      | 6 mo<br>FU | 12 mo<br>FU |          |                          |                            |                          |
| 043    | Gardiner/Ghana<br>Accra          | 85/001          | 10/85                | 11/87                      | 200                         | 200 | 196             | 163        | 174         |          | 7/1/87                   | 9/87 SW                    | CR 623                   |
| 044    | Klufio/Ghana<br>Accra            | 84/003          | 10/85                | 7/87                       | 200                         | 199 | 191             | 185        | 157         |          | 6/22/87                  | 6/86 PL                    | Closed                   |
| 440    | Draoune/Traore<br>Bamako/Mali    | 83/031          | 1/85                 | 7/87                       | 100                         | 99  | 79              | 58         | 37          |          | 5/5/87                   | 10/87 KJ                   | Closed<br>CR in Progress |
| 457    | Toure/Traore<br>Kaya/Mali        | 84/002          | 9/85                 | 4/87                       | 200                         | 76  | 22              |            |             |          | 7/7/87                   | 8/86 KJ                    | Closed                   |
| 460    | Sarake/Traore<br>Bamako/Mali     | 85/003          | 9/85                 | 9/88                       | 200                         | 196 | 153             | 65         | 42          |          | 3/08/88                  | 12/87 KJ                   | Active<br>(Adm. Closed)  |
| 8060   | Ruscowsky/Brazil<br>Porto Alegre | 84/001          | 3/85                 | 12/86                      | 300                         | 149 | 101             | 51         | 28          |          | 5/5/87                   | 4/87 DB                    | Closed                   |

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

Closed\*- Closure form not complete.

FOLDES  
OCTOBER 1988

STUDY STATUS LIST  
VAGINAL CONTRACEPTION  
3172

Description of Study: DIAPHRAGM WITH SPERMICIDE VS. DIAPHRAGM WITHOUT SPERMICIDE VS. SPERMICIDE ONLY (DELFEN FOAM)

Study Number: 7788

Total Number of Cases: 432

Total Number of Studies: 1

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| Center | Investigator/<br>Country | Index<br>Number | Date<br>Initiated/<br>Date Active | Expiration<br>Date | Proposed<br>No. of<br>Cases | Forms Processed |            |            |              | Date<br>Last<br>Shipment | Date<br>Last<br>Site Visit | Status/<br>Comments |        |
|--------|--------------------------|-----------------|-----------------------------------|--------------------|-----------------------------|-----------------|------------|------------|--------------|--------------------------|----------------------------|---------------------|--------|
|        |                          |                 |                                   |                    |                             | 1 mo<br>ADM     | 3 mo<br>FU | 6 mo<br>FU | 12+ mo<br>FU |                          |                            |                     |        |
| 298    | Guillebaud/England       | 85/004          | 9/84 / 9/85                       | 1/90               | 432                         | 121             | 117        | 118        | 93           | 43                       | 09/12/88                   | 6/88                | Active |

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FOLDES  
OCTOBER 1988

STUDY STATUS LIST  
VAGINAL CONTRACEPTION  
3170

Description of study: VAGINAL SPERMICIDE ACCEPTABILITY TRIAL OF DELFEN FOAM VS. CONCEPTROL GEL  
Study Number: 0799

Total Number of Cases: 220

Total Number of Studies: 2

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| Center | Investigator/<br>Country | Index<br>Number | Date<br>Active | Expiration<br>Date | Proposed<br>No. of<br>Cases | Number of Cases Completing |              |                  |              | Date<br>Last<br>Shipment | Date<br>Last<br>Site Visit | Status/<br>Comments |        |
|--------|--------------------------|-----------------|----------------|--------------------|-----------------------------|----------------------------|--------------|------------------|--------------|--------------------------|----------------------------|---------------------|--------|
|        |                          |                 |                |                    |                             | 2 Week<br>ADM              | 2 Week<br>FU | 4 Week<br>Survey | 4 Week<br>FU |                          |                            |                     |        |
| 857    | Gomez/Columbia           | 88/003          | 06/88          | 12/88              | 110                         | 59                         | 39           | 40               | 32           | 32                       | 09/21/88                   | 5/88                | Active |
| 8044   | Cordero/Dom. Rep.        | 88/004          | 07/88          | 12/88              | 100                         | 24                         | 11           | 11               | 0            | 0                        | 09/06/88                   | 9/88                | Active |

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*M*

FOLDES  
OCTOBER 1988

STUDY STATUS LIST  
VAGINAL CONTRACEPTION  
3609

Description of study: ACCEPTABILITY TRIAL OF CONDOMS AMONG US MILITARY MEN  
Study Number: 7801

Total Number of Cases: 130

Total Number of Studies: 1

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| Center | Investigator/<br>Country | Index<br>Number | Date<br>Active | Expiration<br>Date | Proposed<br>No. of<br>Cases | Number of Cases Completing |               |               | Date<br>Last<br>Shipment | Date<br>Last<br>Site Visit | Status/<br>Comments |
|--------|--------------------------|-----------------|----------------|--------------------|-----------------------------|----------------------------|---------------|---------------|--------------------------|----------------------------|---------------------|
|        |                          |                 |                |                    |                             | 1 Month<br>ADM             | 2 Month<br>FU | 2 Month<br>FU |                          |                            |                     |
| 0028   | Magruder/Ft. Bragg NC    | 88/005          | 08/88          | 03/89              | 130                         |                            |               |               | 8/88                     | Starting                   |                     |

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11-18

FOLDES Y  
OCTOBER 1988

STUDY STATUS LIST  
VAGINAL CONTRACEPTION  
3608

Description of study: PHASE I LEA'S KAP HUMAN POST-COITAL TEST

Study Number: 0798

Total Number of Cases: 10

Total Number of Studies: 1

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| Center | Investigator/<br>Country | Index<br>Number | Date<br>Active | Expiration<br>Date | Proposed<br>No. of<br>Cases | Number of Cases Completing |                  |                   | Date<br>Last<br>Shipment | Date<br>Last<br>Site Visit | Status/<br>Comments |
|--------|--------------------------|-----------------|----------------|--------------------|-----------------------------|----------------------------|------------------|-------------------|--------------------------|----------------------------|---------------------|
|        |                          |                 |                |                    |                             | ADM                        | Pre-coital<br>FU | Post-coital<br>FU |                          |                            |                     |
| 922    | Schulman/Mineola NY      | 88/001          | 12/87          | 8/88               | 10                          | 7                          | 6                | 6                 | 05/20/88                 | 5/88                       | Cancelled*          |

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\* Another site is currently being recruited.

**APPENDIX D**  
Expenditures

APPENDIX D

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

Expenditures

1 October 1987 - 30 September 1988

|  |                            |
|--|----------------------------|
| Salaries and Fringe Benefits                     | \$ 2,381,351               |
| Service Centers                                  | 414,084                    |
| Consultant and Professional Fees                 | 99,701                     |
| Contracted Labor                                 | 22,961                     |
| Travel - Domestic                                | 106,029                    |
| Travel - Foreign                                 | 558,230                    |
| Supplies - Office                                | 16,785                     |
| Supplies - Medical                               | 61,324                     |
| Printing and Reprints                            | 45,579                     |
| Office/Medical Equipment, Maintenance and Repair | 32,364                     |
| Freight  | 12,534                     |
| Dues and Registration Fees                       | 17,564                     |
| IJGO Subscriptions                               | 13,603                     |
| Other Purchased Services                         | 185,216                    |
| Keypunching                                      | 32,858                     |
| Other Expenses and Bank Service Charges          | <4,484>                    |
| Data Purchases                                   | 245,869                    |
| Subcontracts                                     | 1,494,827                  |
| General and Administrative Costs                 | <u>1,570,192</u>           |
| TOTAL  | \$ <u><u>7,306,587</u></u> |