PD-ABC-414

ANNUAL REPORT

1 October 1989 – 30 September 1990

Cooperative Agreement

AID/DPE–0537–A–00–4047–00

FHI FAMILY HEALTH INTERNATIONAL • Durham, NC 27713 USA

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I. INTRODUCTION

The Cooperative Agreement charges Family Health International (FHI) with providing the Office of Population with research support "directed toward fostering the development and introduction of methods of fertility control, the assessment and evaluation of fertility control technologies, and the strengthening of such capabilities on an international basis". In consultation with the Research Division, FHI manages a complex program designed to enable the Office to make decisions relating to contraceptive technology that are solidly based in reliable data. In order to carry out this research in the most program-relevant, as well as most cost-effective manner possible, FHI conducts the great majority of its studies in the developing world through an extensive international network of research institutions and investigators, and collaborates closely with other Cooperating Agencies and international research organizations. Finally, FHI also has leveraged its expertise with other funding sources, especially in the fields of contraceptive technology and reproductive epidemiology, and is thus able to bring additional resources to complement the generous support it receives from A.I.D.

The following is a brief synopsis of the highlights of our program by division during the current reporting period:

A. Clinical Trials Division

The NET (norethindrone) products continue to be a major focus of our development efforts. The most advanced of the two products currently is the NET-90 injectable contraceptive. A problem with achieving a reliable level of reproducability in the manufacturing process has required more stringent quality control measures to be taken before the large and expensive Phase III trials can commence. But the advantages of the method, particularly its extremely low total dose and its low compliance requirements, coupled with the high level of demand for an injectable product in the developing world combine to encourage our continued commitment to this product. Similarly, experience with NORPLANT[R] suggests that the biodegradable feature of the NET implant ("Annuele") will be most welcome in the field; reformulation efforts were the focus of recent work, and Phase II studies of presentations designed to give the optimum blood levels are scheduled to begin shortly.

Sterilization continues to be of high priority in Clinical Trials, and an iodine formulation for sclerosing the Fallopian tubes nonsurgically was developed during this period and will enter acute safety studies shortly. Preparation of a marketing approval application for a new occlusive device, the Filshie Clip, continued; submission to the FDA is projected for later in 1991.

NORPLANT[R] studies continue in a number of countries under several kinds of arrangements, including collaboration with AVSC and JHPIEGO and add-on funding from the missions. Several issues continue to demand our attention, including a continued demand for local data, an obligation for continued monitoring of clients who received NORPLANT[R] under a research protocol, the maintenance of the world-wide NORPLANT[R] data set, and the WHO/HRP, Population Council, and FHI post-marketing surveillance.

Considerable interest has been expressed in the efficacy trial we have begun in collaboration with CONRAD on the female condom, "Reality." A no-scalpel vasectomy technique is under evaluation in several countries, coincidentally with its introduction.

B. Reproductive Epidemiology and Sexually Transmitted Diseases Division

RESTD continues to work in areas of considerable concern to the Office of Population and to the international family planning community generally. A particularly worrisome indication that hormonal contraception may enhance a woman's susceptibility to HIV arose in Nairobi; the study was not designed to address that question directly, but the hypothesis is biologically plausible. With funding from this

Cooperative Agreement supplemented by WHO, NIH, and Ortho Pharmaceuticals, FHI fielded a pilot study in Kenya to determine whether the hypothesis can be tested directly.

In the same interface between contraceptive technology and HIV infection, RESTD examined whether spermicides may be safely used with the frequency and in the quantities required by commercial sex workers. A preliminary study in a small number of low-risk women in Thailand showed that frequent use may result in a dangerous erosion of vaginal tissue. A larger, statistically valid study will follow.

An interesting study of discordant couples in Zambia is examining the efficacy of barrier contraceptives in preventing HIV infection. A companion study among high risk women in Cameroon will give comparable data for HIV and other STDs.

A continuing interest in RESTD is the non-contraceptive effects - particularly the risks - of contraceptives. Largely because of the widespread use of oral contraceptives around the world, RESTD is adapting a computer model that will estimate the effect of OC use on overall mortality rates, given estimates of incidence of other, relevant pathology. In the United States where the risk involved in pregnancy and birth are relatively low and the incidence of breast

cancer relatively high, taking into account the protective effects of OCs on ovarian and endometrial cancers, it appears that OC use probably does not impact appreciably on death rates. On the other hand, in the developing world where these parameters are quite different, OC use is likely to have a measurably positive effect.

C. Program Evaluation Division

The active program areas for this Division are method acceptability, contraceptive choice and use, program effectiveness, breast-feeding and postpartum contraception, and AIDS and family planning. Within these areas, PE works to improve the quality of programming and increase the impact of service delivery programs.

The focus of the acceptability work is on condoms, both male and female. While the physical characteristics of condoms are the subject of study in the Material Technology Division, PE studies the behavioral factors affecting the acceptance and use of condoms. Several studies of the female condom among a variety of populations, for example, will yield data on how women actually use the female condom, what problems they encounter and how likely they are to adopt the method and use it properly; these data will directly complement the clinical trial being conducted in collaboration with CONRAD which is evaluating the safety and efficacy of the product for an FDA submission.

PE is working closely with the Materials Technology Division in the development of the plastic condom. This work permits MTD to evaluate design features of the new condom with human subjects; critical performance features, such as breakage and slippage, as well as more subjective parameters such as comfort and sensation, can be tested and measured. PE also provides data on the acceptability of new latex condom design (such as different sizes or thicker films) to assists the Office of Population in procurement decisions.

PE has also carried out important acceptability studies involving NORPLANT[R], as well as broader areas which impact on the acceptability of contraceptives in a more general sense.

PE plays FHI's most active role in quality of care issues and has been especially involved in the areas of compliance and informed consent. Several FHI studies of compliance for oral contraceptive use - as well as other studies showing OC failure rates as high as 20 percent - led to an expert meeting at FHI in July of 1990. The meeting, in turn, resulted in a request from the FDA for FHI to coordinate a meeting of the FDA's Fertility and Maternal Drugs Committee. The objective of the meeting will be to simplify and standardize OC labeling by all U.S. pill manufacturers. FHI is working closely with other Cooperating Agencies in this effort, as well as with IPPF and WHO/HRP, to insure

that this effort toward more usable information for pill users also has impact on international family planning programs.

PE's activities in informed choice grew in large measure out of A.I.D.'s Task Force on Informed Choice. An important focus of the work is on programs which show a clear predominance of one method of family planning; diagnostic studies to examine the factors leading to this condition have been carried out in Nepal and the Dominican Republic and the Division has assisted in bringing the results of these studies to the attention of policy makers for appropriate consideration. Communications material that addresses this important component of quality of care is being produced, and a conceptual framework for guiding informed consent and quality of care assessments is being tested empirically.

As national family planning programs become more common and fundamental and resistance to their implementation more rare, PE's emphasis has shifted from studies meant to sensitize policy makers to the need for such programs to studies meant to enhance the effectiveness and sustainability of these programs. Of particular interest are those factors which can be controlled or modified to improve service delivery programs. USAID Missions are especially interested in subjects such as fees for service, client screening, laboratory tests for acceptors of hormonals, education and counseling, availability and accessibility, and knowledge and attitudes of clinical staff. An FPI study of the

efficacy of expensive laboratory screening of prospective OC clients in Senegal and the presentation of the results at a symposium organized by FHI resulted in recommendations for eliminating the requirement for such testing; the results of the effort are being disseminated to other countries in Francophone West Africa.

Such program-related work in PE is often requested by the Missions and is frequently funded through add-ons to the Cooperative Agreement. Not surprisingly, one area of particular concern at the Mission level (as well as elsewhere) is the costing of family planning. The squeeze on resources is felt throughout, and studies which help program managers make decisions that are more firmly based in empirical data are especially welcome. New methods are particularly challenging in that changes in method mix may have profound impact on the costs of a program. FHI will help to project the impact of NORPLANT^{R} in this context, and in particular the trade off between a relatively higher initial cost, and a presumably much higher rate of compliance (and therefore effectiveness). Variations in its delivery will be examined for their cost implications, both costs directly to the family planning program and opportunity costs elsewhere, as, for example, one encounters when using nurses rather than physicians to do the implantation procedure.

Cost recovery also demands a great deal of interest and FHI has developed a methodology for projecting the impact of price increases as programs feel the need for generating more income from their activities. Shifts in use patterns may be expected from such changes, and FHI will attempt to study these, as well: if a social marketing project increases its prices significantly, will governmental free service programs experience an increased demand? Can method mix be manipulated through pricing, or will one method show an increased demand if another is perceived as too expensive? Similarly, is condom misuse (or non-use) affected by price, or are free condoms less well used than condoms that are purchased? These issues will be addressed in a study planned for Bangladesh.

FHI believes that the AIDS epidemic is having an impact on many family planning programs and that it is often the case that program managers feel the need for assistance in dealing with the risk of HIV infection in a responsible way. The issue of counseling often arises and FHI is frequently asked for guidance. The need for condoms in this area represents a challenge in logistics and cost for many programs and many family planning programs have not given proper condom use adequate consideration in the past. Risk assessment seems required in the setting of many programs, and PE is attempting to help BEMFAM in Brazil develop acceptable screening tools that can be used in their clinics.

Breast-feeding continues to be an effective method of controlling fertility and, indeed, in some parts of the world prevents more births than modern contraceptives. As breast-feeding declines, the need for family planning services increases - just to hold fertility rates constant. FHI continues to publish widely used material on breast-feeding and to study the factors that affect breast-feeding patterns. Active studies continue in Pakistan and the Philippines.

D. Field Development and Training

The area of responsibility for FDT is broad and covers the following areas: institutional development; training and support for conferences, seminars and expert meetings; contraceptive introduction; and information dissemination. It is FHI's position that the spread of contraceptive technology to a diverse, sometimes skeptical target group made up of academics, managers, providers and clients, is a demanding and expensive proposition. FDT endeavors to manage a complex and coordinated program to insure that the appropriate technology and information is received by the appropriate audience.

The Family Health Research Centers (FHRCs) are an important component of this program. Originally, FHRC's started as sites at which to implement clinical trials, they continue to perform this critical role

with important results. These organizations have grown in size and capability to the point that they generate their own research agenda, relate in some cases at a policy level to their own governments, and attract funding from other international research organizations. FHI continues to provide a reduced level of core support to the FHRCs, but having in most cases succeeded in organizing their financial management so that they can now document a realistic overhead charge, much of our support is in the form of payment for specific research subcontracts; it is significant that FHI often finds itself in competition for such services with other international donors. Some direct support continues, particularly in the areas of financial management and computer technology, but enhancing these capabilities is seen as assistance that will further their managerial and scientific independence. Thus, while these centers have clearly been the beneficiaries of substantial support over the years, and in a few instances the center has not survived (notably the one FHI attempted to start in the Sudan), it must be conceded that the FHRCs represent a successful investment in institutional development.

FDT's training activities relate directly to FHI's overall need to conduct research in the technology of contraception in the most cost-effective and acceptable manner possible. The fact is that it is less expensive to implement the various phases of research in the

target country than to limit the in-country activity to data gathering. Equally important, local investigators (and their governments) have become less tolerant of being treated as less important and less competent components of the research enterprise. FHI has developed a series of course that enable local investigators and institutions to play an increasingly meaningful role in quality research work. These curricula are recognized both by the target groups as well as by other organizations to be important steps to carrying out research at internationally recognized standards. For example, **The Application of Epidemiologic Methods to Studies of Reproductive Health: An Eleven Part Series** will be published in English, French and Spanish shortly as a collaboration between FHI, the Centers for Disease Control and the World Health Organization. Workshops on clinical trials research methods have been held periodically since 1985, most recently in Portuguese, and the curriculum has been translated and reproduced locally for use in Indonesia. Standardized training material for clinical trials data analysis has also been developed and has been in use since 1988. A number of workshops and seminars in these fields have been held during this reporting period.

A discrete area of activity within FDT has been designated "contraceptive introduction". It is understood that a good part of FHI's role has always been to assist in the introduction of new contraceptive technology. Indeed, many of the clinical trials FHI has

carried out over the years have had as an important component the introduction of new (and sometimes not so new) contraceptive methods to the academic and clinical leaders of the developing world. But with NORPLANT[R] about to become widely available and FHI's relatively new emphasis on the advantages of postpartum contraception, a more explicit framework for introductory activities was in order.

The purpose is to provide support to national programs as they begin to integrate new technology into their various systems. A review of the steps required has been undertaken, and consideration given to each, including national strategy development, addressing logistics requirements, generating interest in the method, insuring training for the relevant staff, developing information and education material, establishing appropriate surveillance programs, and defining needed programmatic and policy research. At no time did FHI contemplate being directly involved in the management of these various components of a comprehensive introduction program, but it was apparent that an efficient and effective program would require a conceptual framework that did not appear to be in place at the time. Subsequent discussions with A.I.D./W and other Cooperating Agencies confirmed this view, and FHI and the Population Council were appointed lead agencies for NORPLANT[R] introduction, even though neither agency was expected to assume an active role in service delivery. FHI is also attempting to facilitate the widespread adoption of postpartum contraception through a comprehensive approach that takes into account the complex and varied needs of programs which do not presently encourage such use.

Finally, the information dissemination activities of FDT continue to be an important factor in insuring the appropriate and effective use of FHI's broad research program and to enhance technical competence within the field of international reproductive health. This effort is focused on encouraging regulatory and health policy change, improving service delivery programs through better technical information, counteracting misinformation about contraceptives, helping to identify priorities for research activities, and fostering the development of better informed training and health education strategies. Regular publications, articles in international media, training of FHRC staffs in research utilization, scientific writing workshops, journalist workshops, and technical assistance in library science and CD-ROM data bases are all used to pursue these objectives.

E. Materials Technology Division

The newest of FHI's divisions continues to work in two broad areas, each at the end of a broad spectrum running from contraceptive development to use in service delivery programs. The development work is pointed toward a thermoplastic condom, one that is expected to withstand the rigors of storage in the tropics, to be acceptable at least in the same range of satisfaction as latex condoms, and to be competitive in cost with the latex product. This work is carried out

in close collaboration with the Program Evaluation division which provides rapid feed-back to MTD on consumer reactions to the design features and materials of the developing product. Work on one design is near completion, and MTD expects to submit a 510K application to the FDA for marketing approval early in 1991.

The other program area in MTD consists of work in quality assurance of latex condoms. A.I.D. currently is purchasing some 850 million condoms at a cost that approaches $40 million. In close collaboration with the Commodities and Program Support Division of the Office of Population and with the manufacturers, FHI is now managing a surveillance program for these two procurement contracts; the volume of testing that the sampling requires has led FHI to establish its own testing laboratory (at significant savings over using commercial testing firms). MTD also is continuing to examine the whole range of issues involved in using laboratory tests to examine the suitability of a given population of latex condoms. Both of the most common tests leave much to be desired in their challenge to the product, one stretching the condom in excess of 625% of its normal dimensions, the other inflating the condom with more than 24 liters of air; that is, the stress of neither test seems obviously related to the stresses intercourse would place on the device. A large human use test was started during this reporting period which is getting breakage rates on twenty different lots of condoms; these rates will be compared with the massive laboratory data

on these lots in an attempt to determine which of the tests (or combinations of tests) best predict breakage. Efforts also continue to develop better, more predictive laboratory tests. Finally, a real time aging test was begun which is subjecting new condoms to a variety of climatic stress at three different sites in Mexico; samples will be taken at semiannual intervals, and it is hoped that a better estimate of shelf-life for condoms under different storage conditions will emerge.

II. CLINICAL TRIALS

The Division of Clinical Trials remains involved both in introductory trials of marketed contraceptives and in the development of new products, through US-FDA approval.

The most advanced of the new products is the NET-90 day injectable microspheres. A Phase IA study of a new formulation began at CONRAD in April 1990. If upon completion this study shows adequate NET release rates, a Phase II study will commence at two U.S. sites.

The problems of NET release in the biodegradable pellets have been addressed. Seeking to increase the NET release rates, a Phase IIA study has been designed using 8mm long pellets of two diameters, 2.75mm and 3.0mm. Endocon has indicated that the new pellets will be delivered in early December 1990. The clinical trials will commence immediately after in two U.S. sites. This study will continue for 24 months to document the 'tail' of NET release. A Phase IIB study is scheduled to follow the initiation of the Phase IIA to evaluate the efficacy of the product formulations.

The Division continues its efforts to develop a safe and effective method of non-surgical female sterilization. Formulation problems with the iodine system are being resolved and a Phase I study is planned. The Phase I study will be initiated in two already selected U.S. sites early in 1991.

Studies of the Reality Female Condom have begun at 9 sites in collaboration with CONRAD. FHI is responsible for the monitoring of the three overseas sites and for two of the US sites, for analysis of all the data and for regulatory affairs. This study is the basis for FDA approval of the product.

The NORPLANT^{R} studies continue in a number of countries using either central or USAID Mission support. We have made plans to follow-up all the subjects enrolled in centrally supported sites until removal of the implants or completion of the 5-year period. Special efforts are being directed at the collection of data on five-year removals of the NORPLANT^{R}.

Data cleaning and analysis continues on the large Filshie Clip data set in preparation for the submission of a Pre-Marketing Application (PMA) from the FDA. This work involves the coordinated efforts of the Clinical Trials, Scientific Support Services, Regulatory Affairs and Biostatistics and Quality Assurance Divisions. The submission of the PMA is scheduled for the fall of 1991.

In the area of introductory clinical trials, the termination of a large number of studies involving oral contraceptives, intrauterine devices and female sterilization resulted in more than 30 consultant reports written by the Division in the last year. The analysis of these large data sets continues, to be followed with a proper dissemination of the results.

Several studies are being conducted to introduce new methods to developing countries. Trials of the no-scalpel technique of male sterilization are ongoing. Trials designed to evaluate the breakage rates of latex condoms in human use are also continuing. The Investigator Network Needs (INN) strategy has been modified to include two modalities, one geared to the formation of new clinical investigators and the other oriented to meet the needs of established investigators by supporting projects designed, conducted and analyzed at the local level.

A. Systemic Contraception

1. Long-acting Steroids

a) NET 90-Day Injectable Microspheres

Stolle Research and Development Corporation has conducted baboon tests of 12 new formulations with four baboons per formulation. At a NET 90-day Injectable Microspheres management committee meeting on 16 February 1990, the committee decided to begin a Phase IA study at CONRAD using the 18D formulation in doses of 50, 65 and 80 mg. This one injection study began in April with 6 subjects per dose. Preliminary results from the first month for half the subjects show a somewhat low but even NET release pattern with minimal burst effect. A full review of the early results will be possible in early October. Following the identification of an acceptable formulation in a Phase IA study at CONRAD, a Phase II study is planned at three sites using two injections of microspheres produced in a larger 1 to 2 kg batch.

b) NET Pellet Implants

Data from the Phase I clinical trial at CONRAD for the 15 subjects using the larger diameter (2.75 mm) pellets showed a 12 month mean serum NET level of 0.4 ng/ml.

At a meeting in Washington on 17 August 1990, it was agreed that Endocon, Inc. would produce 8 mm long pellets of 2 diameters: 2.75 mm and 3.0 mm. A Phase IIA study is planned to begin early 1991 at CONRAD and Cornell University Medical School among 40 subjects to primarily document serum NET, P and E_2 levels. Several months later, a Phase IIB study will start among 160 subjects at 4 clinics (including the Phase IIA clinics) to assess the overall efficacy of the two formulations without collecting pharmacokinetic or ovulation detection data. The Phase IIA study will continue for up to 24 months to fully document the characteristics of the post-effective 'tail' of NET release and return of ovulation.

c) NORPLANT^R Implants

FHI continues to monitor pre-introductory, Phase III clinical trials of NORPLANT^R contraceptive subdermal implants. Studies are ongoing at 37 sites in 11 countries; data have been collected on almost 8,000 insertions. A summary of admissions is given in Table 1. The objectives of the studies were to introduce the NORPLANT^R six-capsule system into countries that had 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 both A.I.D. and non-A.I.D. support, is providing data for local regulatory approval of NORPLANT^{R}. As a direct result of FHI's support of pre-introductory clinical trials, NORPLANT^{R} has now been approved for marketing in Haiti, Nepal, Sri Lanka and Bangladesh.

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.

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^{R} system and to bridge the gap until local regulatory approval of the method is obtained and wider distribution can be undertaken. The largest expansion program is in Bangladesh where over 2,300 insertions have been done at 7 clinics since April 1988.

The development of user-oriented materials specific to the cultural characteristics of each country's client populations has been accomplished through the Program for the Introduction and Adaptation of Contraceptive Technology (PIACT). Prototype counseling materials, brochures and handouts, are adapted for local use. A standardized training curriculum has also been tested and is now available for local adaptation.

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

Insertions have been performed in 7,991 women to date. There have been a total of 2,272 removals, 42 due to accidental pregnancy, 666 for menstrual problems, 367 for medical reasons, 429 for planned pregnancies, 438 for other personal reasons and 330 were removed upon completion of five years. One of the 42 pregnancies was ectopic and clearly a method failure. Of the remaining 41 pregnancies, 35 were intrauterine and 6 are not known. Of the 42, twenty-one are possible method failures; in 18 the women were likely pregnant at admission and 3 are not known. Twenty-three pregnancies resulted in live births, one ended in stillbirth, and 7 in abortion. Eight pregnancies are presumed to have ended, but the pregnancy outcome is presently unknown; 2 pregnancies were still continuing at the time of this report.

Three of the 23 live births ended in neonatal death within six weeks of delivery. 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^{R} use.

A summary of cumulative life-table event rates across all study sites is presented in Table 2. The one-year pregnancy rate is 0.3 per 100 users. Removals for menstrual-related problems account for the greatest number of discontinuations with the method; the one-year rate is 3.7 per 100 users. The pooled continuation rates are 99.8, 96.3, 91.0 and 75.2, respectively, after 1, 6, 12 and 24 months of use. The corresponding follow-up rates are 96.6, 84.7, 70.0, and 41.2. The low 24 month follow-up is largely due to subjects whose scheduled 24 month visit has not yet arrived.

A 100-case study of the NORPLANT^{R}-2 rods was initiated in Singapore in June 1987 and discontinued in August 1987, although follow-up of 12 women already inserted with NORPLANT^{R}-2 sets will continue for three years (the effective use-duration) or until removal of the implants.

d) Egypt: Introduction of Long-Acting Steroids

The project was originally developed with the support of an in-country FHI field office (since dissolved) jointly with the National Population Council (NPC) of Egypt and the Egyptian Fertility Care Society (EFCS), which now has full management responsibility for the project. Two in-country training centers, Assiut and Alexandria, were established. The planned comparative cohort study to evaluate long-term side effects is now being funded by WHO.

Although originally designed to evaluate NORPLANT^R-2 covered rods, the EFCS and NPC, in consultation with FHI, the Population Council and Egyptian physicians and government officials, have opted to substitute NORPLANT^R capsules for NORPLANT^R-2 covered rods since NORPLANT^R-2 has been discontinued. Initiation of the clinical trial began in five university teaching hospitals in July 1988, and nearly all 1,500 cases have completed 2 year follow-up. The EFCS issued 6 month reports to the Ministry of Health and the Egyptian drug regulatory agency, the Supreme Organization of Pharmaceutics.

Future Plans

NORPLANT^R pre-introductory and expanded trials will continue with the goal of local regulatory approval. The New Drug Application (NDA) for NORPLANT^R was submitted by the Population Council to the FDA in the fall of 1988 and is expected to be approved before the end of 1990. Upon FDA approval of the NDA, FHI will renew its efforts to gain regulatory approval in countries where local regulatory approval has not yet been received. FHI will also begin to study the efficacy and safety implications of NORPLANT^R use that exceeds the prescribed five-year period.

TABLE 1

Status of Ongoing NORPLANT[R] Clinical Trials

	Initiation Date	Planned Caseload	Insertions Performed
Bangladesh			
Center 166	Jun. 1988	200	269
Center 167	Jul. 1988	400	204
Center 704	Feb. 1985	700	727
Center 718	Feb. 1985	700	571
Center 721	Feb. 1985	700	678
Center 722	Apr. 1988	200	277
Center 766	Apr. 1988	300	258
El Salvador			
Center 800	Feb. 1988	50	49
Center 821	Feb. 1988	100	99
Center 823	Feb. 1988	150	150
Center 824	Feb. 1988	100	103
Ghana			
Center 041	Oct. 1985	100*	4
Center 468	Jun. 1987	100	100
Haiti			
Center 8017	Nov. 1985	250	243
Center 8331	Nov. 1985	400	394
Center 8332	Nov. 1985	50	50
Nepal			
Center 729	Feb. 1985	500	507
Center 731	May 1985	100	100
Center 735	Feb. 1987	200	200
Center 736	Feb. 1987	200	196
Center 742	Feb. 1987	200	200
Nigeria			
Center 040	Oct. 1985	370	247
Center 042	Oct. 1985	355	114
Center 435	Jan. 1986	355	119
Center 437	Oct. 1985	355	138
Center 453	Nov. 1985	350	186

TABLE 1 (continued)

	Initiation Date	Planned Caseload	Insertions Performed
Pakistan			
Center 674	Sep. 1988	100	136
Center 675	Jul. 1988	100	120
Center 676	Aug. 1988	100	30
Center 677	Sep. 1988	100	108
Center 678	Aug. 1988	100	121
Philippines			
Center 600	Feb. 1985	150	150
Center 602	Feb. 1985	150	150
Senegal			
Center 482	Dec. 1986	300	138
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		8,765	7,991

*Study has been canceled.

TABLE 2

NORPLANT[R] Clinical Trials
Cumulative Life-table Event Rates

Event	Rate per 100 users
Accidental pregnancy	
1 month	0.0
6 months	0.3
12 months	0.3
24 months	0.3
Removal for menstrual problems	
1 month	0.0
6 months	1.1
12 months	3.7
24 months	11.6
Removal for medical reasons	
1 month	0.2
6 months	1.4
12 months	2.4
24 months	5.3
Continuation	
1 month	99.8
6 months	96.3
12 months	91.0
24 months	75.2
Follow-up*	
1 month	96.6
6 months	84.7
12 months	70.0
24 months	41.2

*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-dose estrogen pills and their acceptability in the developing world continues, but recent emphasis has been on evaluating progestogen-only pills in breast-feeding women, triphasic pills, and the clinical impact of changing from standard- to low-dose estrogen products.

a) Loestrin versus Lo-Femenal

FHI has completed a comparative evaluation of two low-dose estrogen oral contraceptives, Loestrin and Lo-Femenal. Loestrin (Parke-Davis) has a composition of 30 mcg ethinyl estradiol and 150 mcg norethindrone acetate. Lo-Femenal (Wyeth) has a composition of 30 mcg ethinyl estradiol and 300 mcg of the progestin norgestrel. Low-dose estrogen oral contraceptives are being introduced in government programs throughout the world in an attempt to reduce long-and short-term side effects. A 1,350 case comparison was conducted at five centers, located in Malaysia, Egypt, Thailand, Indonesia, and Mexico. The center in Indonesia was closed due to inactivity. However, the other centers successfully completed the study and data analysis is complete. Of the proposed 1,350 cases, the study enrolled and successfully followed up 892 women.

Although follow-up visits were scheduled at 1, 4, 8, and 12 months after admission to the study the majority of the women returned for their last follow-up visit at 11 months. This was due to the fact that while pill cycles are 28 days, follow-ups are scheduled by calendar months (30-31 days). Women returning at 11 months for their last follow-up had completed 12 pill cycles. Rates are reported at 11 months.

The total discontinuation percentage at 11 months was 36.3 in the Loestrin group, including a lost to follow-up percentage of 8.8, and 29.7 for the Lo-Femenal group, including a lost to follow-up percentage of 7.6 (Table 3), with over ninety percent of the women having returned for the 11-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 common 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. Gross cumulative life table discontinuation rates are presented in Table 4. The life table discontinuation rates for accidental pregnancy was 2.3 and 0.3, respectively, for 12 pill cycles of Loestrin and Lo-Femenal.

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 had been expressed before this trial 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 was 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. Noriday 1/50 is comprised of 50 mcg mestranol and 100 mcg norethindrone. The trial was conducted at four centers located in Yugoslavia, the Philippines, Mexico and Thailand; all four sites have completed the study. A total of 908 women were admitted and successfully followed up. Women were assigned either Noriday 1/50 or Lo-Femenal for three months and then crossed to the other pill. At one center, some women were mistakenly assigned to Norminest (35 mcg ethinyl estradiol and 50 mcg norethindrone) or Femenal (50 mcg ethinyl estradiol and 500 mcg norgestrel) for three months and then crossed to the other pill. Total discontinuation percentages at three months after crossover are 34.7 for the Noriday 1/50 to Lo-Femenal group, including a lost to follow-up percentage of 32.6, and 37.8 for the Lo-Femenal to Noriday 1/50 group, including a lost to follow-up percentage of 32.2, 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. Data to date indicates that switching from Noriday 1/50 to Lo-Femenal should pose no efficacy, safety, nor continuation rate concern.

c) Progestogen-only Oral Contraceptives

A.I.D. is now making progestogen-only pills available to programs that request them and FHI continues to evaluate these pills around the world, with particular emphasis on the contraceptive needs of breastfeeding women. A 3,900 case, 20 center noncomparative clinical trial of the progestogen-only oral contraceptive, Ovrette (Wyeth), has been completed. Ovrette has a composition of 75 mcg of the progestin, norgestrel. Nineteen centers completed the study; one center was closed due to inactivity. Also, results from one center in Senegal were excluded from analysis due to the local practice of dosing women with steroids (Synergon) to induce menses in order to contracept.

Although follow-up visits were scheduled at 2, 6, and 12 months after admission to the study the majority of the women returned for their last follow-up visit at 11 months. This was due to the fact that while pill cycles are 28 days, follow-ups are scheduled by calendar months (30-31 days). Women returning at 11 months for their last follow-up had completed 12 pill cycles. Rates are reported at 11 months.

Final data on 3,413 women from 19 centers in Latin America and Africa show an 11-month total discontinuation percentage of 53.7 including a lost to follow-up percentage of 26.5 (Table 5). 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. More than half of the women returned for the eleven-month visit. Gross cumulative life table discontinuation rates are presented in Table 6.

In order to establish the acceptability of the progestogen-only pill in a large population of breastfeeding women, a 1,200-case expanded strategy was developed to distribute and evaluate Ovrette in several countries, often through a community-based or health post system. The strategy is complete. The majority of women in this strategy also returned for their last follow-up at eleven months, thus rates are reported at 2, 6, and 11 months. Data on the 916 women who were admitted to the study, and successfully followed-up, show an eleven-month total discontinuation percentage of 52.8 including a lost to follow-up percentage of 30.1 (Table 7). The majority of discontinuations were for the same "other personal reasons" as described above; 61.5 percent of the women have returned for the eleven-month visit. Gross cumulative life table discontinuation rates are presented in Table 8.

An 800-case comparative study of progestogen-only oral contraceptives (POCs) versus non-hormonal methods in lactating

women was conducted at three centers located in Egypt and Argentina. All three centers have completed the study. The objectives of this trial were to evaluate and compare the overall acceptability and reported side effects of the progestogen-only oral contraceptive Ovrette versus nonhormonal methods. Additionally, the differences over time in the weight of breastfed infants for both groups are being compared. Final data on 766 women admitted to the study show a six-month follow-up rate of 81.1 for the POC group and 80.9 for the nonhormonal group. Table 9 presents final data on the complications and complaints reported for 702 women and their infants, who were followed-up throughout the study period. 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 10 shows final data on mean infant weight for women and their infants followed-up thus far in both groups. Four infant deaths were reported; these were all in the nonhormonal group. One infant death reported was due to Sudden Infant Death Syndrome (SIDS). The mother was an IUD user and the death was not related to the contraceptive method. Two other reported infant deaths were due to pneumonia. 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. The aforementioned infant deaths were all reported by the Argentine centers. The one infant death reported by the Egyptian center was attributed to gastroenteritis. The mother had been

surgically sterilized and the death was not related to the contraceptive method.

A small study designed to assess the effect of a progestogen-only pill (MICROLUT) on milk yield and composition was recently completed. Microlut is comprised of 30 mcg levonorgestrel. The final report has been received from the study center at the University of Western Australia. Twenty-seven subjects successfully completed the study, 14 in the experimental group and 13 in the control group; eight subjects withdrew from the study for various reasons. Data from two subjects were rejected due to incompleteness, unreliability or deviation from the study schedule.

No significant differences in milk yield were found between the groups at any of the five measurement points. Also, no significant differences were found between the growth rates of either the female or male infants of the experimental or control mothers.

There were no significant differences in the mean protein, triacylglycerol, or lactose concentrations of the experimental pill group compared to the controls at any of the five assessment points. There were no significant differences in the energy values of the 24 hour milk productions between the two groups at any assessment point. There appeared to be no changes in the number of feeds demanded or the time spent feeding once the

mothers started using Microlut. No adverse experiences were reported.

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 oral contraceptives and careful clinical research is required to determine whether A.I.D. should offer triphasic pills under its commodity purchases. A 1,350-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. Triquilar is comprised of 6 pills containing 50 mcg levonorgestrel (LNG) and 30 mcg ethinyl estradiol (EE); 5 pills containing 40 mcg LNG and 40 mcg EE; and 10 pills containing 125 mcg LNG and 30 mcg EE. One center is still active; all others have completed the study and 1,118 women have been admitted. The 8-month cumulative total discontinuation percentages are similar, 33.8 for the Triquilar group, including a lost to follow-up percentage of 22.7, and 35.5 for the Lo-Femenal group, including a lost to follow-up rate of 21.7 (Table 11). Approximately 40% of the women 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; in the Lo-Femenal group most of the discontinuations were for common side effects, followed by "other personal" reasons and planning pregnancy. Gross cumulative life table discontinuation rates are presented in Table 12. These data indicate that Lo-Femenal is as safe and effective as Triquilar. Given the added cost of having an additional product (Triquilar) in terms of distribution cost, counseling cost, and the concern of switching pills, these data indicate that Lo-Femenal should continue to be offered and not Triquilar in A.I.D.'s commodity purchases.

Future Plans

There is great interest in studying the progestogen-only oral contraceptive in the postpartum period, with emphasis being placed on the time of initiation of such treatment. Clinical and programmatic issues would be considered in such research. FHI will, however, continue to evaluate research proposals from field centers on a project-by-project basis. Also, if promising new agents are worthy of investigation, FHI will consider conducting clinical trials if the product has potential to improve the efficacy and/or safety profile of currently available oral contraceptives.

Table 3

Lost To Follow-Up and Total Discontinuation Percentages for Loestrin versus Lo-Femenal Studies

Category	Loestrin (N = 444)	Lo-Femenal (N = 448)
Lost to Follow-up Percentage[1]		
1 month	2.0	2.5
4 month	3.2	3.8
8 month	5.6	5.4
11 month	8.8	7.6
Total Discontinuation Percentage[2]		
1 month	3.8	4.5
4 month	14.0	11.4
8 month	30.9	25.4
11 month	36.3	29.7
Woman Months		
1 month	437.5	440.0
2 month	1,628.0	1,642.5
8 month	2,989.0	3,085.5
11 month	3,854.5	4,038.5

[1]Percentage of women lost to follow-up among the total number who entered the study.

[2]Percentage of women not returning to the clinic among the total number of women who entered the study (including lost to follow-up).

Table 4

Gross Cumulative Life Table Discontinuation Rates
for Loestrin versus Lo-Femenal Studies

Event	Loestrin (N = 444)	Lo-Femenal (N = 448)
Accidental Pregnancy		
1 month	0.0	0.0
4 month	0.3	0.0
8 month	2.3	0.0
12 month	2.3	0.3
Menstrual Problems		
1 month	0.2	0.2
4 month	3.6	0.5
8 month	7.1	1.9
12 month	7.1	1.9
Side Effects		
1 month	1.2	0.9
4 month	4.3	2.4
8 month	5.1	4.1
12 month	5.1	4.4
Other Medical Reasons		
1 month	0.0	0.7
4 month	0.5	1.0
8 month	2.8	2.6
12 month	3.8	2.9
Planning Pregnancy		
1 month	0.0	0.0
4 month	0.3	0.3
8 month	0.8	2.2
12 month	1.9	2.8
Other Personal Reasons		
1 month	2.6	1.9
4 month	5.1	4.1
8 month	7.1	7.4
12 month	7.4	7.7
Method Unrelated Reasons		
1 month	1.6	2.8
4 month	3.7	3.5
8 month	4.8	5.1
12 month	5.4	5.7

Table 5

Lost To Follow-Up and Total Discontinuation Percentages for Progestogen-Only Studies (Ovrette) in Lactating Women

Category		(N = 3,413)
Lost to Follow-up Percentage[1]		
	2 month	10.4
	6 month	20.7
	11 month	26.5
Total Discontinuation Percentage[2]		
	2 month	14.9
	6 month	40.4
	11 month	53.7
Woman Months		
	2 month	6,117.5
	6 month	15,320.5
	12 month	23,915.5

[1]Percentage of women lost to follow-up among the total number who entered the study.

[2]Percentage of women not returning to the clinic among the total number of women who entered the study (including lost to follow-up).

Table 6

Gross Cumulative Life Table Discontinuation Rates for Progestogen-Only Studies (Ovrette) in Lactating Women

Event	Rate ± S.E. (N = 3,413)
Accidental Pregnancy	
2 month	0.1 ± 0.0
6 month	0.6 ± 0.2
11 month	1.3 ± 0.3
Menstrual Problems	
2 month	1.8 ± 0.2
6 month	5.0 ± 0.4
11 month	7.4 ± 0.6
Side Effects	
2 month	1.2 ± 0.2
6 month	3.4 ± 0.4
11 month	4.3 ± 0.4
Other Medical Reasons	
2 month	1.2 ± 0.2
6 month	2.5 ± 0.3
11 month	3.0 ± 0.4
Planning Pregnancy	
2 month	0.2 ± 0.1
6 month	0.5 ± 0.1
11 month	0.8 ± 0.2
Other Personal Reasons	
2 month	3.9 ± 0.4
6 month	10.3 ± 0.6
11 month	16.8 ± 0.8
Method Unrelated Reasons	
2 month	1.8 ± 0.2
6 month	5.6 ± 0.5
11 month	6.9 ± 0.5

Table 7

Lost To Follow-Up and Total Discontinuation Percentages for Expanded Progestogen-Only Study (Ovrette)

Category	(N = 916)
Lost to Follow-up Percentage[1]	
2 month	15.7
6 month	23.5
11 month	30.1
Total Discontinuation[2]	
2 month	19.5
6 month	40.8
11 month	52.8
Woman Months	
2 month	1569.5
6 month	3936.0
11 month	6251.0

[1]Percentage of women lost to follow-up among the total number who entered the study.

[2]Percentage of women not returning to the clinic among the total number of women who entered the study (including lost to follow-up).

Table 8

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

Event	Rate ± S.E. (N = 916)
Accidental Pregnancy	
2 month	0.0 ± 0.0
6 month	0.3 ± 0.2
11 month	0.5 ± 0.3
Menstrual Problems	
2 month	1.2 ± 0.4
6 month	2.2 ± 0.6
11 month	2.9 ± 0.7
Side effects	
2 month	0.5 ± 0.3
6 month	0.8 ± 0.3
11 month	1.3 ± 0.5
Other Medical Reasons	
2 month	1.9 ± 0.5
6 month	3.9 ± 0.8
11 month	5.1 ± 0.9
Planning Pregnancy	
2 month	0.1 ± 0.1
6 month	0.5 ± 0.3
11 month	0.7 ± 0.4
Other Personal Reasons	
2 month	5.0 ± 0.8
6 month	9.1 ± 1.1
11 month	12.3 ± 1.3
Method Unrelated Reasons	
2 month	3.2 ± 0.7
6 month	7.7 ± 1.0
11 month	10.4 ± 1.2

Table 9

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

Event	POC (N=368) No.	%	Nonhormonal (N=334) No.	%
Complications				
Pain in iliac area	0	0.0	44	13.2
Endometritis	1	0.3	0	0.0
Parametritis/Pain in adnexa	0	0.0	1	0.3
Small fibroid lump in breast	0	0.0	1	0.3
Small abcess in breast	1	0.3	1	0.3
Cystitis	21	5.7	26	7.8
Pruritus Vulvae	1	0.3	0	0.0
Intense Vaginitis	1	0.3	0	0.0
Vaginal discharge	1	0.3	1	0.3
Kidney Disease	0	0.0	1	0.3
Gastrointestinal Problems	1	0.3	0	0.0
Diarrhea	4	1.1	5	1.5
Intermenstrual Bleeding				
Staining/spotting	188	51.0	154	46.1
Moderate	114	31.0	89	26.6
Heavy	7	1.9	7	2.1
Complaints				
Nipple abrasion	103	28.0	97	29.0
Flu-like symptoms	32	8.7	23	6.9
Abdominal pain	0	0.0	17	5.1

Table 9 (continued)

Event	POC (N=368) No.	%	Nonhormonal (N=334) No.	%
Infant Health				
Gains little weight	59	16.0	76	22.8
Gastrointestinal	16	4.3	25	7.5
Diarrhea	1	0.3	7	2.1
Gastroenteritis	1	0.3	1	0.3
Severe weight loss	1	0.3	0	0.0
Flu/fever	12	3.3	18	5.4
Ear infection	4	1.1	6	1.8
Bronchitis	2	0.5	1	0.3
Pneumonia	6	1.6	11	3.3
Lung infection	0	0.0	1	0.3
Death (pneumonia)	0	0.0	2	0.6
Death (SIDS)*	0	0.0	1	0.3
Death (gastroenteritis)	0	0.0	1	0.3

*Sudden Infant Death Syndrome

N = the number of women followed-up.

Multiple symptoms may be reported per woman.

Table 10

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

Time	Mean Infant Weight (g)	
	POC (N=368)	Nonhormonal (N=334)
FU 1	5422	5492
FU 2	6362	6516
FU 3	6758	6733
FU 4	7331	7425
FU 5	7737	7761
FU 6	8270	8248

Table 11

Lost To Follow-Up and Total Discontinuation Percentages for Triquilar versus Lo-Femenal Studies

Category	Triquilar (N = 556)	Lo-Femenal (N = 557)
Lost to Follow-up Percentage[1]		
1 month	9.9	11.3
4 month	16.2	17.1
8 month	22.7	21.7
12 month	63.1	61.6
Total Discontinuation Percentage[2]		
1 month	11.3	12.4
4 month	20.7	24.1
8 month	33.8	35.5
12 month	76.3	77.6
Woman Months		
1 month	517.0	517.5
4 month	1856.0	1838.0
8 month	3449.0	3371.0
12 month	4600.5	4482.0

[1]Percentage of women lost to follow-up among the total number who entered the study.

[2]Percentage of women not returning to the clinic among the total number of women who entered the study (including lost to follow-up).

Table 12

Gross Cumulative Life Table Discontinuation Rates for Triquilar versus Lo-Femenal Studies

Event	Triquilar (N = 556)	Lo-Femenal (N = 557)
Accidental Pregnancy		
1 month	0.0	0.0
4 month	0.0	0.2
8 month	0.0	0.2
12 month	0.3	0.2
Menstrual Problems		
1 month	0.0	0.0
4 month	0.0	0.0
8 month	0.2	0.3
12 month	0.2	0.6
Side Effects		
1 month	1.6	2.3
4 month	3.6	4.2
8 month	5.8	6.2
12 month	6.0	7.5
Other Medical Reasons		
1 month	0.0	0.7
4 month	0.0	0.9
8 month	1.0	1.1
12 month	1.3	1.3
Planning Pregnancy		
1 month	0.4	0.2
4 month	0.6	3.0
8 month	2.1	3.5
12 month	2.8	4.0
Other Personal Reasons		
1 month	0.6	0.2
4 month	1.5	1.6
8 month	3.5	3.1
12 month	4.1	3.9
Method Unrelated Reasons		
1 month	0.8	0.0
4 month	1.5	1.1
8 month	2.4	2.7
12 month	2.7	2.7

B. Barrier Contraceptives

1. Contraceptive Efficacy Trials

The National Research Institute of Fertility Control (NRIFC) in Pakistan requested the assistance of FHI in evaluating the contraceptive efficacy of menfegol and nonoxynol-9 vaginal tablets. Two hundred sexually active women will be randomly assigned to use either the menfegol or the nonoxynol-9 tablets as their sole means of contraception for one year. The study was initiated in July 1989, and approximately 105 women have been enrolled in the study. FHI is providing technical assistance, and USAID/Islamabad is providing the funds for on-site costs.

2. Comparative Diaphragm Study

Interim data for the study conducted at the Margaret Pyke Center in London comparing the fitted diaphragm with or without spermicide and spermicide alone (foam) are presented in Table 13. Enrollment has increased to a total of 209 women, and the center continues to recruit informed volunteers. Although pregnancy rates are high in the two diaphragm study groups, more pregnancies have been reported among diaphragm-without-spermicide users than among diaphragm-with-spermicide users. FHI continues to monitor the trial closely. Thus far, no statistically significant differences in pregnancy rates have been observed. Due to slow enrollment, the spermicide only group was eliminated. Currently,

209 women have been enrolled in the study, and 79 women have completed the full 12 month follow-up period.

3. Development of D-propranolol as a Spermicide

At a meeting between FHI, AID and NIH in March of 1989, it was decided that the next studies on D-propranolol should determine the bactericidal activity of D-Propranolol against N. gonorrhea, the concentrations of D-Propranolol needed in cervical mucus to inhibit sperm migration through the cervix, and the presence of any clinical advantages of D-Propranolol over nonoxynol-9.

To determine the concentrations of D-propranolol in cervical mucus, several discussions were held with Dr. K. Katz of the University of California - Davis to identify suitable methodology. Dr. Katz submitted a research proposal to FHI, but because much of it was considered outside the scope of the D-propranolol project, the proposal was sent to CONRAD for consideration.

A protocol has been prepared for the comparative study of D-propranolol and nonoxynol-9. The study will compare the spermicidal activity of a 4% D-propranolol cream and a 4% nonoxynol-9 gel. The cream or gel will be applied intravaginally by female volunteers either immediately or 6 hours before sexual intercourse. It is anticipated that the study will be initiated late in 1990. Dr. R. Blackwell, University of Alabama at Birmingham, has replaced Dr. G. Bernstein as the principal

investigator.

4. Phase II Study of Reality Vaginal Pouch

An Investigators' Meeting was held in Atlanta, Georgia on 23 January 1990. In collaboration with CONRAD, the outstanding regulatory documents are being collected from the various study centers. Product was shipped in March so that volunteer recruitment could begin. Four of the five domestic centers and all three of the international centers are active.

Two clinics in Mexico and one in the Dominican Republic are participating in the study. The principal investigators and their study coordinators visited FHI in May of 1990 for study initiation.

5. Lea's Shield

Lea's Shield is a cup-shaped reusable silicone device that is larger than a cervical cap and is held in place near the cervix by the walls of the vagina. It has a valve at the bottom to allow the escape of cervical mucus. It does not require a spermicide and is intended to be worn for up to three days.

FHI completed a Phase I evaluation with Dr. Gerald Bernstein in which midcycle cervical mucus was examined for the presence of sperm shortly after coitus with the device in place. A

preliminary draft report indicated that the device was effective in excluding sperm from the mucus of most women. In the women in whom sperm were detected, only a few sperm were found and most of the sperm were dead or with poor motility. Based on the results, Dr. Bernstein concluded that the shield was comparable to other mechanical barrier contraceptives.

A safety study was planned at CONRAD for the winter 1990. Implementation of the study was delayed due to questions of product liability and provision of indemnification by the manufacturer to the investigator and his institution.

Future Plans

In the coming months, a Phase I clinical study to compare the potency and duration of spermicidal activity of D-propranolol to that of nonoxynol-9 will be conducted. Dr. R. Blackwell will examine cervical mucus for the presence of sperm in women who apply a D-propranolol cream or nonoxynol-9 gel intravaginally immediately or several hours prior to coitus. A Phase II study is planned for Lea's Shield. The study will compare the pregnancy rates of the Lea's Shield used without spermicide to the Prentif cervical cap used with spermicide. Volunteers will be followed for six months and will use the assigned methods as their sole form of contraception.

FHI will continue to study the effectiveness, safety, and acceptability of several barrier contraceptives in the coming year. The diaphragm comparative study in England will continue as will the safety and efficacy study of vaginal spermicide tablets in Pakistan. A study on the concurrent use of spermicides and latex condoms as protection against STDs in Bogota, Colombia was expected to begin in Spring 1990. The investigator and the study coordinator were brought to FHI for study initiation in May of 1990; the study will begin upon receipt of clincial trials materials.

TABLE 13

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 w/Spermicide (n=75)	Diaphragm only (n=82)	Spermicide only (n=52)
Reasons for Discontinuation			
Accidental pregnancy	11	19	12
Planned pregnancy	13	14	13
Medical	1	0	1
Discomfort	1	1	1
Product-related	0	0	1
Other personal	5	6	7
Twelve-month Cumulative Life-table Rates per 100 Women			
Discontinuation			
Accidental Pregnancy	19.1	34.0	31.5
Planned pregnancy	26.6	25.6	33.4
Other medical	1.8	0.0	4.5
Discomfort	1.3	1.2	2.0
Product-related	0.0	0.0	2.4
Other personal	9.4	11.5	20.5
Continuation rate	52.2	42.9	33.1
Woman Months of Use	598.0	614.0	429.5

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 was compared with the tubal ring, the Wolf Clip, the Secuclip, bipolar electrocautery and the Pomeroy method of tubal ligation. Analysis will examine the ease of use, and the complications and pregnancy rates as reported by 33 centers in which trials were conducted. Comparative trials with other devices (Wolf Clip and tubal ring) are the pivotal efficacy trials for the Pre-Marketing Application (PMA) submission; these as well as all other Filshie clip trials will be analysed for safety in requesting FDA approval for marketing.

a) Filshie Clip versus Wolf Clip

Follow-up has been completed for a comparative study of the Filshie Clip and the Wolf Clip in minilaparotomy procedures in interval women in the Dominican Republic, Mexico, Panama and Malaysia. To date 865 interval case records have been loaded onto the computer. There were technical failures in one Wolf Clip and three Filshie Clip procedures. Table 14 details the surgical difficulties. Sixteen women, five from the Filshie group and 11 from the Wolf group, were reported to have surgical injuries or major complications. These are also detailed in Table 14.

Approximately 90% of the women returned for their early follow-up visits (<31 days post-sterilization). About 14% of the Wolf Clip cases and about 19% of the Filshie Clip cases reported one or more complications, mostly minor, at this contact. However, one luteal phase pregnancy was reported in the Filshie Clip group, and two women in the Filshie Clip group and two women in the Wolf Clip group were readmitted to the hospital. One woman in the Wolf Clip group had additional pelvic/abdominal surgery for metrorrhagia. Over eighty-one percent of the women in both groups have returned for long-term follow-up (>31 days post-sterilization). Two pregnancies were reported in the Wolf Clip group; one was a luteal phase pregnancy. Seven women in the Filshie Clip group were readmitted to the hospital as was one woman in the Wolf Clip group. In all, 40 (11.3%) Filshie Clip cases and 32 (9.2%) Wolf Clip cases reported one or more complications at the long-term follow-up visits. Adverse experience reports were filed for the following cases in this strategy: two cases of Filshie Clip displacement have been reported at the Dominican Republic center and were detailed in previous reports, one Wolf Clip patient underwent a total salpingectomy following confirmation of unoccluded tubes due to unclosed clips, one case of temporary apnea in a Wolf Clip patient, and one case of a malignant cerebral tumor resulting in death in the Filshie Clip group.

The two clips were also compared in laparoscopic procedures. Studies are complete in Mexico, Venezuela, Guatemala and Haiti; a short report has been prepared for the latter. Interval sterilizations were performed on 1,215 patients. Surgical

difficulties were reported in 9.7% of the Wolf Clip cases and in 6.8% of the Filshie Clip cases (Table 15). Twenty-two women, 8 from the Filshie Clip group and 14 from the Wolf Clip group, were reported as having sustained surgical injuries or complications. Over 90% of the women in both groups returned for early follow-up visits (<31 days post-sterilization). Forty-six Filshie Clip cases (7.6%) and 60 Wolf Clip cases (9.9%) reported one or more complications at early follow-up. There were two hospital readmissions, both in the Filshie Clip group. Over 85% of the women returned for their long-term follow-up visits (>30 days post-sterilization); there were 12 hospital readmissions, 7 in the Filshie Clip group, and 10 pregnancies, including three luteal phase pregnancies as shown in Table 15.

Adverse experience reports were received for the following cases in this strategy: five cases of application difficulty in the Filshie Clip group and one case in the Wolf Clip group, one case each of incisional infection, mental anguish, pelvic pain and ovarian cystectomy in the Wolf Clip group.

TABLE 14

Filshie Clip versus Wolf Clip via Minilaparotomy

	Filshie Clip (N=435)		Wolf Clip (N=430)	
	No.	%	No.	%
A. Events at Surgery				
Surgical difficulties				
With equipment	0	-	1	0.2
Entering the peritoneum	2	0.5	5	1.2
Visualizing/grasping tubes	9	2.1	5	1.2
Occluding tubes	2	0.5	1	0.2
Occlusive technique to wrong structure	1	0.2	0	-
Ovarian Cyst	0	-	1	0.2
More anesthesia required	1	0.2	0	-
Surgical Injuries/Complications				
Tubal injury without bleeding	2	0.5	2	0.5
Tubal bleeding	1	0.2	2	0.5
Uterine tear	1	0.2	1	0.2
Apnea	0	-	1	0.2
Uterine perforation	1	0.2	6	1.4
Blood loss > 100 ml	1	0.2	0	-
Total women with 1+ surgical injuries/ complications	5	1.2	11	2.6

TABLE 14 (Continued)

Filshie Clip	Wolf Clip			
	(N=435)		(N=430)	
	No.	%	No.	%
B. Events Reported at Early Follow-up*				
Women returning	392	90.1	381	89.2
Readmissions	2	0.5	2	0.5
Pregnancy	1**	0.2	0	-
Complications				
Serous discharge	19	4.9	16	4.2
Hematoma	8	2.1	4	1.1
Inflammation at incision	22	5.7	13	3.4
Abscess	6	1.5	3	0.8
Perineo-plastic surgery	0	-	1	0.3
Bleeding	1	0.3	0	-
Complete dehiscence	0	-	1	0.3
Urinary tract infection	1	0.3	2	0.5
Other infection	3	0.8	7	1.8
Vaginal bleeding	12	3.1	4	2.4
Women with 1+ complications	75	19.1	55	14.4
C. Events Reported at Long-term follow-up*				
Women returning for 6-month follow-up	354	81.4	349	81.2
Women returning for 12+month follow-up	312	71.7	310	72.1
Readmissions	7	1.6	2	0.6
Pregnancy	0	-	2***	0.6
Total women with 1+ complications	40	11.3	32	9.2

*Thirteen non-interval cases are excluded from analysis.
**Luteal phase
***One luteal phase

TABLE 15

Filshie Clip versus Wolf Clip via Laparoscopy

	Filshie Clip (N=607)		Wolf Clip (N=608)	
	No.	%	No.	%
A. Events at Surgery				
Surgical difficulties				
With equipment	0	-	2	0.3
Entering peritoneum	6	1.0	14	2.3
Visualizing/grasping tubes	15	2.5	19	3.1
Occluding the tubes	8	1.3	16	2.6
Occlusive technique to wrong structure	7	1.2	6	1.0
Adhesions/occluded additional structure	1	0.2	1	0.2
Dropped clips	4	0.7	1	0.2
Total	41	6.8	59	9.7
Surgical injuries/complications				
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	-	2	0.3
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	14	2.3

TABLE 15 (continued)

	Filshie Clip (N=607) No.	%	Wolf Clip (N=608) No.	%
B. Events Reported at Early Follow-up*				
Women returning	557	91.8	548	90.1
Readmissions	2	0.4	0	-
Luteal phase pregnancies	1	0.2	2	0.4
Complications				
Serous discharge	14	2.5	9	1.6
Hematoma	5	0.9	7	1.1
Inflammation at incision	11	2.0	20	3.3
Bleeding at incision	0	-	4	0.7
Ecchymona	4	0.7	7	1.1
Vaginal bleeding	12	2.2	15	2.5
Abscess	1	0.2	2	0.4
Urinary tract infection	3	0.5	6	1.1
Gastrointestinal	1	0.2	0	-
Drug Allergy	1	0.2	0	-
Infection in Adnexa	1	0.2	0	-
Other	4	0.7	8	1.4
Total women with 1+ complications at follow-up	46	8.2	60	10.0
C. Events Reported at Long-Term Follow-up**				
Women returning at 6 months	438	72.2	463	76.1
Women returning at 12+ months	482	79.4	495	81.4
Readmission	7	1.5	5	1.0
Pregnancy	3****	0.6	7***	1.3
Total women with 1+ complications at long-term follow-up	70	14.5	62	12.5

*Technical failure cases (2) and non-interval cases (34) are excluded from follow-up analysis.
**> 31 days post-sterilization
***1 luteal phase
****2 luteal phase

b) Filshie Clip versus Tubal Ring

Studies have been completed for a comparative trial of the Filshie Clip and the Tubal Ring via laparoscopy in interval procedures in Indonesia, Mexico, Panama and the Dominican Republic. Two centers in Thailand also conducted this comparison under the direction of the Thailand Fertility Research Association; their data were sent to FHI, but are not included here. In all 1,055 interval procedures were performed. There were 13 technical failures, three in the clip group. Surgical injuries and complications were reported in 17 (3.3%) of the clip patients and 29 (5.4%) of the ring patients and surgical difficulties were reported in 37 Filshie Clip procedures (7.0%) and in 29 tubal ring procedures (5.3%) as shown in Table 16.

About 80% of the women in each group returned for their early follow-up visit (<31 days post-sterilization). In both groups the most frequently reported complication/complaint was serous discharge from the incision site. Over 93% of the women returned for one or more long-term follow-up visits. There were 9 readmissions in the Filshie Clip group and 10 in the ring group. Eight pregnancies (6 Filshie Clip, 2 Tubal Ring) were reported; two were luteal phase.

Three cases of displaced clips were noted in previous reports. Adverse experience reports have also been reported for the following: one case of pneumonia in a ring patient, one case of

food poisoning in a Filshie Clip patient, and one death due to trauma from a head injury in the ring group.

Four centers in Latin America and one in Kenya completed comparative studies of the Filshie Clip and Tubal Ring via minilaparotomy. Of the 841 interval procedures performed (Table 17), 23 resulted in technical failures which occurred between three centers, seven in Filshie Clip procedures and 16 in Tubal Ring procedures. Surgical difficulties were reported for 36 women in the Filshie Clip group and for 63 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 88% of the women returned for their early follow-up visit (<31 days post-sterilization). The percentage of women reporting one or more complications at the early follow-up visit was 16.6% in the clip group and 13.6% in the ring group. Two luteal phase pregnancies, one in each group, were reported at early follow-up. Approximately 83% of the women returned for at least one long-term follow-up visit. The rate of complications reported at long-term follow-up visits was 11.8% in the clip group and 14.5% in the ring group. There were 7 readmissions reported including one for an ectopic pregnancy in a ring patient. One other ectopic pregnancy occurred in the clip group. The majority of reported complications were for infection and adnexal pain. One case each of clip displacement and clip expulsion in the Filshie group were

described in a previous report. Other adverse experiences reported include one case of cervical dysplasia and one case of bladder injury in the ring group, and one case each of abdominal pain, lymphoma of the small intestines and death from metastatic lymphoma in the clip group.

TABLE 16

Filshie Clip versus Tubal Ring
Via Laparoscopy

	Filshie Clip (N=523) No.	%	Tubal Ring (N=532) No.	%
A. Events at Surgery				
Technical Failures				
Change in approach	2	0.4	0	-
Change in technique	0	-	3	0.4
Two techniques used	0	-	4	0.8
Procedure discontinued	1	0.2	2	0.4
Surgical Difficulties				
Entering the peritoneum	8	1.5	5	0.9
Visualizing/grasping the tubes	15	2.8	18	3.4
Occluding tubes	8	1.5	4	0.8
With equipment	2	0.4	1	0.2
Occluding wrong structure	4	0.8	0	-
Total	37	7.0	29	5.3
Surgical injuries/complications				
Cervical laceration	6	1.1	3	0.6
Uterine perforation	3	0.6	2	0.4
Tubal bleeding	2	0.4	14	2.6
Bladder injury	1	0.2	0	-
Lesions	0	-	1	0.2
Soft tissue emphysema	5	1.0	6	1.1
Blood loss > 100 ml	0	-	1	0.2
Tubal injury without bleeding	0	-	2	0.4
Total	17	3.3	29	5.4
Total women with 1+ injuries/complications	16	3.1	27	5.1

TABLE 16 (Continued)

	Filshie Clip (N=523)		Tubal Ring (N=532)	
	No.	%	No.	%
B. Events Reported at Early Follow-up*				
Women returning	409	78.2	428	80.5
Readmissions	2	0.5	1	0.2
Complications				
Serous discharge	16	3.9	16	3.8
Hematoma	0	-	2	0.5
Incomplete dehiscence	3	0.7	3	0.7
Inflammation/infection	2	0.5	8	1.9
Eczema	1	0.2	0	-
Urinary tract infection	1	0.2	0	-
Vaginal bleeding	4	1.0	6	1.4
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	30	7.4	38	8.9
Luteal phase pregnancies	1	0.2	1	0.2
C. Events Reported at Long-Term Follow-up				
Women reporting for 6-month follow-up*	445	85.1	438	82.3
Women reporting for 12+ month follow-up*	460	87.9	463	77.0
Pregnancy	6	1.2	2	0.4
Total women with 1+ complications at long-term follow-up**	16	3.3	12	2.5
Readmissions**	9	1.7	10	1.9

*Excludes technical failures and non-interval women.
**Includes 6-,12- and 24-month data.

TABLE 17

Filshie Clip versus Tubal Ring Via Minilaparotomy

	Filshie Clip (N=420)		Tubal Ring (N=421)	
	No.	%	No.	%
A. Events at Surgery				
Technical Failures				
Change in approach	2	0.5	2	0.5
Two techniques used	5	1.1	10	2.4
Change in technique	0	-	4	0.9
Total	7	1.7	16	3.8
Surgical Difficulties				
With equipment	1	0.2	2	0.5
Visualizing and/or grasping tubes	26	6.2	35	8.3
Occluding tubes	2	0.5	13	3.1
Entering peritoneum	4	1.0	9	2.1
Closing incision	0	-	1	0.2
Ovarian cyst	1	0.2	0	-
Ectopic Pregnancy	1	0.2	1	0.2
Other	1	0.1	2	0.5
Surgical Injuries/Complications				
Tubal injury without bleeding	9	2.2	11	2.7
Tubal injury with bleeding	9	2.1	16	3.8
Uterine perforation	4	1.0	3	0.7
Cervical laceration	0	-	3	0.7
Spasm of larynx	0	-	3	0.7
Blood loss > 100 ml	1	0.2	0	-
Vasovagal reaction	1	0.2	0	-
Lesions	2	0.5	0	-
Laceration	1	0.2	2	0.5
Laceration of ovary	1	0.2	0	-
Cardiorespiratory arrest	1	0.2	0	-
Total women with 1+ surgical injuries/complications	26	6.1	38	9.0
Total women reporting major complications during recovery	15	3.6	15	3.7

TABLE 17 (continued)

	Filshie Clip (N=420) No.	%	Tubal Ring (N=421) No.	%
B. Events Reported at Early Follow-up*				
Women returning for early follow-up	361	88.9	366	88.8
Readmissions	3	0.8	3	0.9
Pregnancy (luteal phase)	1	0.3	1	0.3
Complications/Complaints				
Serous discharge/abscess	9	2.3	8	2.6
Inflammation	20	5.8	13	3.7
Hematoma	10	2.9	5	1.4
Incomplete dehiscence	6	1.7	13	3.7
Complete dehiscence	2	0.6	0	-
Infections	3	0.8	3	0.9
Urinary tract infection	1	0.3	1	0.3
Vaginal bleeding	2	0.6	3	0.9
Bleeding	0	-	2	0.6
Gastrointestinal	1	0.3	0	-
Other complications	6	1.7	10	2.3
Total women reporting 1+ complications at early follow-up visit	59	16.6	56	13.6
C. Events Reported at Long Term Follow-up				
Women returning for 6-month follow-up*	366	83.8	354	84.1
Women returning for 12+ month follow-up*	354	84.0	358	84.6
Readmissions	2	0.5	5	1.4
Pregnancy	1	0.3	1***	0.3
Total women reporting 1+ complications at long-term follow-up**	46	11.8	55	14.5

*Excludes technical failures and non-interval women.
**Includes 6- and 12-month follow-up visits.
*** Ectopic pregnancy

c) Filshie Clip versus Modified Pomeroy Method

The Filshie Clip was compared with the modified Pomeroy method via minilaparotomy in postpartum women in Taiwan, the Philippines, Thailand and Panama. A total of 1,403 procedures were performed; data on 1,396 cases are provided in Table 18. All four centers have completed follow-up. Consultant reports were completed for the studies. The 7 technical failures are detailed in Table 18. 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 18); 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 (<31 days post-sterilization) were completed for more than 88% of the women. During the early follow-up period, 68 (10.6%) Filshie Clip patients and 79 (12.8%) Pomeroy patients reported one or more complications. Two hospital readmissions were reported among Filshie Clip cases and three readmissions were reported among Pomeroy cases.

Over 72% of the women in each group returned for their 12-month follow-up visit; 94 women in the Filshie Clip group (15.6%) and 100 women in the Pomeroy group (16.9%) experienced one or more complications since one-month post-surgery.

During long-term follow-up visits, 18 women, 12 in the Pomeroy group and 6 in the Filshie Clip group, were readmitted to the

hospital. 86.8% women in the Filshie Clip group and 84.5% in the Pomeroy group returned for their 24+ month follow-up visit. Eleven pregnancies have been reported, nine in Filshie Clip cases and two in the Pomeroy group.

TABLE 18

Filshie Clip and Modified Pomeroy

	Filshie Clip (N=696)		Modified Pomeroy (N=700)	
	No.	%	No.	%
A. Events at Surgery				
Technical Failures				
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	0.6
Surgical Difficulties				
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
Surgical injuries/complications				
Tubal injury without bleeding	1	0.1	1	0.1
Tubal injury with bleeding	8	1.1	6	0.9
Soft tissue emphysema	0	-	1	0.1
Total women with 1+ injuries/complications	9	1.3	9	1.3
B. Events Reported at Early Follow-up*				
Women returning for follow-up*	642	92.2	620	88.6
Readmissions	2	0.3	3	0.5
Incision Complications				
Serous discharge	32	5.0	38	6.1
Inflammation	17	2.6	17	2.7
Abscess	8	1.2	12	1.9
Bleeding	1	0.2	1	0.2
Hematoma	1	0.2	0	-
Incomplete dehiscence	4	0.6	8	1.3
Gastrointestinal	1	0.2	0	-
Drug allergy	1	0.2	0	-
Other	1	0.2	0	-
Total women with 1+ complications*	68	10.6	79	12.6

TABLE 18 (Continued)

	Filshie Clip (N=696)		Modified Pomeroy (N=700)	
	No.	%	No.	%
C. Events Reported at Long Term Follow-up**				
Women returning for 6-month follow-up visit*	515	74.0	523	74.7
Women returning for 12-month follow-up visit*	501	72.0	518	74.0
Women returning for 24+-month follow-up visit	604	86.8	591	84.5
Long-term** complications/ complaints				
Abdominal/Pelvic Surgery	5	0.8	9	1.3
Infection	5	0.8	12	1.8
Keloids	93	14.1	94	13.9
Total women with 1+pelvic problems	45	6.8	34	5.0
Total Women with 1+complications	94	15.6	100	16.9
Readmission to the hospital**	6	1.0	12	2.0
Pregnancy	9	1.5	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 has been completed at two centers, one in Brazil and the other in Peru; a brief report was written on the 75 case study in Peru. 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 August 1985.

Long-term (> 24 months post-surgery) follow-up data were collected for 62 of the 85 (73.0%) Filshie Clip cases and 55 of the 73 (75.4%) Secuclip cases. Two pregnancies were reported among Secuclip patients and one luteal phase pregnancy was reported in the Filshie Clip group. At long-term follow-up visits, 21.1% of the Secuclip patients and 20.2% of the Filshie Clip patients reported complications. Most of these were keloids or adnexal pain. Three readmissions to the hospital, one for a cholecystectomy, one for observation and one for pregnancy termination were reported.

e) Filshie Clip versus Bipolar Electrocoagulation

Bipolar electrocoagulation is the most commonly used method of sterilization in industrialized and in more advanced developing nations. Comparative studies of the Filshie Clip versus bipolar electrocoagulation have been completed at five sites. Four

hundred sixty-two bipolar procedures and 473 Filshie Clip procedures were done. There were five technical failures (Table 19). Surgical difficulties were reported for nine women in the Filshie Clip group and for 13 women in the cautery group; the most common difficulty was entering the peritoneum. Four women in the Filshie group and 5 women in the cautery group had surgical injuries or complications.

About 94% of the women in each group 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 3.0% in the clip group and 7.6% in the cautery group. Two readmissions were reported in the Filshie group; one was for termination of pregnancy and the other for pelvic surgery. Three readmissions were reported within the cautery group; two of these were for pelvic surgery. Over 95% of the participants returned at 12+ months post-surgery. The rate of complications reported at the long-term follow-up visits was 4.0% in the clip group and 10.5% in the cautery group. Adverse experience reports have been received for the following conditions: curretage for excessive bleeding, uterine bleeding, metrorrhagia(2), ectopic pregnancy(2), and migration of clip to the abdominal wall. adnexal pain, reported by 2.9% of clip patients and 9.4% of cautery patients, was the major complaint recorded at the long-term follow-up visit. five pregnancies have been reported, two in the filshie clip group and three in the cautery group.

table 19

filshie clip versus bipolar electrocoagulation

	filshie clip (n=473)		bipolar electrocoagulation (n=462)	
	no.	%	no.	%
a. events at surgery/recovery				
technical failures				
change in approach	1	0.2	0	0.2
two techniques	0	-	2	0.4
change in technique	1	0.2	1	0.2
surgical difficulties				
entering peritoneum	4	0.8	8	1.7
visualizing tubes	3	0.6	2	0.4
grasping tubes	1	0.2	2	0.4
occluding tubes	0	-	1	0.2
combination	1	0.2	0	-
surgical injuries/complications				
uterine perforation	2	0.4	0	-
soft tissue emphysema	2	0.4	2	0.4
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 injuries/complications	4	0.8	4	0.9
total women reporting major complications during recovery	8	1.7	23	5.0

table 19 (continued)

	filshie clip (n=473) no.	%	bipolar electrocoagulation (n=462) no.	%
b. events reported at early follow-up*				
women returning for follow-up*	444	93.9	433	93.7
complications/complaints				
serous discharge	1	0.2	4	0.9
inflammation	1	0.2	4	0.9
bleeding	2	0.5	0	-
hematoma	1	0.2	3	0.6
incomplete dehiscence	0	-	1	0.2
complete dehiscence	0	-	1	0.2
infections	3	0.7	15	3.5
vaginal bleeding	5	1.1	5	1.0
total women with 1+ complications*	13	3.0	33	7.6
c. events reported at long term follow-up**				
women returning for 6-month follow-up visit*	446	94.3	432	93.5
women returning for 12+ month follow-up visit*	454	96.0	439	95.0
total women with 1+ complications**	18	4.0	46	10.5
readmission to the hospital**	3	0.7	3	0.7
pregnancy	2	0.4	3	0.7

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

f) noncomparative filshie clip studies

long-term follow-up is complete 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 1,455 interval patients. there were 12 technical failures. table 20 details events at surgery and at follow-up. surgical difficulties have included 27 cases of difficulty with the equipment, 17 cases of difficulty entering the peritoneum, 41 cases of difficulty visualizing or grasping the tubes, 67 cases of difficulty in occluding the tubes and 10 cases of clip application to the wrong structure. in 88 cases two clips were used on one tube. the rate of surgical injuries/complications is 1.8%. over 83% of the patients returned for the early follow-up visit; 12.6% of the 1,204 women returning reported one or more complications. there were three readmissions and one patient reported a luteal phase pregnancy. three luteal phase pregnancies were reported among the 1,185 women who returned more than 30 days post-sterilization. four other pregnancies were reported at eight weeks, one year (2 cases) and 2 years post-surgery. in two cases it was possible to determine that the tubes were not fully occluded. hospital readmissions occurred for: hysterectomy (8 cases), bronchitis, pelvic pain (3 cases), urethral dilation, foot problems, stress incontinence, pregnancy termination, polypectomy, cervical stenosis, a d&c (3 cases), draining of an ovarian cyst (3 cases), lymph node biopsy, breast lump removed (3 cases), resterilization, blackouts, cone biopsy, a

blood transfusion for menorrhagia, an ulcer (2 cases), a drug reaction and gallstones. besides hospitalizations, adverse experience reports have been received for: abdominal pain, fecal impaction, dermoid cyst, vaginal discharge, moderate dysplasia, leg pain, pyrexia, inflamed sutures, dyspareunia, irritable bladder, urinary tract infection, psoriasis, vaginal bleeding and hemolytic anemia. about 10.5% of the patients have reported complications at a long-term follow-up visit. over half of these were adnexal pain or menstrual problems.

table 20

noncomparative filshie clip trials

	filshie clip (n=1,455) no.	%
a. events at surgery		
technical failures		
change in approach	8	0.5
two techniques used	2	0.1
procedure discontinued	2	0.1
surgical difficulties		
with equipment	27	1.9
entering peritoneum	17	1.2
visualizing/grasping tubes	41	2.8
occluding tubes	67	4.6
occluding wrong structure	10	0.7
more than 2 clips needed	88	6.0
surgical injuries/complications		
cervical laceration	2	0.1
uterine perforation	2	0.1
tubal bleeding	10	0.7
tubal injury w/o bleeding	3	0.2
ruptured ovarian cyst	1	0.1
vasovagal reaction	2	0.1
soft tissue emphysema	1	0.1
other perforation	1	0.1
cardiac arrest	1	0.1
total women with 1+ surgical injuries/complications	26	1.8

table 20 (continued)

	filshie clip (n=1455) no.	%
b. events reported at early follow-up*		
women returning for early follow-up	1,210	83.2
readmissions	3	0.2
complications		
serous discharge	42	3.5
inflammation/abcess	40	3.3
bleeding	6	0.5
incomplete dehiscence	5	0.4
pregnancy	1**	0.1
hematoma	10	0.8
infection	13	1.1
complete dehiscence	1	0.1
other	8	0.7
women reporting 1+ complications at early follow-up	153	12.6
c. events reported at long-term follow-up*		
women returning for 6-month follow-up	1,185	81.4
women returning for 12+month follow-up	1,024	70.4
total women with 1+ complications	125	10.5
readmissions	60	5.1
pregnancies		
luteal	3	0.2
possible method failure	4	0.3

*technical failure cases are excluded
**luteal

g) Other Sterilization Studies

A retrospective evaluation of the Filshie Clip has been completed in Malaysia. Admission, early and one-year follow-up data on 639 women sterilized with the Filshie Clip from 1980-1985 was transferred from clinic records to FHI forms. Attempts were made to contact these women and ask them to return for a long-term follow-up visit; about 36% (228 women) returned. Ten surgical difficulties, two surgical injuries and eleven cases of blood loss greater than 100 ml were recorded. Five pregnancies were reported at 84, 82, 69, 12 and 6 months post-surgery. Four readmissions were reported including one for observation only, two for termination of pregnancy and one for other pelvic surgery. The following complications were 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). Two hundred twenty women (34.3%) returned for exams at 12 or more months after surgery. Adverse experience reports were filed for the following conditions: cholecystectomy, an endometrial cyst and an ovarian cyst.

Future Plans

Most studies ended in June 1989. Data cleaning and report writing continue as does the four divisions' (Clinical Trials, Scientific Support, Biostatistics and Regulatory Affairs) efforts to produce the Filshie CLip PMA. Long-term follow-up of women who took part

in the Filshie Clip trials has been proposed to begin when funds become available. Several papers have been proposed which would utilize this data. A new clip, the Cambridge Clip, is under development. Future comparative studies of this clip have been proposed.

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 commonly known as no-scalpel vasectomy (NSV) results in less blood loss and in most cases does not require a suture. Comparative studies will examine the standard incision and ligation technique with the puncture and ligation technique.

a) Puncture Method (No-scalpel) versus Standard Incision

A study with the PDA in Bangkok, Thailand, has ended. A consultant report has been completed. The study in Sri Lanka is also complete. A 300 case study is underway with APROFAM in Guatemala. An additional study began with PROPATER in Brazil in April 1990. The PKMI (an AVSC affiliate) in Indonesia is interested in studying the no-scalpel method in four clinic

settings. Development of this project is underway. In all, vasectomies have been performed on 933 patients. There were two technical failures with the no-scalpel procedure. Surgical difficulties and injuries were reported in 26.4% of the standard incision group and in 36.4% of the puncture group (Table 21). Approximately 80% of the men in the standard incision group and 80% in the puncture group have returned for early follow-up visits (<15 days post-sterilization). One hundred five complications were reported, 82 among standard incision patients (21.8%) and 23 among puncture patients (6.2%). Two hospital readmissions were reported, one in each group. Approximately 75% of both groups have returned for long-term follow-up. There have been ten failed sterilizations, 4 among standard incision patients (1.1%) and 6 among puncture patients (1.7%).

Future Plans

The IMSS in Mexico City is interested in the cautery vs. ligation comparison using the NSV approach. A protocol has been prepared.

TABLE 21

PUNCTURE METHOD VERSUS STANDARD INCISION TECHNIQUE

	Puncture Method (N=464)		Standard Incision Technique (N=469)	
	No.	%	No.	%
A. Events at Surgery				
Surgical Difficulties/Injuries				
With Equipment	4	0.9	3	0.9
Isolating Vas	57	12.3	22	4.7
Entering Scrotum	32	6.9	23	4.9
Occluding Vas	9	1.9	5	1.1
Closing Incision	6	1.3	12	2.6
Excessive Bleeding	3	0.6	3	0.9
Other	58	12.5	56	11.9
Total	169	36.4	124	26.4
B. Events Reported at Early Follow-up				
Men returning	371	80.0	376	80.2
Complications				
Hematoma	3	0.8	25	6.6
Incision infection	0	-	6	1.6
Epididymitis	3	0.8	1	0.9
Scrotal abscess	1	0.3	0	-
Scrotal bruise/swelling	5	1.3	36	9.6
Serous discharge	0	-	1	0.3
Fever	2	0.5	3	1.1
Backache	1	0.3	1	0.3
Other	8	2.2	9	2.4
Hospitalization	1	0.3	1	0.3
C. Events Reported at Long-term Follow-up				
Men returning for 10-week follow-up	349	75.2	371	79.1
Complications/complaints				
Scrotal pain	16	4.6	19	5.1
Wound pain/slow healing	3	0.9	3	1.2
Unspecified pain	1	0.3	1	0.4
Men not declared sterile	6	1.7	4	1.1
Pain in abdomen	1	0.3	1	0.3
Testicular pain	3	0.9	3	0.8
Suprapubic ache	1	0.3	-	-

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 an iodine formulation (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 108-month, cumulative life-table pregnancy rates for the two active studies shown in Table 22 range from 7.6 to 8.7 per 100 women. Nine-year follow-up (120 months) is available for some women; no additional pregnancies 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 has closed 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 completed the study; data analysis is in progress.

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 48-month pregnancy rate of 2.9 per 100 women. Six percent of the women have completed 48-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 administered with the FEMCEPT device. Data on the stability of the formulation presented to the FDA in the IND submission were thought too variable; its viscosity changed to an inappropriately high level over time. Efforts are currently underway to develop a stable formulation. Once stability and sterility are assured and FDA approval is given, Phase I trials will commence.

Future Plans

FHI is the major institution doing research in the area of nonsurgical sterilization. Priority will be given to clinical studies of iodine. Phase I through III studies are anticipated for the iodine formulation.

FHI has stopped all research on Quinacrine non-surgical sterilization and has closed its IND with the US FDA.

TABLE 22

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

	12mo. rate	24mo. rate	36mo. rate	48mo. rate	60mo. rate	72mo. rate	84mo. rate
Pellets with Sodium Thiopenthal							
Santiago, Chile							
N=148	4.2	6.4	8.7	8.7	8.7	8.7	8.7
	(94.4)*	(88.5)	(84.7)	(79.4)	(77.9)	(77.2)	(77.2)
Pellets without Sodium Thiopenthal							
Santiago, Chile							
N=123	3.3	6.7	6.7	6.7	7.6	7.6	7.6
	(96.6)	(96.5)	(93.9)	(93.0)	(90.4)	(84.2)	(71.1)

*Follow-up rate

TABLE 22 (continued)

	96mo. rate	108mo. rate	120mo. rate
Pellets with Sodium Thiopenthal			
Santiago, Chile			
N=148	8.7	8.7	8.7
	(76.5)	(70.6)	(30.2)
Pellets without Sodium Thiopenthal			
Santiago, Chile			
N=123	7.6	7.6	
	(43.0)	(20.2)	

*Follow-up rate

E. Intrauterine Devices

FHI continues to conduct 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 under way since 1984 to assess the clinical performance and acceptability of this device by comparing it to locally used IUDs throughout the world. Follow-up was completed for all active investigative sites in October 1989. Final processing of data is underway and results presented in this report are preliminary.

The largest comparison under this strategy was between the TCu 380A and the TCu 200. Data on 2,266 cases have been received from Brazil, Cameroon, Chile, Egypt, El Salvador, Honduras, Mexico and Pakistan. The corresponding cumulative life-table accidental pregnancy rate (Table 23) is significantly lower for the TCu 380A group at 0.7 per 100 women than for the TCu 200 group at 2.4 per 100 women ($P<0.01$). All other event rates are comparable.

The Egyptian Fertility Care Society (EFCS) is also coordinating a randomized, multicenter trial of these two devices. Data on 1,000 cases are being collected, processed and analyzed with EFCS

computer facilities. Follow-up rates at each of the five sites continue to be high. FHI will collaborate with EFCS to continue follow-up of the TCu 380A and TCU 200 users in order to provide the Egyptian Ministry of Health with information on long-term use of this device.

Studies evaluated the TCu 380A with the TCu 220 at one site in Mexico and three sites in the Philippines. A combined total of 889 patients of the planned 900-patient caseload were enrolled into the trial. The preliminary twelve-month continuation rates are 88.0 in the TCu 380A group and 91.0 in the TCu 220 group (Table 24). No significant differences have thus far 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) were conducted in Nigeria, Peru and Turkey. A total of 755 patients were admitted into these studies and twelve-month continuation rates at present are approximately 84.0 in both study groups (Table 25). While the twelve-month expulsion rate continues to be somewhat lower for the TCu 380A group (4.0 per 100 women) than for the LLD group (6.4 per 100 women), the difference is not statistically significant. This is also the case regarding twelve-month accidental pregnancy rates. All other event rates and the continuation rates are comparable for the two groups.

Studies comparing the TCu 380A with the Multiload Cu 250 (MLCu 250) were completed in Malaysia, Sri Lanka and Thailand. A total

of 2,144 women were admitted, with twelve-month continuation rates currently at 90.5 for the TCu 380A users and 88.8 for the MLCu 250 users (Table 26). The twelve-month pregnancy rate remains significantly lower for the TCu 380A compared to that for the MLCu 250 (0.2 and 1.0 per 100 women, respectively, $p<.05$). The two devices continue to perform comparably in terms of all other event 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. Follow-up (24-month) was recently completed for this study. As with the EFCS study, the data will be analyzed in-country with the BKS PENFIN computer facilities. All 3,000 patients were enrolled and the overall follow-up rates were high. Data from both the BKS PENFIN and EFCS studies will be made available to FHI for comparative analysis once data have been processed and analyzed by the respective centers.

One study in Venezuela compared the TCu 380A with the Nova T. A total of 300 women were admitted; twelve-month continuation rates are 85.4 for the TCu 380A group and 89.4 for the Nova T group (Table 27). While the twelve-month pregnancy rate for the TCu 380A group (1.4 per 100 women) was lower than that for the Nova T group (3.3 per 100 women), this difference was not statistically significant. There is a significant difference between the two device groups for removals of bleeding and/or pain. The lifetable rates are 5.5 per 100 women for the TCu 380A group and 0.0 per 100 women for the Nova T group ($p<0.10$).

Table 23

FHI Comparative Trials of the TCu 380A IUD and TCu 200 IUD

Twelve-Month Lifetable Event Rates[1], by Investigative Site and Device Type

Study Site	No. of Cases[2]	Accidental Pregnancy	Expulsion/ Displacement	Bleeding/ Pain	Continuation Rate
			Gross Cumulative Lifetable Rates		
Chile					
TCu 380A	149	1.4	0.0	0.7	92.9
TCu 200	151	0.0	2.6	0.0	96.7
Mexico					
TCu 380A	150	0.8**	4.8	6.6	82.2
TCu 200	148	6.2	4.9	3.2	81.0
El Salvador					
TCu 380A	149	1.7	5.1	7.7	78.7
TCu 200	151	1.7	2.9	8.7	75.8
Brazil					
TCu 380A	148	0.0	1.8	4.0	82.3
TCu 200	152	0.0	4.7	11.4	78.2
Egypt					
TCu 380A	97	2.2	2.1	20.0	72.9
TCu 200	102	1.8	8.0	10.0	78.7
Honduras					
TCu 380A	148	0.0	6.4	9.3**	78.3***
TCu 200	144	5.0	5.1	20.4	61.1
Cameroon					
TCu 380A	139	0.0	6.8	1.0	91.2
TCu 200	138	1.1	1.7	2.7	93.4
Pakistan					
TCu 380A	151	0.0	1.3	11.6	77.9
TCu 200	149	1.5	6.2	10.7	77.1
Total					
TCu 380A	1131	0.7***	3.2	7.1	82.8
TCu 200	1135	2.4	4.0	7.6	80.4

[1]Per 100 women.
[2]Number of cases may have changed due to final data cleaning.
* p<.10; ** p<.05; *** p<.01 level.

Table 24

FHI Comparative Trials of the TCu 380A IUD and the TCu 220 IUD

Twelve-Month Lifetable Event Rates[1], by Investigative Site and Device Type

Study Site	No. of Cases[2]	Accidental Pregnancy	Expulsion/ Displacement	Bleeding/ Pain	Continuation Rate
			Gross Cumulative Lifetable Rates		
Philippines					
TCu 380A	100	0.0	3.0	2.1	85.9
TCu 220	101	0.0	1.1	5.2	90.8
Philippines					
TCu 380A	98	1.1	0.0	11.0	85.0
TCu 220	92	0.0	0.0	7.2	89.5
Philippines					
TCu 380A	100	0.0	6.3	5.6	81.3
TCu 220	100	0.0	6.6	2.2	85.9
Mexico					
TCu 380A	143	0.7	1.4	0.9	96.1
TCu 220	155	2.2	0.0	1.5	94.8
Total					
TCu 380A	441	0.5	2.6	4.4	88.0
TCu 220	448	0.8	1.6	3.7	91.0

[1]Per 100 women.
[2]Number of cases may have changed due to final data cleaning.

Table 25

FHI Comparative Trials of the TCu 380A IUD and the Lippes Loop IUD

Twelve-Month Lifetable Event Rates[1], by Investigative Site and Device Type

Study Site	No. of Cases[2]	Accidental Pregnancy	Expulsion/ Displacement	Bleeding/ Pain	Continuation Rate
			Gross Cumulative Lifetable Rates		
Nigeria					
TCu 380A	152	0.0	7.8	1.3	73.8
Lippes Loop	149	2.8	10.3	1.8	78.4
Peru					
TCu 380A	149	0.7	2.3	3.1	89.5
Lippes Loop	146	2.5	4.9	4.8	84.5
Turkey					
TCu 380A	77	0.0	0.0	5.0	95.0
Lippes Loop	82	0.0	0.0	0.0	100.0
Total					
TCu 380A	378	0.3	4.0	2.7	84.3
Lippes Loop	377	2.3	6.4	2.9	83.9

[1]Per 100 women.
[2]Number of cases may have changed due to final data cleaning.

Table 26

FHI Comparative Trials of the TCu 380A IUD and Multiload Cu 250 IUD

Twelve-Month Lifetable Event Rates[1], by Investigative Site and Device Type

Study Site	No. of Cases	Accidental Pregnancy	Gross Cumulative Lifetable Rates: Expulsion/ Displacement	Bleeding/ Pain	Continuation Rate
Sri Lanka					
TCu 380A	149	0.0	3.5	0.7	95.2
MLCu 250	151	0.7	2.1	1.4	93.2
Sri Lanka					
TCu 380A	150	0.7	3.4	1.5	89.8
MLCu 250	150	2.1	3.5	2.0	91.9
Malaysia					
TCu 380A	74	0.0	0.0	4.1	91.5
MLCu 250	75	1.4	1.3	1.4	87.2
Thailand					
TCu 380A	679	0.2	2.4*	3.8	89.3
MLCu 250	716	1.0	4.6	3.5	86.8
Total					
TCu 380A	1052	0.2**	2.6	3.0	90.5
MLCu 250	1092	1.0	3.9	2.7	88.8

[1]Per 100 women.
* $p<.10$; ** $p<.05$ level.

Table 27

FHI Comparative Trials of the TCu 380A IUD and Nova T IUD

Twelve-Month Lifetable Event Rates[1], by Investigative Site and Device Type

Gross Cumulative Lifetable Rates

Study Site	No. of Cases	Accidental Pregnancy	Expulsion/ Displacement	Bleeding/ Pain	Continuation Rate
Venezuela					
TCu 380A	150	1.4	3.9	5.5*	85.4
Nova T	150	3.3	3.7	0.0	89.4

[1]Per 100 women.
*p<.10

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 IUD to an untrimmed (standard) TCu 200 IUD. Trimming the horizontal arms to fit the width of a woman's uterus is thought to reduce the potential of the IUD arms extending into the opening of the fallopian tubes and subsequent associated problems. Measurements of 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. A total of 172 patients were admitted and follow-up of patients was completed in 1989. Final processing of data will be completed once final queries have been answered and returned. Preliminary follow-up rates at twelve months are 54.4 for the TCu 200 and 64.5 for the adapted T IUD. While the twelve-month lifetable pregnancy rate remains much higher in the adapted T IUD group (3.6 per 100 women) compared to that in the TCu 200 IUD group (0.0 per 100 women), the difference is not statistically significant due to sample size restrictions. There is a significant difference between the devices for total terminations at 6 months. The lifetable rates are 19.1 per 100 women for the TCu 200 group and 7.6 per 100 women for the Adapted T group ($p<.10$).

3. IUD Insertion With or Without Antibiotics

A site in Nigeria under the supervision of the Clinical Trials Division was added to the Reproductive Epidemiology and Sexually Transmitted Disease 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 study in Nigeria was included in order to provide an adequate sample size to detect a difference between the two groups, should one exist. A total of 1,485 women enrolled and final processing of data is completed. Twenty-one cases of PID have been reported, nine occurring in the placebo group and 12 in the doxycyline group. Of these, 15 were diagnosed at the one-month visit and six at the three-month visit. The study did not find that the use of a systemic antibiotic at the time of IUD insertion significantly reduced the incidence of PID among this population. While unclear, this finding may be due to a combination of factors: effective screening of patients, using a population at lower risk for sexually transmitted deseases, sterile insertion procedures, and prompt medical follow-up of patients.

4. IUD Surveillance in Mali

A surveillance study of IUD acceptors in Mali was initiated in May 1988. A total of 231 women have been admitted into the trial, with 134 women choosing the TCu 380A, 73 choosing the TCu 200 and 25 the Lippes Loop. To date, no accidental pregnancies have been reported. Interim twelve-month life-table expulsion/displacement rates are 12.3 per 100 women among TCu 380A users, 11.9 per 100 women among TCu 200 users, and 9.3 per 100 women among Lippes Loop acceptors. Bleeding/pain removal rates were 3.4, 7.8, and 14.6 for TCu 380A, TCu 200 and Lippes Loop users, respectively. Twelve-month continuation rates are approximately 70 per 100 women for each of the three groups.

Future Plans

The planned long-term follow-up (up to ten years) of the 1,400 patients enrolled in Thailand's multicenter trial of the TCu 380A and Multiload Cu 250 IUDs and follow-up is continuing through 48 months. FHI is also looking into the necessity of conducting clinical trials assessing the long-term effects of TCu 380A use. There is increased interest in the potential of postpartum IUD insertion and FHI is planning to support introductory clinical trials on this modality. Lastly, FHI is assessing the potential of conducting clinical trials comparing the newly developed Cu-SAFE 300 IUD with the TCu 380A IUD. The Cu-SAFE 300 is a smaller, more flexible device whose primary benefit is the possible reduction in menstrual bleeding and in lower removal rates for bleeding and pain associated with use of other IUDs.

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 pursued. The INN strategy helps medical practitioners gain experience with various methods of contraception in many different parts of the world in addition to permitting FHI staff to help train them in conducting clinical trials research. This strategy also helps FHI to evaluate new investigators and permits them to assess the type of caseload and degree of follow-up a new investigator can achieve.

Eleven studies were being conducted under FHI's Investigator Network Needs Strategy during this fiscal year; only two studies remain active. These studies encompass a variety of contraceptive methods and, according to the objectives of the strategy, address special research interests of the investigators. In some cases they have served to introduce the investigators to the clinical research process. These are reported here by study area.

1. IUD studies

Three investigators trained at FHI-sponsored Clinical Trials Workshops are conducting IUD studies under the INN strategy, one each in Nepal, Colombia and Burkina Faso. Each study is a programmatic evaluation of the TCu 380A versus the TCu 200, having a combined total of 800 cases. To date, data have been received for 636 cases. The combined twelve-month follow-up rates are 63.4 and 65.0, respectively. A statistically significant difference has emerged in the twelve-month

cumulative life-table rates for removal of the IUD for personal reasons: (0.0 per 100 women in the TCu 380A group compared to 3.0 per 100 women in the TCu 200, $p<.05$). No other significant differences between the two device groups have been detected at this point.

Follow-up in the Colombia trial was recently completed, and final data processing is underway. The trial in Burkina Faso was initiated in late July and admissions have been slow. The Nepal trial will conduct an additional 12 months of follow-up at the request of the investigator and the local AID mission.

2. Sterilization Studies

Follow-up has been completed for a surveillance study of 205 sterilization patients in Nigeria. One hundred twenty-seven women were sterilized with the tubal ring, 60 with the Filshie clip and 18 by the Pomeroy method. Follow-up rates at six-months were 65.5, 50.0, and 75.0 for patients in the respective groups. FHI is currently completing analysis of these data.

3. Systemic Studies

A study in Mali at the Maternal and Child Health Center associated with the Ministry of Health was conducted to compare Noriday and Lo-Femenal, two locally available oral contraceptives. Data analysis has been completed for 199 women and a final report has been written. The twelve-month follow-up rates were 48.6 and 51.0 for the two groups, respectively. There were no significant differences between the pills

concerning reasons for discontinuation or for side effects. A comparison of Micronovum and Ovrette, two types of progestogen-only oral contraceptives, was conducted in Zimbabwe. One thousand one hundred fifty-seven women were admitted to this study. The study and data analysis have been completed and the final report was written. Six-month follow-up rates were 57.3 and 53.4 for the respective study groups. The six-month lifetable rate for discontinuation due to menstrual problems was significantly higher ($p<.01$) for Ovrette users (3.5 per 100 women) than for Micronovum users (0.3 per 100 women). No other significant differences at the six-month visit have been detected between the two pill groups.

A surveillance study in Niger to collect data on the use of locally available standard-dose and low-dose contraceptives, Minidril and Stediril has been completed. A total of 146 patients were admitted into the trial. Twelve-month follow-up rates were 42.9 in the Minidril group and 32.8 in the Stediril group. There were no accidental pregnancies reported and two women discontinued pill use to plan pregnancy. There were no significant differences detected.

Two investigators in the Philippines who participated in FHI-sponsored Clinical Trials Workshops have completed their studies of two locally available oral contraceptives, Triquilar (a triphasic pill) and Lo-Ovral (a low-dose combination pill). A total of 383 patients have been enrolled out of a proposed combined caseload of 400. Follow-up percentages at 12 months were 72.3 among Triquilar users and 68.9 among Lo-Ovral users. Discontinuation rates were 33.0 and 35.5 per 100 women, respectively. No pregnancies have been reported to FHI at this time.

Data has been processed and analysed for both sites.

One additional study, a noncomparative surveillance trial of Lo-Femenal in Indonesia, has closed. Ninety-four patients were admitted out of a proposed 100-case study. One pregnancy has been reported during the study. The twelve-month follow-up rate is 91.1.

Future Plans

FHI's policy will be to continue to attempt, whenever possible, to meet local needs for research as identified by USAID Missions and/or local investigators. In an effort to further expand this activity, FHI has initiated the Local Projects Funding strategy to enhance the research skills of proven investigators by providing support for conducting locally developed research projects. These projects will be designed, conducted and data analyzed using in-country facilities. The INN strategy will continue to answer locally defined questions, in addition to recruiting proven investigators for new studies. Five studies in Mexico (2 sites), Egypt, El Salvador and Brazil have been proposed for FY 1991.

G. Special Studies

1. Filshie Clip Preclinical Toxicity Studies

In 1985, the FDA requested that carcinogenicity studies be performed with two sterilization devices, the silicone ring (Falope Ring/Cabot Medical Corporation) and the titanium and silicone clip (Filshie Clip/Femcare Ltd.). The study, jointly sponsored by FHI, Cabot Medical Corporation and Femcare Ltd., was designed to evaluate the potential tumorigenic effects of both devices in mice and rats. FHI's responsibilities included monitoring the study, financial management of the study, and preparation of the final study reports including statistical analysis.

The testing facility contracted to conduct this study was the Department of Pathology, University of Nottingham Medical School, Queen's Medical Center, Nottingham, England. Dr. Graham Robinson, Senior Lecturer in the University of Nottingham Medical School's Department of Pathology, was the Study Director. The study was conducted under Good Laboratory Practices. Quality Assurance during the conduct of the study was contracted to an independent third party, Toxicol Laboratories Ltd., Herefordshire, England. Additional Quality Assurance review following completion of the study was conducted by Family Health International.

Both the silicone ring and the titanium and silicone clip sterilization devices used in this study were modified in size (i.e., each was a smaller version of the devices used in human trials) by the respective manufacturers. The mouse and rat studies were not designed as comparative studies between the devices. Rather, the studies were designed to separately compare the results obtained from each device group to a common control group. Histologic evaluation of all tissue samples in the mouse and rat studies were performed by two pathologists at the University of Nottingham Medical School's Department of Pathology. Whenever there was a tissue slide in question the pathologist doing the primary reading of that set elicited the opinion of the other pathologist.

The mouse study was conducted using 600 Charles River CD-1 strain female mice, approximately 6 to 7 weeks of age. The mice were divided into three groups of 200 mice each. All three groups underwent laparotomy. One group had a silicone ring device implanted near the fallopian tube in the anterior uterus region. The second group had a titanium and silicone clip device implanted near the fallopian tube in the anterior uterus region. The third group had no device implanted; these animals served as controls. Tissue samples obtained during post-mortem examination were fixed and prepared for histologic evaluation. The surgical procedures on these mice began on April 21, 1986; all of the mice in the study had a post-mortem examination conducted by December 21, 1987.

The rat study was conducted using 600 Sprague-Dawley strain female rats, approximately 6 to 7 weeks of age. The rats were divided into three groups of 200 rats each. All three groups underwent laparotomy. One group had a silicone ring device implanted near or on the fallopian tube. The second group had a titanium and silicone clip device implanted near or on the fallopian tube. The third group had no device implanted; these animals served as controls. Tissue samples obtained during post-mortem examination were fixed and prepared for histologic evaluation. All of the rats in the study had a post-mortem examination conducted by June 26, 1988.

Histologic evaluation of all tissue samples in the mouse and rat studies were completed in February 1990. All data generated from the studies were received by FHI in August 1990. Statistical analysis of the data is being conducted by the Biostatistics Division of FHI. Draft study reports have been written for the rat studies, one for the silicone ring device (Falope Ring/Cabot Medical Corporation) and one for the titanium and silicone clip (Filshie Clip/Femcare Ltd.). These draft study reports are expected to be finalized by November 1990. Draft study reports are being written for the mouse studies, one for the silicone ring device (Falope Ring/Cabot Medical Corporation) and one for the titanium and silicone clip (Filshie Clip/Femcare Ltd.). These study reports are expected to be finalized by December 1990.

2. 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 conduct a 2-year study in rats. The study is being conducted at Bio/Dynamics in New Jersey. The animals were autopsied in August 1989 and it will take approximately one additional year to analyze all tissues and prepare the final report. To date, the study has progressed well and uneventfully. Food intake, body weight gain and gross observations were all normal. Although a number of animals have died of natural causes, this is to be expected in a study of this duration. No overt problems of particular significance were detected upon gross necropsy of these rats.

Future Plans

The final report for the NET carcinogenicity study will be completed soom. It is anticipated that a draft report will be completed in the spring, 1990, and the final report will be available the following summer.

III. REPRODUCTIVE EPIDEMIOLOGY AND SEXUALLY TRANSMITTED DISEASES

In addition to pregnancy prevention, family planning methods have a wide range of health consequences for their users. As more years of contraceptive experience are accumulated by ever more users, we learn more about the non-contraceptive effects of family planning, both benefits and risks. It has taken years of careful research, for instance, to understand the complex relationship between IUD use and pelvic inflammatory disease. Unfortunately, in some cases incomplete or inaccurate information about family planning still abounds, such as the widespread fears about the Pill and cancer. In other cases, a more balanced picture has been drawn, as for the benefits of barrier contraceptive use against sexually transmitted diseases (STDs).

The Division of Reproductive Epidemiology and Sexually Transmitted Diseases (RESTD) provides this much-needed information on the risks (disease promotion) and benefits (disease prevention) of family planning methods. A major emphasis of the RESTD division is STDs, including HIV. We seek to determine the extent of protection against STDs that is provided by barrier contraception, and whether hormonal contraception increases susceptibility to HIV infection. Other areas of interest are reproductive cancers, contraception for women with special needs, and morbidity associated with pregnancy and childbirth.

A. Ongoing Projects

1. Reversible Contraception and Risk of HIV in Women

Because HIV infection occurs in women of childbearing age, many of whom use contraception, the question arises whether contraceptives modify the probability of HIV transmission. Little is known about the association between contraceptive methods and HIV. One widely reported study found that oral contraceptive use increased the risk of HIV infection three-fold. That finding was incidental in a study of another issue, and a study designed specifically to investigate the OC-HIV association is critical. Although we are reasonably certain that condoms reduce the risk if HIV infection, the ~~in vivo~~ data are weak and the magnitude of protection is unknown. Likewise, questions remain about the magnitude of spermicide protection against HIV (if any) and the long-term acceptability of spermicides.

The RESTD division, with the Department of Obstetrics and Gynaecology at the University of Nairobi, is conducting a pilot study to demonstrate the feasibility of a planned three-year, multi-center research project to examine the relationship between various methods of contraception--especially oral contraceptives, condoms and spermicides--and HIV transmission.

The purpose of the pilot study is to determine if enough women will agree to participate in the study, if follow-up rates are sufficient, if the number of seroconversions is large enough for statistical analysis and whether the data collection instruments

are appropriate. A cohort of 1,500 seronegative women who attend the family planning clinic at Kenyatta National Hospital will be followed for one year and re-tested for HIV quarterly. Those who seroconvert during the observation period will be designated cases in the case-control study. Three controls will be randomly selected from women remaining seronegative. Cases and controls will undergo a detailed interview including contraceptive, reproductive, sexual and medical histories.

The protocol and data collection instruments have been finalized, and the study staff is in place. Recruitment into the cohort began in late July and is proceeding briskly. Follow-up will begin late in October 1990.

2. Barrier Contraceptives and HIV in High-risk Women

Conclusive epidemiologic data to support the assertion that barrier methods can effectively prevent the sexual transmission of HIV are lacking. The National AIDS Control Service (NACS) of Cameroon, the RESTD Division and FHI/AIDSTECH are conducting a prospective study of the association between barrier contraceptive use and HIV infection in high-risk women. The objectives of the study are: 1) to measure the incidence of HIV infection in a cohort of high-risk Cameroonian women; 2) to evaluate the effectiveness of condoms in preventing infection with HIV and other STDs, primarily syphilis and gonorrhea; and 3) to evaluate the effectiveness of spermicides in preventing infection with HIV and

other STDs. Women with multiple sexual partners are advised to use both condoms and spermicidal suppositories at every sexual encounter. Coital logs are used to record information on how many coital episodes took place, and whether the barrier methods were used.

Admission into the study is complete (N=303), and follow-up will continue for 15 months, or until HIV infection occurs. The HIV seroprevalence at admission was 9.2%, and syphilis seroreactivity was 38.3%. The HIV seropositives have been excluded from follow-up. Extensive follow-up data have been received but are not yet computer loaded.

3. Barrier Contraceptives and HIV in Discordant Couples

The Division is evaluating the effect of barrier contraceptive use by HIV-discordant couples in Zambia. These are couples in which one member is HIV-positive and the other is HIV-negative. Couples making regular clinic visits to the University Teaching Hospital in Lusaka have been counseled on use of spermicides and condoms. They maintain a pictorial coital log between visits that denotes when coitus occurred and whether the barrier methods were used. The couples return quarterly for physical examinations and testing of the seronegative partner.

An interim analysis was done for a poster at the San Francisco AIDS conference in June 1990. At that time, 125 couples had been

enrolled, but due to loss to follow-up and false negative ELISA tests, only 90 couples provided evaluable data. Mean follow-up was 9.7 months per couple. 75% of coital episodes were protected by condoms, and 87% by spermicides. Only 3% of coital episodes were protected by neither method.

There were 7 seroconversions (7.8%), for a Pearl rate of 9.6 seroconversions per 100 couple-months. Three new infections occurred among women, and four among men. Among 31 couples reporting perfect condom use, there was one seroconversion (3.2%), while six of the remaining 56 couples seroconverted (10.7%). We performed a survival analysis adjusting for age and gender of the seronegative partner, condom use, spermicide use, and clinical stage of the seropositive partner. The relative rate of seroconversion for more compliant condom users (top two tertiles) compared with less compliant condom users was 0.48 (95% CI 0.14, 1.61). The relative rate of seroconversion for more compliant spermicide users (top two tertiles) compared with less compliant spermicide users was 0.82 (95% CI 0.25, 2.70).

The width of the confidence intervals make interpretation of these findings difficult. More follow-up of more couples and more seroconversions will lead to more precise measures of effect, and more stable incidence rates of seroconversion. There appears to be a trend of diminishing barrier compliance over time, though. Follow-up of this cohort continues.

4. Prevalence of HIV and HTLV-1 in Gonaives, Haiti

Data on the prevalence of HIV infection in Haiti are scarce, mostly obtained 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 education programs.

A cross-sectional clinic-based study was conducted to determine the seroprevalence of HIV-1 and HTLV-1 among 2,000 adults aged 15-45 who attend two comprehensive health centers in Gonaives, Haiti. Initial analyses showed that 8.8% of the study population were positive for HIV-1 and 4.3% were HTLV-1 positive (1.5% were infected with both HIV-1 and HTLV-1). Men and women were equally likely to be infected with HIV-1. HIV-1 prevalence was greatest among persons aged 25-34, but the prevalence of HTLV-1 infection increased in succeeding age groups. The prevalence of HIV-1 was slightly higher among persons who had received one or more injections during the 12 months preceding the interview. This study provided the impetus for an AIDS and STD education program in Gonaives.

Additional analyses are in progress, and a manuscript will be

prepared and submitted to an appropriate journal later in 1990.

5. Nonoxynol-9 and STDs in High-risk Women

In 1986, FHI conducted a clinical trial of the effect of the contraceptive sponge on the incidence of STDs in high-risk women in Bangkok, Thailand. The study showed that the incidence rates of gonorrhea and chlamydial infection were reduced by 69% and 33%, respectively, in the sponge users. The RESTD Division plans to conduct trials at multiple sites to test the effect of nonoxynol-9 spermicidal products (and possibly NeoSampoon foaming vaginal tablets) on the incidence of bacterial STDs. Condoms will also be offered in these studies.

Data collection is complete in the first such study (conducted in Bangkok) and the data are being readied for analysis. We tested the effect of N-9 delivered in the form of a film. From pilot data and the early reactions of study participants, we believe that the film was well-accepted by the women, since it dissolves quickly and is often unnoticed by the male partner.

6. Balancing the Risks and Benefits of Contraception

Information has been accumulated from many sources on immediate and long-term benefits and risks of oral contraceptive use. FHI has developed a computer simulation model (OCRISK program) which takes into account the risks and benefits reported in the

literature for various diseases and estimates the net effect of oral contraceptive use on life expectancy and other mortality variables.

Work is in progress to use the program to estimate the number of deaths caused or averted by oral contraceptives for each of nine broad categories of cause of death. Relative risks comparing the risk of mortality among users and nonusers of the new lower dose OCs are not yet available, but may well demonstrate that oral contraceptives avert more deaths than they cause. 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 who were under age 25 at first birth).

Unfortunately, running the OCRISK simulation model is time-consuming and requires hand calculations and the use of intermediate programs and computer hardware. FHI is developing a streamlined analysis system which will integrate the OCRISK program. The new software will facilitate data entry and file management, automate the complex computations, provide user-friendly access for other FHI staff, and reduce the time required to perform the analyses.

RESTD staff have designed the software specifications, and testing will begin shortly. We will use this new software to evaluate the effects of newly reported associations between OC use and specific diseases. Furthermore, we will provide USAID missions with

country-specific data on the impact of OC use on women's health. FHI is disseminating up-to-date perspectives on the Pill to users and providers working with other AID-funded agencies.

7. 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).

A total of 581 women were interviewed (212 cases and 369 controls). All data have been transferred to FHI for processing and analysis. Data management and cleaning are in progress, along with the creation of numerous analysis variables. Preliminary results of the analysis of the relationship between DMPA and risk of cervical cancer will be presented at the VIIth International Meeting of the Society for the Advancement of Contraception to be held in Singapore in November 1990.

In addition to the main analysis, RESTD has undertaken two validation studies to assess information bias in the case-control

data. The first methodologic study evaluates the accuracy of the cervical cancer diagnoses for cases. Biopsy specimens used to make the original diagnosis have been reviewed by a panel of pathologists at the University of the West Indies Department of Pathology. Data collection for the second study, which focuses on measuring recall bias in self-reported history of hormonal contraceptive use, was completed in August 1990. For a sample of cases and controls, contraceptive histories reported by respondents during interviews are being compared with prescription histories in family planning records. Data from these two validation studies will be analyzed and two manuscripts prepared in 1991.

8. Contraception and Sickle Cell Disease

Many doctors consider oral contraception to be contraindicated in women with hemoglobinopathies such as sickle cell disease. But 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 the injectable benefits women who are homozygous for sickle cell disease by decreasing the frequency of sickling crises.

Building on this study, FHI has conducted 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 were 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 and data collection ended in August 1989. Twenty-six patients completed phase 1 and four terminated the trial before finishing phase 1. One died during the washout phase. Of the 25 patients who entered the second phase of the trial, 18 completed phase 2, and seven terminated the trial before completing phase 2. Data are being processed, and results will be available later in 1990.

A study in Nigeria of women with sickle cell disease who use the NORPLANT[R] contraceptive system is underway. The active ingredient of NORPLANT[R] is levonorgestrel, a progestogen. 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[R] insertion, and for up to five years of observation after insertion. Twenty-one participants have had the implants inserted, and recruitment and follow-up continue.

Following their NORPLANT[R] insertions, 13 women reported their physical conditions are much better, 3 women said they are slightly better, and 5 said their disease has not changed. None reported a worsening. The prevalence of complications and complaints that are common to sickle cell patients, such as headaches, dizziness and limb pain, are lower post-insertion than pre-insertion. Chronic problems with the shipping and importation of laboratory reagents still preclude hematologic tests on the stored blood samples.

9. The Male Influence on Spontaneous Abortion

This study used the Finnish hospital discharge registry and census data to examine the relationship between fetal loss and male occupational exposure to agents with recognized reproductive toxicity. The registry permitted use of a sample of 73,000 exposed and 1.5 million unexposed men and enabled us to control for maternal history and exposure to substances associated with an increase in spontaneous abortion.

An exposure classification system was developed to assign specific exposures to men on the basis of their occupation. To estimate the relative risk of spontaneous abortion among various groups of fathers exposed to any mutagen and to specific mutagens, odds ratios were obtained using logistic regression analysis, adjusting for the potentially confounding effects of maternal age, maternal occupational exposures and socioeconomic status. When wives of men exposed to mutagens and wives of men not exposed to mutagens were compared, paternal exposure had no overall effect on the risk of spontaneous abortion. However, paternal exposure to four of the 25 exposures evaluated (ethylene oxide, rubber chemicals, solvents used in refineries and solvents used in rubber manufacture) was associated with increased risk of spontaneous abortion. The manuscript summarizing the study findings was submitted to and given a favorable review by the American Journal of Public Health. At the request of the journal's reviewers we are shortening the

manuscript and will resubmit it.

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

Women who discontinue oral contraceptive use often do so because of early side effects, and Vitamin B_6 may reduce the incidence and/or severity of those side effects. In collaboration with the Zacatecas (Mexico) General Hospital, the Division conducted a double-blind, randomized clinical trial of the effect of taking Vitamin B_6 on the early side effects associated with OC use. Women in the treatment group received 150 milligrams of vitamin B_6 each day during their initial three months of OC use; other women received a placebo. Study outcomes recorded on daily symptom logs included the frequency and severity of OC side effects including nausea, irritability and headache.

Data collection concluded in June, 1990. The first draft of the report by the Principal Investigator should be ready in October, 1990. Of the 120 subjects, 42% of the participants completed the three-month observation period. There appears to be no difference in the incidence of side effects between the vitamin B_6 and placebo groups.

11. Oral Contraceptives and Bone Mineral Density

Estrogen therapy is known to retard bone loss 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 (BMD) 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 lumbar spine BMD was measured by dual photon absorptiometry; two sites on the radius were measured by the single photon method. Information on other risk factors for osteoporosis and a contraceptive history was collected on a self-completed questionnaire. Three hundred and fifty-two women participated.

Adjusting for known determinants of bone density by multiple linear regression, the mean spine BMD of ever users was greater than that of never users. The difference was greatest among women with low current calcium intake or low lifetime levels of breastfeeding (60 mg/cm^2 [95% CI 10-110]). Adjusted lumbar BMD was higher among users who reported lifetime OC use of 48 months or more than among women with shorter durations of OC use.

In a second analysis of the same data set, we examined the effect of lactation on BMD in these women. Among women who had not used OCs, those who had breastfed had substantially higher lumbar BMD

than those who had never breastfed. The increase was greatest for those women with the longest duration of breastfeeding. The difference was smaller and not significant among women with a history of OC use.

These two papers are being finalized for publication, and two other analyses of the data set are planned.

12. 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 initiated a study of the acceptability of three spermicidal products containing nonoxynol-9 among both men and women attending a Zambian STD clinic. Each participant will be asked to use one product at every intercourse for two weeks, and then use a second product for another two week period. Participants will be interviewed to reveal problems with spermicide use and any preference s/he may have. Three months after active participation ceases, each person will be re-contacted to determine whether s/he is using a spermicidal product.

Preliminary results are encouraging, in that a surprising enthusiasm has been expressed by both male and female participants. Four of the first five participants reported at the three-month

contact that they had purchased and were using a spermicide. They cited the lack of worry about STDs and pregnancy that attended spermicide use. The National STD Control Programme will consider providing a widely accepted spermicide product at STD clinics nationwide.

13. Reproductive Cancers

Depending on the region of the world, breast cancer is the first or second most common cancer in women. Its incidence is increasing rapidly in developing countries, and is related to patterns of reproduction, including the timing of childbirth in relation to menarche and the duration of breastfeeding. Unanswered questions about the long-term safety of oral contraception in relation to breast cancer persist, especially for a few groups of women. Use of oral contraceptives also affects the incidence of other reproductive cancers; it is well established that OCs reduce the risk of endometrial and ovarian cancer, yet the Pill may be associated with a slight increase in the risk of cervical cancer. FHI has conducted or supported three relevant studies.

Some studies suggest that OCs may be associated with an increased risk of breast cancer among women less than 45 years of age (a small fraction of all breast cancers). FHI, in collaboration with CDC, undertook a decision analysis to determine whether women should continue to use the Pill if it causes breast cancer in premenopausal women. The decision analysis was constructed to

weigh the risks and benefits of OC use ~~versus~~ non-use in terms of the reproductive cancers. Our results show that even if OCs do prove to be causally related to breast cancer among women younger than 45, users would still experience fewer reproductive cancers during their lifetimes than non-users.

The decision analysis was then extended to evaluate the effects of OC use on reproductive cancers in the developing world, taking into account maternal mortality -- a major problem in poorer countries. In each of the developing countries we studied (Senegal, Colombia, Jamaica, Singapore and India), we found that OC use reduces mortality. In Senegal, for instance, 500 maternal deaths were averted by OC use while 18 additional reproductive cancers occurred in OC users; thus a total of 482 deaths were averted. The protective effect of OC use was most pronounced in countries with high maternal mortality (India and Senegal), whereas fewer deaths were averted in countries with lower maternal mortality (Singapore and Jamaica).

Both of these analyses were presented at the 1990 American Public Health Association meeting, and will now be submitted for publication.

We have also investigated cohort trends in reproductive cancer incidence and OC use in 14 developed and developing countries. We developed log-log graphic plots of breast cancer by age for selected birth cohorts of women, using data published from cancer

registries that collaborate with the International Agency for Research on Cancer. We found that the women born in cohorts likely to be exposed to OCs had no more breast cancer at age 45 or younger than women in birth cohorts in which OC exposure could not have occurred.

14. Breast Cancer and Oral Contraceptives in Perimenopausal Women

Recent studies of this association have focused on relatively young women, since it is they who have had the opportunity to use OCs for long durations and at early ages. It is important to assess the effect of OCs among women in the age group when breast cancer is much more common. If an adverse effect of OC use persists into the ages at which the incidence of breast cancer becomes high, then the implications for the public health would be far more serious. RESTD funded the Slone Epidemiology Unit of the Boston University of School of Medicine to analyze data from a multi-hospital case-control study of breast cancer in women aged 45-59. Results show an elevated relative risk in women with 5-9 years of OC use, but not in women with 10 or more years of use. Furthermore, the findings were not consistent across geographical areas. The study provides little support for the hypothesis that there is an adverse effect of previous OC use among older women. These results appeared in the proceedings of the Royal Society of Medicine's conference on breast cancer (edited by Mann, 1990).

B. Planned Projects

In the coming year, work will continue in contraception and STDs, with a major emphasis on the influence of hormonal and barrier contraceptives on the transmission of STDs. As funding permits, we will also broaden our scope of work in reproductive health. Areas of special interest are contraception for older women and other groups with special needs, breast cancer, maternal morbidity and mortality, disease prevention, and previously unstudied associations between disease and contraceptive use.

1. Maternal Morbidity

The burden of maternal morbidity is great; it has been estimated that there are 15 serious morbidities for each maternal death. RESTD is developing (with USAID/New Delhi and Ford Foundation funds) three surveys of maternal morbidity in India, Bangladesh and Egypt. The surveys will measure the prevalence of maternal morbidity in those countries, determine the causes, and identify solutions that are feasible, effective and culturally acceptable. Standardized survey instruments are being developed in consultation with the local investigators and medical anthropologists, following focus group discussions with local women.

The Indian project has governmental approval and will shortly get funding approval from the Ford Foundation (New Delhi). Bangladesh will receive funding from the Ford Foundation (Dhaka) as soon as

government approval is given. Egypt is still developing the proposal in collaboration with FHI and the Ford Foundation (Cairo). An Investigators' Meeting was held in New Delhi in July 1990 and was attended by the investigators from the three sites. USAID/New Delhi funds were used for this meeting. A second meeting will be held in early 1991.

2. The Effects of Frequent Use of Nonoxynol-9

There is great concern about providing women with methods for protecting themselves from STDs, because condom use is not always acceptable. One suggestion has been that women should use a chemical barrier with or, if need be, in place of a physical barrier. N-9 may be effective in preventing STDs, but it has the potential to irritate mucosal tissues, and a recent report suggested an increase in the risk of genital ulcers among women who used a product containing N-9.

RESTD conducted a small (N=15) phase I local toxicity study to determine if frequent use of N-9 affected the vaginal or cervical mucosa. Low-risk women inserted four N-9 suppositories nightly for two weeks. Six of the 14 women followed (43%; 95% CI 18%-71%) had significant physical findings that included disruption of the epithelium, bleeding, inflammation and edema.

We plan to conduct a larger phase II local toxicity study using N-9 suppositories. The larger study will allow us to measure more

precisely the incidence of substantial vaginal and/or cervical irritation with frequent N-9 use. Also, we will determine whether there is a dose-response relationship between frequency and incidence of irritation. Using a protocol developed by the RESTD division, the World Health Organization intends to conduct a similar study of frequent insertion of NeoSampoon (menfegol) suppositories.

3. Low-dose Oral Contraceptives in Older Women

Contraceptive options for older women are limited. Many physicians are reluctant to give OCs because of fear of cardiovascular side effects. Reanalysis of old data suggests this risk is not as great as it was thought to be. Furthermore, a study in Israel has shown that women treated with triphasic OCs for symptoms of menopause not only had remission of symptoms, but also had greater bone mineral density compared with women presenting with menopausal symptoms but not treated.

We have developed and submitted for funding a replication of the Israeli study. We will follow women from 40-49 years of age, comparing users of a low-dose OC with women using other methods of contraception. Potential investigators have been identified. We plan to evaluate blood pressure, serum lipids, coagulation factors and glucose tolerance, in addition to bone density and menopausal symptoms.

4. Contraception and Other Diseases

Long range plans of the Division include exploration of the association between contraceptive use and occurrence of other diseases, such as systemic lupus erythematosus, endometriosis and testicular or prostate cancer.

IV. PROGRAM EVALUATION

The five priority research areas in the Program Evaluation Division are: acceptability and demand for contraceptive methods; improving the use of contraceptive methods; improving the effectiveness of family planning programs; breastfeeding and postpartum contraception; and AIDS and family planning. Several studies on the economics of family planning, a cross-cutting issue, are also being done through the Program Evaluation Division.

The emphasis of PE studies is on understanding factors associated with contraceptive acceptance, correct use, and continuation within the **general** population. This complements the research in Clinical Trials which focuses for the most part on **clinical** populations.

The highest priority activities for each of the five areas are:

(1) Acceptability/Demand: acceptability of latex and plastic condoms (male and female).

(2) Improving Contraceptive Use: pill compliance and informed choice.

(3) Improving Program Effectiveness: reasons for continuation/ discontinuation, evaluation of social marketing, assessing the impact of family planning and health programs and cost-effectiveness studies.

(4) Breastfeeding/Postpartum Contraception: testing of the Bellagio consensus and support of programmatic research on postpartum programs.

(5) AIDS and FP: research on the feasibility of adding HIV risk assessment to FP programs and on the impact of the HIV epidemic on condom distribution by FP programs.

Most studies of the Program Evaluation Division are designed to provide practical information to improve service programs. Research methods range from in-depth interviews and focus groups to hospital-based studies and large household surveys. As part of each project, technical assistance is provided to local investigators so they can develop the capability to evaluate their own programs.

A. Acceptability of New and Already Developed Methods

The Associate Director for Market Research and two Research Analysts plan, coordinate and implement the acceptability and market research within the Program Evaluation Division. The studies in this section have dealt with a wide range of contraceptive methods including NORPLANT[R] and male and female condoms. When methods such as the new NET products are further developed, we will also study their acceptability.

The vast majority of FHI's work on acceptability currently focuses on male and female condoms due to the upsurge in interest in barrier

methods brought about by the STD/AIDS crisis. The purpose is to find out which types of condoms are most preferred by consumers and which ones provide the best performance. NORPLANT[R] acceptability studies are looking at satisfaction with the method, providers' attitudes, the impact of husband counselling, and reasons for continuation and discontinuation.

1) Egypt: NORPLANT[R] Acceptability

As part of the pre-introductory clinical trials of NORPLANT[R] contraceptive implants in Egypt, the acceptability of NORPLANT[R] to previous users and new acceptors has been assessed. The purpose of the research is to understand the reactions of users to the product, identify any problems with insertion or removal, and evaluate user perceptions of counseling received before and during use. The study was conducted by five universities in Egypt, coordinated by public health physicians working closely with the clinical trials investigators.

Stages I and II of the NORPLANT[R] acceptability study have been completed in Egypt: Stage I included focus group discussions with NORPLANT[R] users, their husbands and the service providers who had experience with NORPLANT[R] between 1982 and 1988; stage II involved focus group discussions with those participating in the current NORPLANT[R] clinical trial; a survey of the 1,500 women in the clinical trial; and participant observation at the clinical trial sites.

In the Stage I focus groups, the majority of respondents agreed that NORPLANT[R] had advantages over other contraceptive methods since it is a long-acting method suitable for women who want no more children, is reversible and does not cause sterility. Side effects, including menstrual irregularities, dizziness, and headaches, were found to decrease with increased duration of use. Husbands tended to be supportive of their wives using NORPLANT[R] as many husbands did not want more children.

The Stage II focus group discussions among clients in the current clinical trials found that most users and discontinuers were satisfied with NORPLANT[R] and would consider using the method again. Problems associated with NORPLANT[R] included irregular or excessive bleeding, amenorrhea, headaches, weight loss or gain, and weakness. Few women reported social problems associated with NORPLANT[R]. Worries and doubts about NORPLANT[R] tended to increase after one year of use, mainly due to the spread of rumors, the main source of which were doctors not associated with the clinical trials and relatives. Discontinuation was due mainly to side effects, especially menstrual irregularities.

Results from the Stage II survey, which was completed for 1,351 of the 1,537 clients in the clinical trial, suggest that, overall, 93 percent of the women are satisfied users, and that even among those experiencing problems, 89 percent are still satisfied users. Women in the survey tended to be in their early 30s. Most had no education, and worked at home. They had an average of four children, and few wanted any more children. Most had used family planning before

trying NORPLANT^R, generally the pill or IUD. Many had had problems with the other methods. By the time of the survey, more than half of the women had experienced a problem with NORPLANT^R, usually menstrual disturbance. Only seven percent had had NORPLANT^R removed, again due to menstrual or other medical problems. When asked if they would consider using NORPLANT^R in the future, an average of 67 percent said they would, and an additional 22 percent said they were not sure. An average of 89 percent said they would recommend NORPLANT^R to others. EFCS is currently working in a final report of the survey, which will have more information on NORPLANT^R removals.

A series of papers on NORPLANT^R acceptability has been planned. The first, a paper about the general acceptability of NORPLANT^R in Egypt, has been drafted. An abstract will be submitted to the Population Association of America.

2) Bangladesh: NORPLANT^R Acceptability Research

This project has four phases that relate to both the first cohort of NORPLANT^R acceptors in Bangladesh and a second cohort representing an expanded clinical investigation. The first phase consisted of an in-depth investigation of 300 discontinuers and continuers participating in a NORPLANT^R clinical trial conducted by the Bangladesh Fertility Research Programme and supported by FHI's Clinical Trial Division. The second phase was an expanded clinical trial (N=1,200). The clinical trial was designed so that it would be possible to study whether the addition of a special counselling program for husbands that

might possibly improve women's experience with NORPLANT^R. The third phase is a replication of the first phase, but will focus on the experience of women in the expanded NORPLANT^R trial. This will be undertaken during FY'91. The fourth phase is a survey of the reproductive health and contraceptive behavior in geographical areas where NORPLANT^R implants have been introduced. The survey is being conducted by BFRP with technical assistance by FHI. Field work for this survey was completed in September 1990.

The first cohort of NORPLANT^R acceptors was recruited into the pre-introductory clinical trial during February 1985-March 1986, with a total of 673 NORPLANT^R acceptors in three clinics. During the first 18 months, a total of 100 women had discontinued the use of the implants. An in-depth follow-up interview of 74 discontinuers of the first cohort of NORPLANT^R users and a sample of those still continuing with the implants was conducted in their homes. A small sample of husbands was also interviewed. The survey investigated a host of factors potentially affecting the discontinuation and continuation of the implants.

A central concern of this study was whether women found it difficult to get the implants removed when they wished to discontinue. In answer to the open-ended question, "When you made the request for removing NORPLANT^R 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 did not 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). This indicates room for improvement in training providers to respond to clients' desires to discontinue the method although the problem affected a relatively small percentage (10%) of the discontinuers--all of whom did get their implants removed.

A joint BFRP-FHI paper was prepared on these results and will be presented at the APHA meeting, October 1990.

Dr. Larry Severy, an FHI consultant, will be visiting BFRP in December, 1990 to help with the reproductive health survey data analysis.

3) Secondary Analysis: Menstrual Behavior and Beliefs: Analysis of Multi-country Data

The purpose of this analysis is to develop robust and reliable indices of menstrual patterns and perceptions that will be useful in analyzing the reproductive health survey in Bangladesh. The work is being done by an FHI consultant, Dr. Larry Severy. The data set is the WHO multi-country study of menstruation perceptions conducted in the early 1980's.

4) Haiti: Condom Acceptability Study

To look at issues relating to the acceptability and use of condoms distributed free of charge at a family planning clinic in the low-income Cité Soleil district of Haiti's capital and largest city, Port-au-Prince, a retrospective, household-based survey of acceptors and of community residents was undertaken in 1986-87 with technical and financial assistance from FHI. The study obtained information from over 700 men.

A final report, Perceptions and Practices Relating to Condom Use Among Men in Cité Soleil, Haiti was prepared with the Centre Pour le Développement et la Santé and distributed in October, 1989. Findings showed near universal knowledge yet very low use of condoms in Cité Soleil. Among men whose wives or partners had received condoms at the local family planning clinic during the previous three months, fewer than one half said they had ever used them. Only five percent were current users. Condoms were considerably less popular than systemic methods--pills, injectables and implants--in Cité Soleil. Among men not currently practicing any method of contraception, only one percent said they planned to use condoms in the future, compared with 25 percent who intended for a partner to use pills and over half who planned for a partner to be protected by injectables. These data were collected before widespread publicity about AIDS in Haiti and many of the intervention programs to slow the spread of the virus which causes the disease. More recent surveys show that condom use has increased considerably.

Among the conclusions of this report is the urgent need to promote the use of condoms among Haitian males in urban settings such as Cité Soleil. In addition to their role as a family planning method which can be provided safely in a non-medical distribution system, condoms are important in limiting the spread of sexually transmitted diseases, including AIDS, a major problem in Haiti. A shorter version of the final report is being prepared for publication in 1991.

5) Use of New Barrier Contraceptives

Given the tremendous investment required to develop new methods of contraception, as well as the large A.I.D. investment in contraceptive commodities, it is important to evaluate the acceptability of these methods early in the development process, or before procurement of large supplies for program distribution. The first FHI acceptability study of condoms involved spermicidally-lubricated condoms. (See section on AIDS studies.) Since this initial study, FHI has expanded its efforts to include several small studies to examine the acceptability of various prototype plastic condoms, latex condoms of different sizes, female condoms and stronger latex condoms. We are conducting these studies both locally and internationally to provide essential preliminary information on product acceptability to help in procurement decisions or before these methods are distributed widely. In subsequent phases of the evaluation process, increasing emphasis will be placed on marketability of the new methods in developing countries. Further studies will include planners and providers as well as users.

a) Stronger Condoms

FHI conducted a two phase study of a thicker (and presumably stronger) condom for A.I.D. In the first phase, 12 couples from FHI did a blind comparison of two standard condoms and two condoms which were 30% thicker. While the couples were unable to differentiate the thickness as such, most respondents preferred the thinner standard condom on every index of acceptability except strength. Seventy-five percent preferred the standard condom.

The second phase of this project was a study of these stronger condoms in Sri Lanka, Mali and the Dominican Republic to determine perceptions of comfort, fit, and breakage as well as overall preference. This study was directed toward the question: if a social marketing (or commercial) organization added the stronger condom to its product line and described it as stronger, would consumers prefer it to their usual condom? A critical issue was to determine whether local concern about breakage and protection against unwanted pregnancy, HIV infection and STDs would result in a preference for the stronger, thicker device. Seventy-two percent of participants indicated a preference for the stronger condom due to the perceived added protection against pregnancy. Eighty-one percent of subjects cited this preference due to perceived added protection against AIDS. It is interesting to note that many of the participants would pay more for a stronger product. The next stage is to see whether the stronger condoms have a lower breakage rate. (See "Future Plans" section.) An unanswered question

is whether condom users in developing countries would prefer the "stronger" condoms over standard ones if the former were simply offered with no explanation. This question could be addressed in a future study if the stronger condoms come out favorably in the breakage study.

b) Female Condoms

PE is evaluating the acceptability of a female condom, the WPC-333 (now called Reality™), while CT is looking at its efficacy in preventing pregnancy. The female condom was developed to give women a barrier method to protect themselves against both STDs (including HIV infection) and unwanted pregnancy, without having to rely on the direct cooperation of their partners. FHI has sponsored two female condom acceptability studies in Thailand, each with 20 women at high risk of STDs. Results of the first study indicated that participants experienced few problems using the condoms, but objected to the bulkiness of the device and the inconvenience of self-lubrication. Some of their partners objected to the female condom as well as to the standard male condom. Nevertheless, 80% of the participants in the study said they would recommend these to a friend, especially if the devices were smaller and pre-lubricated.

A second study was conducted in the same population with a modified, pre-lubricated device. Results show that the smaller device was properly sized for this population, but that the Thai volunteers still have some complaints about the method. For the most part, these complaints center on the inner ring. Sixteen (80%) of the twenty women

stated that the inner ring caused pain, interfered with intercourse and that their partners could feel the inner ring as well. While all of the participants felt that the male condom was more convenient, approximately half of the women would use the device in the future.

We have received requests from several other countries, including the Dominican Republic, Kenya, Cameroon and India, to evaluate the acceptability of the female condoms and hope to pursue several of these opportunities. At the same time, the Clinical Trials Division, in collaboration with CONRAD, will continue to assess the contraceptive efficacy of this device.

c) Larger Condoms

One issue regarding condom usage centers on adequate fit and its relationship to comfort and breakage. In some populations, men may find a larger condom more comfortable. A better fitting, more comfortable product may lead to reduced breakage and increased acceptability. In order to not place anyone at risk due to device slippage, we conducted a small in-house study in an attempt to determine whether the slightly larger (55mm as opposed to the standard 52mm) would remain on the penis during coitus. We compared the larger condom to a standard condom on aspects of comfort and overall product satisfaction, as well. Results indicated that the larger size had minimal impact on retention -- with only one reported case of slippage. Most participants found the device to be comparable in comfort and fit to currently available products. This study was repeated in Mali,

Kenya and Ghana. Preliminary results indicated that 60% of participants in Kenya and Ghana preferred the standard (52mm) device. Conversely, 60% of the Malian participants found the larger device to be more acceptable. Though it was a blinded study, virtually all participants were able to differentiate the condom sizes (i.e. recognizing that the 55mm device was larger). When selected, the larger devices were preferred based on comfort, conversely, the standard condom was preferred because tighter fit equated to security. The results of the study indicate an interest and possible need for devices in multiple sizes.

d) Plastic Condoms

Preliminary function tests are underway on various prototype plastic condom designs being developed by FHI. In a series of studies, local couples have volunteered to test the acceptability of prototype condoms made of polyurethane film. Several designs have been evaluated and have been continuously refined with respect to study participants' suggestions and preferences. Most problems reported with one of the prototypes (e.g., donning difficulties, bunching, excessive noise) appear to be related to its single size and the material (film) used. Future work on this product will center on finding a better film that will minimize bunching and noise and provide improved elastic properties.

A second polyurethane prototype condom has been well received. This device was found to be adequately sized. The treatment of the material

to impart softness produced a condom which 78% of participants (N=50) preferred and would buy over latex. Studies now in development will determine breakage rates of this device as compared to latex and will assess preference for minor modifications made to the prototype. Acceptability tests of the prototype plastic condom will be conducted at FHI and other sites in the United States as well as internationally.

e) Smaller Condoms

Smaller condoms (49mm) are currently being provided to several Asian countries. In its attempt to streamline procurement and distribution, A.I.D./Washington is considering eliminating the smaller size. To data, studies have not been done to assess either the acceptability or the performance of these condoms in actual use. FHI will conduct such research on the smaller condoms in three countries: The Philippines, Nepal and Sri Lanka.

Future Plans: New Method Acceptability: Condom research will continue to have high priority because of the condom's important role in AIDS prevention as well as family planning. FHI's prototype condom development and research on the female condom, as well as studies of latex condoms will all continue, along with research on the acceptability of other contraceptive methods as they are readied for introduction. As the prototype condom is refined, it will be tested by a wider range of users at centers in the U.S. and other countries. To facilitate condom testing, we have set up a local (tri-county area)

test panel with over 300 participants. We have begun to set up similar panels and centers internationally.

As with currently available products, acceptability will be examined at all stages of product development to determine what market potential exists for the new products and how acceptability can be increased. 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. Specific projects that are planned or have just begun include a comparative breakage study of the standard vs. stronger latex condoms and a study of the acceptability and functionality of condom re-use.

1) Standard vs. Stronger Condoms

Though many laboratory studies have collected data on condom breakage, few have been designed to assess breakage in actual use. We have recently begun a study to statistically determine breakage rates in use of a standard (52mm) USAID condom versus an Extra-Strong (ie, thicker) device. An additional component of the study is to assess consumer preference for these two condoms. The study will be conducted at seven international sites.

2) Re-usable Condoms

Information on the practice of re-using latex condoms is largely anecdotal but estimates from a few published studies indicate that the

incidence of re-use could be as high as 16 to 20 percent in less developed countries. To confirm whether condom re-use is prevalent, we have designed a study to assess incidence, reasons for re-use and hygenic practices associated with the behavior. Only if Phase I determines that re-use is an important issue will we consider going on to Phase II which would determine product life and user acceptability of a re-usable plastic condom. Phase II studies would be conducted at four sites in Asia and Africa. These studies will need to be tabled until funds become available.

3) Multi-country Contraceptive Acceptability: Secondary Data Analysis

The Program Evaluation Division is providing financial support to Professor Lawrence Severy to further analyze data from the WHO ten-country study on behavioral patterns and beliefs and perceptions of menstruation. The data assessing these two domains will be subjected to factor and cluster analytic procedures, followed by formal scaling analyses, to develop indices with acceptable estimates of reliability.

Resulting refined scales will be validated with a pilot sample of low income women representing three different ethnic groups. The final product will be a set of technically robust scales available for use by those attempting to assess menstrual behavior and beliefs.

The result of this work can be utilized to develop and refine survey instruments aimed at assessing the relationship between beliefs and

perceptions of menstruation (and menstrual changes) and contraceptive use in surveys.

A visit by the FHI staff member involved in this study to the University of Florida is planned for October 1990 in order to complete the analysis and paper.

B. Improving the Use of Contraceptive Methods

As family planning programs master the rudiments of delivering different methods, their attention turns to the quality of care provided. FHI is making two forays into this area with our work on oral contraceptives - particularly the problem of pill compliance - and our concern with encouraging informed choice. We are working closely with other family planning Cooperating Agencies to define, measure and improve quality of care.

1) Pill Compliance

Although oral contraceptives (OCs) have been used by hundred of millions of women in LDCs since their introduction 30 years ago, there has been very little systematic effort to understand how women actually use the pill and what mistakes are most common. Incorrect use may contribute to increased side effects, discontinuation and method failure. Pregnancy rates as high as 15-20% has found in some settings due to incorrect pill use.

a) Colombia: Pill Compliance

FHI's first study on pill compliance was done in Magdalena, Colombia in 1986, when the last group of the Ministry of Health's rural health promoters in that region completed their training to provide OCs. We found that four out of 10 of 500 new users had discontinued the pill by the end of that study. The most common errors made by continuing users over a two-week period were incorrect transition time between pill packets, followed by incorrect use during the cycle (eg, only when they had sex, alternate days, forgot, etc.). Neither the new users nor the rural health promoters fully understood how to take the pill correctly. One of the most important recommendations of the final report of the study was for more intensive training of the providers in correct OC use, and that providers be accountable for that knowledge before they are allowed to distribute pills and counsel women.

The final report of that study and a 12-page executive summary are available in Spanish and English; a paper on the relationship of OC compliance to knowledge of providers and users was published in the March 1988 International Family Planning Perspectives.

In large part because of this study, the Colombian Ministry of Health (MOH) is revising the training curriculum for its rural health promoters; and, in November 1989, the MOH held a workshop to make the nurses who conduct the training aware of the gaps in the providers' knowledge and the need for the revised curriculum. That workshop was funded by FHI and Pathfinder.

b) Egypt: Pill Compliance

A qualitative study of OC use in Egypt was completed in March 1990. The study involves focus groups with 96 users and discontinuers in four governorates and interviews with 34 providers working in the same villages. Findings of that study were similar to those in Colombia. Most importantly, both users and providers were found to lack understanding of correct use of OCs. None of the users and only three of the providers knew to wait seven days between 21-day pill packets, for example. The focus groups also documented the fears women have about daily OC use, based on their perceptions of the pill as toxic. Their perceptions were reinforced by the advice of two-thirds of the providers to "rest" from the pill at least yearly.

This study culminated in a March 1990 workshop attended by representatives of family planning training institutes, service agencies, social marketing and public information organizations to discuss the implications of these findings. Their recommendations for improving correct pill use emphasized revision and coordination of provider training, better information for pharmacists, and new counseling materials and media messages to reduce fears about the safety of the pill and to provide correct information on OC use.

Also presented at the workshop were complementary quantitative data from the 1988 Egypt Demographic and Health Survey that verified the findings of the qualitative study. For example, only one in 10 of the

999 OC users interviewed in the DHS knew how long to wait between pill cycles. The questions on OC compliance in the Egypt DHS had been included at the request of FHI.

c) Secondary Analysis of OC Data from 1987/88 DHS

We are beginning a secondary analysis of oral contraceptive compliance using data from the Demographic and Health Surveys in four countries: Egypt, Indonesia, Botswana, Zimbabwe. The pill compliance modules were added at FHI's request in order to have data on a large sample of OC users, about 1,500 in each country. These data will be analyzed in the context of personal, method and service delivery characteristics in each country.

d) Papers

A paper "What Do We Know About How Women Take the Pill?", was presented at a Workshop on Compliance sponsored by the Tufts University in November 1988. It has recently been submitted for publication. A second, "The Role of Compliance in the the Use-Effectiveness of Oral Contraceptives," was presented at a Drug Information Association Compliance Symposium in Philadelphia, Pennsylvania in September 1989. That paper will be published as a chapter in a book on Patient Compliance in Clinical Trials and Medical Practice. A shorter version of that paper is in press for the IPPF Medical Bulletin.

e) Expert Meeting on OC Use

FHI brought together 18 biomedical and behavioral experts in the field of oral contraceptive use for a meeting at FHI in July 1990 to identify gaps, set priorities and recommend areas for further research. Recommendations made by this group included improving and standardizing manufacturers' and providers' instructions for pill use (especially with regard to the start date, what to do about missed pills, and use of back-up contraceptive methods). The second priority of the group was behavioral research to identify the specific errors being made by OC users, the reasons for those errors, and interventions to correct them. This meeting also resulted in a request from the U.S. Food and Drug Administration (FDA) for FHI to coordinate a meeting of the FDA's Medical Advisory Committee on Fertility and Maternal Health Drugs to recommend standard labeling for all U.S. manufacturers of OCs. This meeting is now scheduled for February, 1991.

f) Meeting of OC Manufacturers

As a follow-up to the Expert Meeting and in preparation for the FDA meeting, FHI invited representatives from pharmaceutical companies that manufacture OCs to attend a second meeting, in August 1990. Six of the nine companies sent representatives, who discussed the reasons for the instructions they currently provide in patient package inserts (PPIs) and itemized the advantages and disadvantages of the most commonly given instructions for pill use and developed suggestions for how to improve the PPIs. The listing of pro's and con's of various

instructions became the basis for a more extensive version prepared by FHI for the FDA.

2) Informed Choice

A.I.D. has strongly emphasized the importance of informed choice in international family planning programs. At A.I.D.'s request, a Task Force on Informed Choice was convened consisting of representatives of 17 Cooperating Agencies, including FHI. The Task Force issued its report in July, 1989.

The Task Force has underscored the need to develop both qualitative and quantitative instruments and protocols to assess the status of informed choice and identify ways to strengthen it. Informed choice needs to be assessed within the larger framework of quality of care at the clinic-provider level as well as from the user-perspective. Surprisingly few efforts have been made to assess the impact of informed choice and quality of care on increasing the effectiveness of family planning programs.

FHI received an add-on project to do activities to promote informed choice. The Program Evaluation Division's work in the area of informed choice consists of several activities. These include, (1) diagnostic studies in countries where there is predominant use of one method of family planning, (2) illustrative analysis of data on contraceptive method choice, (3) development of materials for strengethening the role of informed choice in family plannng programs, and (4) design and

implementation of studies aimed at assessing informed choice within the larger framework of quality of services.

The PE division has completed diagnostic studies in two countries, Nepal and the Dominican Republic, where there is predominant use of sterilization. The key findings of the Nepal study were published in the journal, Studies in Family Planning, and in December 1989, the Division assisted in disseminating the findings to incourage policy changes and program modification, by sponsoring and organizing three high-level conferences on "Emerging Issues in Family Planning in Nepal".

PATH, under a contract with the Program Evaluation Division, is developing a set of audio video materials on the role of informed choice in family planning programs. As part of the pre-testing phase, PATH presented a slide show at the International Postpartum Conference in Mexico in September, 1990. Further field-testing is planned in 2-3 three developing countries in November-October, 1990. The final product of this activity will be a set of slides and written text which will be distributed to key family planning programs for use in their orientation and training programs.

The final component of the Division's activities in informed choice, is to implement studies designed to evaluate empirically the appropriateness and applicability of a conceptual framework for assessing the quality of services in clinic-based family planning programs and investigate the clients' perceptions of quality of family

planning services and the degree to which the utilization of the services by the clients are affected by the quality of services provided.

The Division has completed three papers on contraceptive method choice and method switching using three data sets from Sri Lanka, including one data set supported by FHI as part of another project. Two of these papers have been published in the Special Supplement of Journal of Biosocial Science, Contraceptive Use Dynamics. The third paper is being published in Demography.

Future Plans: Quality of Care

1. Oral Contraceptive Compliance Follow Up Study in Colombia

After disseminating widely the results from the study in Colombia, the focus group research in Egypt, and DHS data analysis, we plan to do further OC compliance studies as resources permit. In Colombia, we hope to be able to support follow-up focus groups with OC providers to get a better sense of whether they still have problems in delivering OCs despite frequent home visits and to explore other OC delivery and use problems indicated by the 1986-87 survey. We would also like to find out if changes in the rural health promoter training curriculum following our study have brought about meaningful changes in knowledge and practice of OC use.

2. Oral Contraceptive Compliance Follow-up in Egypt:

In about 18 months, we would like to examine what changes have been made in the training curriculum, counseling materials, and media messages on oral contraceptives based on the expert recommendations that resulted from the qualitative study of OC use conducted there in 1988-89.

3. Oral Contraceptive Compliance Strategy

Recognition of problems in correct oral contraceptive use is increasing, in large part because of FHI's work, as is interest in understanding how to improve correct use. FHI plans to develop a series of diagnostic and intervention/impact studies of OC compliance and continuation. Highest priority will be given to whether changes in the delivery of pills and family planning services can improve OC compliance; how modifications of training improve knowledge of correct use among providers and whether modifications in education and counseling materials improve actual use; and how to measure compliance more accurately. For example, a privately funded project will assess the value of a computerized recording device put into an OC packet in studying OC compliance.

Several projects on OC compliance already being explored include: 1) development of educational modules to be used in counseling OC users in family planning clinics, measuring changes in knowledge of users and providers as well as detecting changes in actual pill-taking behavior

due to use of those modules; 2) a case-control study of the previous pill-taking practices of pregnant women attending a prenatal clinic compared to matched non-pregnant OC users from their neighborhoods in order to see which OC errors tend to be associated with unplanned pregnancy. Countries expressing interest include Niger, Mali and Bangladesh.

4. FDA Meeting on OC Package Labeling: Instructions on OC Use.

As a result of the Expert Meeting on OC Use in July 1990, FHI was asked to organize a meeting of the the FDA's Medical Advisory Committee on Fertility and Maternal Health Drugs to make recommendations for improving and standardizing OC use instructions provided by manufacturers in pill packets. That meeting has been postponed until February 1991 but FHI has already prepared a set of background materials for the meeting, including a catalog of OC instructions from 56 brands of pills (representing nine U.S. manufacturers) and 26 other sources (researchers, clinics, medical texts, and family planning organizations), analyzed the readability of those instructions, prepared a catalog of advantages and disadvantages of the predominant current instructions, drafted an alternative set of instructions, and assembled an exhaustive reference list on issues related to correct and continued OC use.

5. Thailand: OC Compliance among Drugstore Clients

An intercept study of OC use knowledge and behavior among 100 purchasers of OCs at drugstores in one province of Thailand is scheduled to begin shortly. Acceptability of OCs is high in Thailand, but so are discontinuation and failure rates, raising concern about how well women understand how to take the pill. This study will also include interviews with 20 drugstore workers to determine if they have the correct knowledge of OC use to pass on to their customers.

6. Informed Choice and Quality of Care

As part of the work supported by the informed choice add on, we plan to disseminate the materials on informed choice. We anticipate that this will help institutionalize the concept of informed choice in the family planning service delivery.

We also plan to implement an intervention study aimed at improving perceptions and use of oral contraceptives (OCs) in Sri Lanka. The purpose of this study will be to test the impact of an information, education, and communication (IEC) intervention on women's perceptions, knowledge, and use of OCs in Sri Lanka.

We plan to implement a study designed to evaluate empirically the appropriateness and applicability of a conceptual framework for assessing the quality of services in clinic-based family planning programs and investigate the degree to which the utilization of the

family planning services by the clients are affected by the quality of services provided. The ultimate purpose of the proposed study is to identify those quality-of-services factors that are critical for improving the utilization of the family planning services. These factors may be related to the policy setups, service delivery or the clients' perspectives, at the national or local level.

Finally, a comparative study that we plan to implement in 2-3 countries is to investigate the clients' perceptions on quality of family planning services provided and examine the degree to which the utilizations of the services by the clients are affected by the quality of services provided.

C. Family Planning Service Delivery

The goals of the Program Evaluation Division's work in reproductive health have been 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 worldwide become better 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.

With various sources of funding, FHI has developed projects in Senegal (AID/W and USAID/Dakar), Niger (USAID/Niamey) and Zaire (OR

Grant/USAID/Kinshasa) to study the reasons for discontinuation of contraceptive methods. Similar projects are being carried out by FHI in The Gambia with funding from the International Development Research Center (IDRC) and in Togo. These projects seek to understand the various factors associated with contraceptive acceptance and continuation among family planning clients. Of particular interest are elements of a service delivery program which can be modified to increase acceptability and continued use by clients: fees; screening practices, including laboratory tests for new acceptors; education and counseling programs; method availability; clinic hours and accessibility; and knowledge and attitudes of clinic staff.

The Program Evaluation Division is pursuing the following projects in the evaluation of family planning service delivery programs:

1) 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 sometimes substantial and follow-up studies are urgently needed to learn the extent and causes of poor compliance and discontinuation.

The regional office of the Zairean Family Planning Association in Kinshasa, the capital of Zaire, carried out a study in collaboration with FHI to examine the characteristics of new clients in five of the

largest clinics delivering family planning services in Kinshasa. All women coming to the clinic for the first time were 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 were followed up at regular intervals during six months. Those who do not return for a scheduled follow-up visit were visited at home by a trained interviewer.

Data collection for the Zaire study began in April 1987 and was completed in September 1988. Data were gathered from more than 1,000 new acceptors of the pill, IUD or injectables. Unfortunately some questionnaires were destroyed before data entry and cleaning were completed so that the exact number of questionnaires completed is not known. A data tape was brought back to FHI for cleaning and linking admission, follow-up and discontinuation visits. Admission questionnaires for 667 were linked with 1134 follow-up questionnaires and 101 home visit questionnaires.

Because of incomplete data, no attempt was made to determine continuation rates. Rather, the data analysis focused on client characteristics and reasons cited for discontinuation. The median age of new acceptors was 29 years; 95% had attended some level of school. Most clients were married, with 63% in a monogamous relationship and 10% in a polygamous relationship. The median age at first pregnancy was 17 years. One third of all clients had a child under one year of age at the time of entering the study and 53% were breastfeeding.

Regarding reasons for using family planning, 71% wanted to space their births while 24% wanted to limit births (and 5% had other reasons). At the time of admission, the clients stated the following preferences for methods: injectable (44%), pill (27%), IUD (26%), and barrier methods (3%). The distribution of methods actually provided differed somewhat, as follows: injectable (38%), pill (21%), IUD (21%), barrier methods (17%) and information only (3%).

Of the 101 women visited at home because they had not returned to the clinic, 13 were pregnant. Of the 88 remaining women, 39 indicated that they were still using the same method received during their last clinic visit and 19 had discontinued using their method; no information was available for the 30 other women. Among those who discontinued, the most frequently cited reason was perceived side effects, followed by absence from partner, family problems, having forgotten, and husband's refusal.

The final report recommends (1) improving dissemination of information to clients about where family planning services can be obtained, (2) expanding voluntary surgical contraceptive services, (3) giving clients more specific instructions about the correct use of methods, (4) giving clients more complete information about side effects and their management, (5) expanding the time of the month during which women can receive a method other than barrier methods, and (6) exploring the possibility of changing the criteria for the eligibility of injectables.

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

Service statistics from the Projet Santé Familiale (PSF) program in Senegal indicate that many family planning 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. 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, and PSF are interested in improving both the number of new acceptors and their satisfaction with and continued use of their chosen method. With technical assistance from FHI, a study has been designed: 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 some women come for family planning services but do not start 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 was delayed at the request of the PSF and USAID/Dakar during 1989. In mid-1990, a Senegalese consultant study coordinator was recruited and clinic sites finalized. Training of interviewers and data collection is expected to begin in late 1990.

3) 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 influence and partial misunderstanding of French medical practices, excessive laboratory tests are required in some Francophone African countries before prescription of systemic methods. The required laboratory tests are expensive, difficult to obtain, and a scientifically unjustified use of scarce resources in desperately poor countries. The tests are virtually unavailable outside of the capitals and large urban areas and they divert medical resources from much more important health care problems. These 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 FHI design and implement an assessment of the 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 was 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 changed its obligatory laboratory test requirements in 1987. Information was gathered on the process of bringing about the decision to abandon systematic lab exams in Burkina Faso. In Senegal, a prospective study of 500 women has been completed. It compares 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). The questions addressed include:

(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?

Lab exams have been recorded for 410 women. Twelve of the 410 women had lab exam results that were outside of the normal range, most often Class III Pap smears (4). Five women had clinical contraindications. Only nine women were able to have confirmatory tests. Of those, only one contraindication was confirmed. These data were presented at a symposium for Senegalese Ministry of Health officials and physicians and regional participants in February 1990. Recommendations from the symposium emphasized that systematic lab exams were not necessary before prescription of oral contraceptives. They also supported the integration of family planning into primary health care, development of a guide for prescribing contraceptives and the necessity of training health personnel in family planning service delivery. The complete report, including a review of the literature, summaries of colloquium presentations and recommendations, as well as the results from the

Senegalese prospective study, will be made available to all francophone countries.

4) Togo: Evaluation of Clinic-Based Family Planning Services

At the request of REDSO/WA and USAID/Lomé, the Program Evaluation Division is supporting a study to assess factors influencing acceptance of family planning methods among clinic clients in Lomé. There is thought to be an "anti-OC prejudice" among many providers, and a consequent high reliance on IUDs. Condoms are also provided, but with virtually no record-keeping.

Field work was initiated in FY'90. Semi-structured interviews with service providers and client surveys have been conducted in four clinics in Lomé and one clinic outside of Lomé. A review of client records was also conducted.

FHI is collaborating with the Ministry of Health, the Statistics Division and the University of Benin in this study. Results will be used by the Ministry of Health and private agencies to improve the quality of family planning services and, we hope, to increase acceptance rates among clinic clients.

Future Plans: FP Service Delivery

1. India: Add-On

Condom use is gradually increasing in India. During the years 1981-86, condoms constituted approximately 10% of the total annual contraceptive prevalence. Social marketing plays an important role in the distribution of condoms. About 40% the total condom couple-years-of-protection (CYPs) is provided by the social marketing sector. Another 10% is provided by the commercial sector. The remaining CYPs, 50%, is accrued from the free distribution sector.

USAID provides support for the social marketing of condoms in selected states in India. It has committed $4.1 million (of which 70% has already been provided) for expansion and distribution of condoms through the Population Services International of India (PSI/I). PSI's primary role is to focus on the states in Northern India where the distribution had previously been done by Union Carbide. PSI is also introducing a new brand of condom (Masti) in the state of Uttar Pradesh, which has a total population of 130 million.

At the request of USAID/India, FHI developed several subprojects to assess the effectiveness of the condom social marketing program in India, with special reference to the PSI program. FHI will work in collaboration with PSI in one of these efforts. In order to give the assessment/evaluation credibility and to avoid a potential conflict of interest between the program and the evaluation, it is important to

carry out the field activities independent of PSI/I although PSI/I can be involved in the planning stage.

MODE Services, a leading marketing research agency, was chosen to conduct an evaluation of consumer preference for condoms, while the Operations Research Group (ORG) was selected to do a study on monitoring of market share of various brands of condoms with special reference to Uttar Pradesh.

Some of the issues of interest are: What is the share of PSI's program to the total condom social marketing program? How much is the cost per CYP? What is the impact of the introduction of a new product? Who are the consumers of the social marketing program? Is the social marketing program largely a substitute for the commercial program? What are the patterns of use? What are the problems encountered by the retailers? How can the program be made more efficient and effective? Finally, what are the lessons learned? These issues relate to the consumers (users), retailers, and the program as a whole.

FHI has submitted two study proposals to the USAID Mission in India for implementation. As part of this add-on project, FHI has also proposed to organize a workshop on social marketing of contraceptives with special reference to India and to condom marketing. The main purpose is to provide a forum and to review substantive findings, discuss lessons learned from projects, critically review evaluation methodologies, and explore alternative approaches for marketing. The participants would represent four major categories: program managers, manufacturers,

distributors/industrialists, and researchers. FHI is awaiting approval of these projects from USAID/New Delhi. A trip is planned for December, 1990 to work with the Mision to get thse projects approved and started.

2) Brazil: Evaluation of BEMFAM's Reproductive Health Approach to Family Planning

BEMFAM, the IPPF affiliate in Brazil, initiated a reproductive health approach to family planning in the state of Pernambuco in 1984. The approach was integrated into a community-based program where health workers assess the risk level of new clients. Those considered at increased risk are referred to physicians who can provide IUDs and minilaparotomy and who have been trained in programs sponsored by JHPIEGO. Since the initial experience, the community-based programs in the states of Rio de Janeiro and in Ceara have also adopted this approach. Until now, these reproductive health activities have not been closely evaluated.

This project will be a collaborative effort between JHPIEGO and FHI to take place in the state of Ceara. Several components will make up the evaluation strategy designed to study:

1) how well the health workers' assessments of risk compares to the physicians' risk assessments;

2) profile of new clients at two points in time to determine how many comply with the referral recommendation and what their contraceptive practices are six months after the initial visit to the health post;

3) knowledge levels, attitudes and practices concerning the concepts of reproductive health and family planning among health agents six months post training;

4) the extent to which the physicians trained in IUD management and minilaparotomy currently use their new skills;

5) the costs and benefits of this reproductive health program.

At the conclusion of the project, a seminar to disseminate results will be held in Fortaleza for local health professionals, decision makers, and political leaders. Field activities will begin in November of 1990 and will conclude about 18 months later.

3) Mali: Adolescent Sexuality Survey

There is a growing concern in Africa about adolescent sexuality and the increasing epidemic of adolescent pregnancy and risk of STDs. Adolescent pregnancy not only poses a health problem, but has a long term social and economic impact. Pregnant adolescents are obliged to drop out of school, compromising their ability to complete their education and successfully compete in the work force. An alternative that is often taken is to have an illegal induced abortion. In Mali, induced abortions are most often used to delay a first pregnancy. A study coordinated by FHI in 1982, examining complications following abortions found that, most often, the women in the study were young, unmarried students. A similar study coordinated by the National Women's Association of Mali found that most young women who admitted having an induced abortion were students. Besides adolescent pregnancy, there is an increasing concern among adolescents about STDs, including AIDS.

Little is known about the level of sexual activity of Malian adolescents and what means, if any, they use to protect themselves from

pregnancy and STDs. Pending availability of funding, the Malian Family Planning Association (AMPPF) proposes to carry out a study in cooperation with FHI to ascertain adolescents' knowledge, attitudes and practices concerning reproductive health and family planning. Five hundred boys and 500 girls between the ages of 14-18 years who attend school in Bamako, would fill out a questionnaire which has been drafted. Four focus groups would be held with parents to ascertain their attitudes about adolescent sexuality, adolescent pregnancy and provision of family planning services to adolescents.

The Ministry of Education is aware of the growing problem of adolescent pregnancy and STDs and wishes to develop a family life program. Information from this study will help the MOE to develop such a program.

4) Cameroon: Physicians' KAP

Contraceptive prevalence in Cameroon is less than 5%, and until recently, a pronatalist policy was in effect. It is hypothesized that the thousand or so physicians in this West African country of 11 million will have a strong influence on the directions family planning will take in the coming years. FHI and the Department of Obstetrics and Gynecology of the Centré Universitaire des Sciences de Santé (C.U.S.S.) in Yaoundé, Cameroon propose a survey of physician's knowledge, attitudes and practices (KAP) of family planning in Cameroon. Pending availability of funds, this first-ever study of the attitudes and practices of physicians concerning the use of

contraceptive in Cameroon would determine: how many physicians recommend and provide contraceptives, which methods they recommend or condemn and why, physicians' knowledge of family planning and the influence of socio-cultural factors on the attitudes and practices of physician's in Cameroon vis à vis contraception. This survey's findings would help C.U.S.S. in making informed recommendations to the Government of Cameroon for a new population policy. This study has the full support of Professor Robert Leke, chief of Ob/Gyn at C.U.S.S. and of Dr. Pierre Sendé, Secretary General of the Medical Society.

D. Cost Studies

With declines or stagnation in donor resources for family planning combined with anticipated increases in demand for contraception, attention is being focused on what it costs to provide family planning and how those costs can be covered. Several projects based in PE address these concerns. One project examines the cost of introducing a new method, NORPLANT^{R}, into an ongoing family planning program and examines impacts on both costs and anticipated impact on contraceptive use. Two projects focus on questions of cost recovery; what happens if programs try to keep their prices in step with the rate of inflation or attempt to shift a higher proportion of costs to the client? Do clients continue to buy contraceptives or does the higher price discourage them from purchasing? A final project takes an in-depth look at condom use and relates use patterns to current and planned price changes.

1) Thailand: NORPLANT^R Delivery by Nurse-Midwives

Although NORPLANT^R contraceptive implants are approved for general use in Thailand, only physicians are trained in their use and until now, the method has been primarily available to hill tribe groups and in low prevalence areas in the south. Now, however, the government of Thailand plans to make the method available more widely. The Thailand Ministry of Health is planning to train nurses to provide NORPLANT^R; one aspect of this project is to determine if they can provide NORPLANT^R safely; i.e., is the rate of complications at an acceptably low level? Other questions concern the impact of NORPLANT^R introduction in raising the number of couple-years-of-protection (CYPs) and in changing the costs of providing family planning. This project will provide information on cost of NORPLANT^R including service delivery and training costs and on the impact of NORPLANT^R in raising contraceptive prevalence and continuation rates.

In this project, 12 nurses at district hospitals will be trained in NORPLANT^R insertion and removal procedures. They will then insert NORPLANT^R in women who opt to adopt the method. The study will look a number of different variables related to making NORPLANT^R available through nurses at district hospitals. Data will be gathered on insertion-related complications and continuation rates, and compared with historical rates of physicians. Contraceptive mix at each test hospital will be compared with a baseline period at the same hospital as well as control hospitals where NORPLANT^R is not being offered. Data will also be gathered on the amount of time spent by hospital

staff in providing NORPLANT^R to see whether this new service places a significant time burden on the staff. Cost information will be gathered in order to calculate the cost of providing this new service, so that the Ministry of Public Health can evaluate the cost effectiveness of NORPLANT^R in the national program. This study will begin in October, 1990, and is being conducted by the Thailand Fertility Research Association (TFRA).

2) Ecuador: Price Elasticity of Demand for Family Planning

Conventional wisdom holds that when prices are increased in clinics that serve middle-class and poor clients, the demand for clinic services will decline. A study will be conducted in FY'91 in which the various impacts of a price increase at several PVO clinics will be analyzed. Specifically, this study will examine changes in total clinic revenues, service-specific revenues and client characteristics. These variables will be measured before the price increase, and one month and three months after the price increase. Study results will be used to help develop a pricing strategy for family planning services provided in PVO clinics. FHI is contributing overhead costs to this study which is being supported by POPTECH.

3) Bangladesh: Price Sensitivity for Condoms/Pills

Because of a decline in USAID population funding for Bangladesh, the Social Marketing Company is considering increasing the prices that it charges for contraceptives. In order to determine what increases to

institute on a national basis, an experiment will be carried out to examine the effects of different price increases. The impact of price changes on volume of contraceptives sold, sales revenue, and on characteristics of clients will be measured; an important question is what happens to sales to those with the lowest levels of income. In addition, the impact of price increases on switching to other methods and other sources will be assessed. The proposed start date for this project is November 1, 1990 and a sub-agreement has been prepared. The project will be supported with funds from the Buffet Foundation.

4) Bangladesh: Use & Misuse of Condoms

This study will describe the uses and misuses of condoms in Bangladesh, including their use for non-contraceptive purposes and their incorrect use for contraceptive purposes. The research will assess how patterns of use and misuse of condoms differ among one group of users who obtain condoms free (or nearly free) from government or NGO distributors and three groups of users who pay for condoms distributed through the Social Marketing Company (SMC). The study will also explore how two levels of increases in the prices of condoms, implemented in conjunction with the companion study, "Assessing the Impact of Price Changes for Condoms and Pills", may affect patterns of misuse and use.

The one-year study will start in November, 1990 and will have qualitative and quantitative components. The qualitative component will involve a local investigator living in a study village for two months, doing in-depth interviews, and conducting group discussions with condom

purchasers and their spouses. The quantitative component will involve interviews with people purchasing condoms or getting them free in the control and the two experimental areas before and after the price changes are implemented in the experimental areas. The study is expected to help the Bangladesh government, the Social Marketing Company, and USAID/Dhaka assess the extent of misuse among those getting condoms free vs. those who purchase than and to identify people's responses to price increases which are part of the cost recovery intiative. It is a companion study to the price sensitivity study just described.

Future Plans: Cost Studies

FHI is hoping to conduct additional research on the costs of NORPLANT[R] and will emphasize cost comparisons of NORPLANT[R] and the IUD. In addition, attention will be paid to assessing the impact of NORPLANT[R] introduction on increasing protection against pregnancy.

Greater attention also needs to be paid to reducing the costs of family planning service provision while at the same time ensuring adequate levels of safety and quality of care. FHI plans to conduct research to investigate the implications for costs, continuation rates and safety of various cost-reducing measures (more flexible follow-up schedules for acceptors, decreases in medical examinations and lab tests, etc.).

Finally both PVOs and government programs will undoubtedly be paying more attention to cost recovery. FHI's work in Bangladesh and Ecuador

can be replicated in other countries to assist planners in making decisions about price changes. We anticipate receiving funding from AID/Ecuador to continue research on pricing and we will investigate opportunities elsewhere.

E. National Multi-Purpose Surveys

Some surveys cover so many subject areas that they do not neatly fit under one of Program Evaluation's topic areas. We have sponsored surveys of young adults that assessed fertility, family planning use, and rates of STDs. Recently, our large surveys have been in Honduras.

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 fertility, contraception, breastfeeding and MCH care. They provide baseline data to show where and what type of services are needed. Repeated 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.

1) Honduras: Follow-up Survey of Pregnant Women and Women With Infants

The Honduran National Epidemiology and Family Health Survey was carried out in 1987. Of the 10,159 women of reproductive age who were interviewed, 2,832 were identified as either pregnant and/or as having a child less than one year of age. These women were contacted between September 1988 and February 1989 as part of the Follow-up Survey to determine survival status of the infant and/or pregnancy outcome. The data have been useful in confirming the results of the 1987 Survey which show a marked decline in infant mortality (IMR). Because only 74% of the eligible women were contacted, the data from the Follow-up Survey have required weighting. The final estimate based on the children under one year of age is 48/1,000, very consistent with the 1985 estimate of 47. The estimate calculated from the cohort of newborns is much lower, 26/1,000. We suspect that either underreporting has occurred in this group or the sample was too small.

A large proportion (24%) of the women in the Follow-up Survey had had an additional pregnancy since the 1987 baseline interview. Since the average duration between surveys was 14 months, this indicates a high number of short birth intervals which are known to be detrimental for the health of both mother and infant.*

The Follow-up Survey also collected information on prenatal care activities, delivery care and complications, and childcare practices. Final reports in English and Spanish were distributed in September, 1990 and several papers are under preparation.

Future Plans: National Multi-Purpose Surveys

Another national MCH/FP Survey is scheduled for 1991 in Honduras. Like the others, it will provide up-to-date information on fertility, child morbidity and mortality, and contraception for the Ministry of Health, The Honduran Association for Family Planning and A.I.D./Honduras. FHI will continue to provide technical assistance through an add-on to FHI.

1) Honduran 1991 National Family Health Survey

The Honduran 1991 National Family Health Survey will be similar to the 1987 National Epidemiology and Family Health Survey and provide estimates for a wide range of topics including contraceptive use, breastfeeding, MCH care, nutritional status of children, fertility and infant mortality. These estimates, when compared to those of 1987, will assist health planners to evaluate their interventions and service delivery capabilities. Like past surveys, the Honduran Ministry of Public Health and the Honduran Family Planning Association (ASHONPLAFA) will organize and administrate the effort. Field work is expected to begin in June 1991.

*In 1987, women were asked about their intention for an additional pregnancy. Of those who stated they wanted no more children, 20% had had an additional pregnancy compared to 31% among those who reported a desire for another child.

2) Sri Lanka: Determinants of Method Choice, DHS Secondary Analysis

The purpose of this study is to analyze the socio-cultural and demographic determinants of contraceptive method choice in Sri Lanka. The study is an update of a previous study on this topic. By extending the analysis to a recent time period (1987), this paper examines changes in the pattern of contraceptive method choice in Sri Lanka. More specifically, we focus on three interrelated questions: (1) Do the demographic and socioeconomic factors continue to exert the same type of influence over the use of any method vs. the use of no method at all? (2) Does the influence of socioeconomic factors continue to be attenuated, and has the effect of family-building stage gained increasingly more in prominence? and, (3) Has the choice of birth spacing methods become more pronounced and sterilization less used in recent years and, if so, which strata of population have experienced these changes? The first two questions deal with the process of the diffusion of contraceptive innovation, while the third reflects on the policy and programmatic issues as the government of Sri Lanka has in recent years attempted to emphasize the use of modern birth spacing methods through its family planning programs. The Program Evaluation Division hopes to carry out similar analyses for 6-8 Demographic and Health Survey (DHS) countries where the DHS surveys were conducted. This will permit an understanding of the recent variations that may exist among countries with respect to continuation and use-effectiveness of contraceptive methods practiced.

F. Consequences of Fertility Decline for Family Welfare

The A.I.D. Bureau for Program and Policy Coordination (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 were supported under this add-on.

The first was conducted by the Institute for Population Studies at Chulalongkorn University (field costs are funded by UNFPA) with the technical assistance of Dr. John Knodel (funded by FHI). Using qualitative and quantitative approaches, this study examined whether Thai families who have limited themselves to two children feel they have benefited economically compared to families with four or more children. Interviews were conducted in two provinces in rural Thailand gathering quantitative data on three dimensions: wealth accumulation, children's education and women's employment. The qualitative component, using focus groups, was subsequently done with a sample of respondents who had participated in the survey.

The report on children's education is complete and was published in September 1989 by the University of Michigan. The report on the quality of housing component was finished in the fall of 1989. A scientific meeting and a briefing meeting were held in Washington, DC on November 16-17, 1989 to present the study findings and their implications. A similar presentation was given to FHI's Technical Advisory Committee in July, 1990.

A dissemination workshop was held in Thailand in February 1990 to discuss the findings with researchers, policymakers, and donor representatives. Some results were published in the Asia-Pacific Population Forum (March, 1990) and another paper was published in the Population and Development Review. The final component, on women's work and family size, has been completed and has been submitted for publication. In short, the results of this study have been very widely disseminated in Thailand and internationally.

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. The final report for this project is overdue, despite our efforts to get TDRI to complete it.

G. AIDS Prevention and Family Planning

The Program Evaluation Division is participating in research and evaluation activities in support of FHI programs in AIDS prevention. Work under FHI's Cooperative Agreement with A.I.D.'s Office of Population includes: the evaluation of an effort in Honduras to educate those at high risk for AIDS and STDs in safer sex practices and to distribute condoms and spermicides; papers on HIV and breastfeeding;

studies to determine the acceptability of a variety of male and female condoms; technical assistance to AIDSTECH projects; and consideration of the effects of AIDS on FP programs as well as the potential contribution of FP programs to preventing the spread of HIV.

Specific AIDS prevention related activities are:

1) 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 HIV to their partners and to rural communities when they return home. Educational strategies are urgently needed to reach this high risk behavior group.

A project carried out at the request of the STD Program of the Honduran Ministry of Health had these objectives: 1) the design and testing of educational materials for use at health centers for the commercial sex workers (CSWs); 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 CSWs; 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 this high risk population.

The study was based at a health center in Tegucigalpa which routinely sees CSWs. The intervention consisted of providing educational materials and promoting condoms to the client population. Pre- and post-tests based on interviews of the client population were used to determine how attitudes and knowledge changed following the intervention. The pre- and post-test interviews also took place at a health clinic in San Pedro Sula, but no intervention was carried out there; it served as a control site. In June and July 1988, Ministry and FHI staff participated in focus groups with 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 took place in late September 1988 and the intervention period extended until January 1989.

The second KAP survey took place in March 1989. At the time of each KAP, the interview asked about the previous week's activities: number of clients, number of condoms used and number of days worked. Based on the 182 women who completed both the first and the second KAP in Tegucigalpa, we have the following information:

Average	KAP I September 1988	KAP II April 1989
Days worked	4.9	4.6
Number of clients	15.6	17.4
Number of condoms used	9.8	10.8
Proportion of sex acts protected with condoms	63%	74%

At the same time, a seroprevalence survey was carried out among both groups of women. Six percent of the women interviewed for the second KAP in Tegucigalpa were HIV+ while 20% of the women in San Pedro Sula were infected with HIV. An in-depth study of the 134 women who participated in the intervention and completed both KAP surveys is underway to determine what are the factors associated with an increase in condom use. The only significant factor was the amount charged per client contact where an increase in charge reflected an increase in condom use. The paper "Condom Use Among High Risk Women in Honduras: Evaluation of an AIDS Prevention Program" will be presented at the 1990 annual meeting of the American Public Health Association.

2) HIV Transmission Through Breastfeeding

FHI staff prepared a paper on breastfeeding and HIV transmission that was first presented as a poster at the June 1988 IV International Conference on AIDS in Stockholm. WHO recommends that mothers in developing countries breastfeed regardless of HIV status, while CDC recommends that seropositive women not breastfeed. Pursuing this controversy, the paper estimated the number of infant deaths (in areas like Africa) due to the transmission of the AIDS virus through breastfeeding (plus all other causes of death to infants) and compared this to the number of deaths that would result if bottlefeeding were substituted for breastfeeding by HIV+ mother. It was concluded that more infant deaths were likely to occur due to not breastfeeding than to continuing to breastfeed despite positive serostatus.

The analysis has since been presented at NICHD, Columbia University, New York City Department of Health, Kenyatta Hospital in Nairobi, and is to be the focus of the next network cover story. It was published in Tropical Doctor in January 1990. Requests for this paper are received by FHI on a regular basis, reflecting the degree of concern of public health authorities and clinicians about breastfeeding and AIDS.

This analysis drew attention to the difficulties in preventing and preparing for the epidemic. Some reaction to the paper underscored the need for hospitals and health departments to understand the local epidemic so that they can advise mothers about infant feeding more appropriately. Accordingly, researchers at FHI have prepared another model which can be used by decision-makers in order to incorporate actual natality, mortality and seroprevalence figures to estimate the impact of advice to breastfeed or not on a local level. The new model used 1987 data from New York City. This new analysis is being done in collaboration with colleagues in breastfeeding research from the NIEHS in the Research Triangle Park.

3) Thailand: AIDS and Family Planning Conference

Thailand is one country which has realized that MCH/FP providers throughout the country need information about AIDS, how to protect themselves from infection, how to assess the risk of clients for infection (and hence, the need to promote safe sex among such clients), how to promote and instruct clients in condom use more effectively. Even though Thailand's private condom promotion program is world

famous, in fact, condoms are little used in Thailand. With partial support from the Program Evaluation Division, FHI supported a national training course on AIDS and FP in which two health officers from each of Thailand's 70 provinces were brought together to explore how MCH/FP providers can better deal with the HIV epidemic.

Future Plans: AIDS Prevention and Family Planning

The HIV/STD epidemic is directly and indirectly affecting family planning programs. Reducing the risk of infection among both FP clients and staff requires changes in clinic procedures including what methods to recommend to whom and the need for staff to follow universal precautions.

The fact that a method of family planning, namely, condoms, has a protective effect against infection is putting new demands on family planning programs for distributing, promoting, and instructing people on correct use of condoms. Condom promotion is new for many FP programs which until recently have been skeptical that clients will be able to use condoms consistently and correctly.

A paper on AIDS and FP was prepared for a seminar on AIDS and population at the World Bank in August, 1990. An earlier version is being published as part of the AIDS Prevention Handbook published by AIDSTECH. FHI also assisted WHO on a monograph, AIDS Prevention: Guidelines for MCH/FP Programme Managers, AIDS and Family Planning which became available in September, 1990.

A panel discussion on AIDS and family planning is being organized for the Cooperating Agency meeting in November, 1990.

Two projects have been developed on AIDS and family planning. The first is a feasibility study with BEMFAM in Brazil to see if clients and providers will accept HIV risk screening. The purpose of the screening is to identify which clients need to be using condoms or reducing their risk behaviors in other ways. This project is awaiting funds.

The second looks at the impact of the HIV epidemic on condom distribution by family planning programs in N. Thailand. It is addressed to questions such as whether there are condom shortages and increased time and resources being required by an increasing demand for condoms due to the HIV epidemic. This project is also awaiting funds.

1) Brazil: Client HIV Risk Assessment in Family Planning Clinics

BEMFAM, the IPPF affiliate in Brazil, has been active in AIDS prevention activities for several years. Their efforts have been widely recognized and well received in a country that ranks second in the number of AIDS cases officially reported.

BEMFAM does not test for HIV infection but they do counsel and treat patients with sexually transmitted diseases (STDs). Routine HIV testing would be prohibitively expensive but if a simple strategy could be found that will identify men and women at risk of HIV, these

individuals could receive, as necessary, counseling and methods that protect their users from STDs as well as unwanted pregnancies.

The proposed project intends to implement and test two methodologies of client risk assessment of HIV infection in order to determine:

1) which methodology is preferred by health care providers and why;

2) how many clients are assessed as being at risk by each methodology;

3) what methods or combinations of methods are selected by the client.

The project will be divided into two phases, one in which a checklist of risk factors will be produced as well as KAP information for the production of educational materials. The second phase includes the testing of the two methodologies to assess risk of HIV infection.

The first methodology involves self-assessment of risk where clients are counseled in small groups, given information about HIV infection and AIDS, and encouraged to ask questions. The clients will be told that the health care provider will ask them if they think they are at risk but that h/she will not inquire as to why the client assesses him/herself at risk. The second methodology entails the same basic counseling in small groups but the client will also complete a short risk index to be shared with the health care provider in a one-on-one setting and to guide his/her assessment of client risk.

The project will be implemented in four different clinics which represent distinct geographical regions and also cities with relatively large numbers of AIDS cases. Ideally each clinic will assign their patients randomly to one or the other methodology. FHI is seeking a source of funds for this project.

2) Thailand: Impact of HIV on Thailand's Family Planning Program.

The purpose of this project is to determine the impact of the HIV epidemic on the national family planning program. Therefore, the project would be conducted in areas in which HIV was known to be a problem. Specifically, the project would obtain data on the characteristics of condom acceptors with emphasis on how they differed from traditional acceptors of condoms and on how the rural health units were coping with the increased demand for condoms. Were the staff also providing counseling to these new acceptors and what problems were the encountering? What logistical problems had arisen as a result of the increased demand for condoms and how were they being solved? Because of funding limitations, this project will not be funded under our cooperative agreement; FHI is currently seeking funding for this project.

H. Natural Family Planning

The goal of current NFP work is to complete scientific research that contributes toward making NFP methods more effective and available for those couples who choose these methods.

FHI's programmatic research creates awareness about the functioning, acceptability and potential impact of NFP programs. Recent emphasis has been put on completion of all NFP studies and 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 recorded 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.

Urine samples for the determination of ovarian hormone levels have been submitted to the laboratory for assay in a manner that successively approximates the estimated date of ovulation. The last share of successive sampling has been completed and the samples sent to the laboratory. The results will be presented at an International NFP Conference at Georgetown University in December, 1990. The main publication has been outlined and will be submitted for publication after the Georgetown Conference.

Future Plans: Natural Family Planning

FHI will participate in a Georgetown University sponsored NFP meeting in December, 1990 presenting papers on completed FHI-supported studies. We will also submit papers for publication on completed NFP studies, including for projects in Kenya, Peru and Egypt.

I. 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. Some countries will have to increase contraceptive use substantially, 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 both as a natural method of birth spacing and as 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. Philippines: Effect of an Education Program on Breastfeeding Practices and Duration of Postpartum Amenorrhea

FHI supported a prospective study with Silliman University in Dumaguete, Philippines, in which rural 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 similarity of frequencies and durations of breastfeeding in the groups was responsible for the similarity in amenorrhea. The breastfeeding education group babies had fewer illnesses, especially gastrointestinal, but growth was comparable between the two groups.

The final report of the major findings of this project has been published and a second paper on the health and growth of the infants has been submitted for publication. The latter analysis shows that breastfeeding education was associated with a reduced frequency of infant illness episodes.

This study was replicated in Manila in order to contrast urban breastfeeding women with the ones studied in Dumaguete. The study was conducted by the staff of the Philippine General Hospital (PGH). The study in Manila found that, contrary to the case in Dumaguete, women who were exposed to educational messages about good breastfeeding practices were able to significantly increase the duration of lactational amenorrhea - by about one month - as well as to make the correct positive changes in infant feeding practices. The findings of this study will be presented at the annual meeting of the National Obstetrics and Gynecologic Association of the Philippines in November 1990.

2. Evaluation of the Honduras Breastfeeding Promotion Program

This research area addresses the question of whether breastfeeding behaviors can be changed through different types of promotion programs. Between 1982 and 1988, the Project to Promote Breastfeeding (PROALMA - Proyecto de Apoyo a la Lactancia Materna) promoted breastfeeding in the major urban hospitals and clinics of the Honduran Social Security Institute and the Ministry of Public Health in Tegucigalpa and San

Pedro Sula. PROALMA activities were 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 PROALMA activities at the community level and among health care professionals, baseline and follow-up surveys were conducted in 1982 and 1985, and again in 1986 and 1988. Examination of breastfeeding trends at a national level were carried out by FHI using three nationally representative surveys: the 1981 ENPA (Encuesta Nacional de Prevalencia de Anticonceptivos), 1984 MCH/FP (Maternal-Child Health and Family Planning Survey), and 1987 EFHS (Epidemiology and Family Health Survey).

In this evaluation of the PROALMA breastfeeding promotion program, both descriptive analyses and multivariate techniques were used. At the national level, between 1981-1987, breastfeeding increased significantly. The greatest increase occurred between 1981 and 1984 and in urban areas. The use of probit analysis showed that the increase in ever/never breastfeeding between 1981 and 1984 was due to behavioral changes rather than changes in the characteristics of the population. The median duration of breastfeeding increased by 2.5 and 1.7 months between 1981-1984, respectively.

At the hospital level, there were also improvements in the knowledge and attitudes of the health care personnel. The largest increase occurred among nurses.

The paper "PROALMA: An Evaluation of a National Breastfeeding Promotion Program in Honduras" has been accepted by the Journal of Biosocial Sciences and will appear in the fall 1990 issue.

3. ESCAP Asia-Pacific Population Journal: Special Issue on Breastfeeding in Asia

FHI has assisted the Population Division of ESCAP (United Nations, Bangkok) with the publication of a collection of papers on breastfeeding in Asia as a special issue of the Asia-Pacific Population Journal. The objective of this joint effort was to disseminate recent research findings as background for policy and program development within the region. About 75 copies of the March, 1990 publication were sent to USAID Missions in selected countries in Asia for distribution to relevant public and private health and family planning agencies, researchers and libraries in each country.

4. Clinical Trials of Bellagio Guidelines and Research to Develop Guidelines for a Longer Lactational Amenorrhea Method

The Bellagio Consensus is the agreement among researchers in the area of lactational anovulation about the conditions under which lactational amenorrhea can be relied upon as an effective contraceptive. The consensus is that there is less than a 2% chance of pregnancy in the first six months postpartum in women who are fully breastfeeding and amenorrheic. These guidelines are based in part on findings from ten

intensive longitudinal studies. In the studies, women were followed up as often as weekly, with blood and/or urine samples taken in addition to information on breastfeeding patterns, menses, supplementation, etc. The Bellagio guidelines do not yet constitute a "family planning method" in the usual sense of the word. A "method" has clear and standardized instructions given by a family planning worker. Follow up is typically not weekly but at some logistically practical interval such as 1, 3, and 6 months. Since lactational infertility is a temporary condition, the guidelines must specify circumstances under which women should start another method.

We do not know whether women will understand when they are to start another method and whether they will actually start at the appropriate time. We also need to know whether the pregnancy rate **estimated** for the method (less than 2% under the conditions specified) will be obtained.

An equally important problem is to determine what guidelines would be useful for women who breastfeed much longer than six months and who have prolonged lactational infertility since at this point, the Bellagio guidelines only deal with the first six months post partum. Development of studies on these two topics is well underway by FHI in collaboration with investigators in a peri-urban area of Karachi, Pakistan and a site in Manila, Philippines.

5. Chile: Growth of BF Babies

Dra. Soledad Diaz and the Instituto Chileno de Medicina Reproductiva have submitted a proposal to analyze nutrition data from existing clinical records and infant feeding diaries to determine the "Influence of the Breastfeeding Pattern Upon Infant Growth and Health During the First Year of Life." FHI will fund this research because one of the most important factors that potentially limits the applicability of the Bellagio Consensus is the extent to which babies can be safely breastfed without supplements.

Future Plans: Breastfeeding

1. Evaluation of Programs to Promote Postpartum Contraception

In the event that funding becomes available, FHI would like to pursue a comprhensive evaluation of postpartum family planning introduction. Such an effort would be both interdivisional within FHI and collaborative with the Association for Voluntary Surgical Contraception (AVSC). While AVSC would give training for new providers, FHI's Field Development and Training Division would organize and coordinate the many logistics of technical training and method introduction. FHI's Clinical Trials Division would analyze data on effectiveness, short-term safety and continuation. The Program Evaluation Division would conduct programmatic research both before and after the training (and method introduction) toward multiple ends, e.g.: 1) in order to assess the knowledge and attitudes of both prospective users and

providers so that the training and counseling materials car be adjusted accordingly; 2) in order to determine whether new users have simply switched from other methods or whether prevalence will increase due to the introduction of the method; 3) to assess client method choice and subsequent satisfaction, including continuation.

FHI would also like to respond to particular needs for programmatic and demographic assessments that do not comprise such a comprehensive evaluation. Some specific topics of interest are (1) the assessment of women's method preferences, especially in the immediate postpartum period; (2) the evaluation of different postpartum family planning counseling strategies; (3) the evaluation of breastfeeding promotion efforts in standard family planning delivery systems; (4) comparative studies of postpartum family planning services delivered by nurses vs. midwives vs. TBAs vs. doctors; and (5) the evaluation of strategies to reach high risk women with postpartum family planning methods, in order to reduce maternal mortality.

J. Other Papers/Publications

The paper "A Community Study of Infant Mortality and Causes of Death in Rural Northeast Brazil" appeared in the July, 1990 issue of the Journal of Biosocial Sciences. Another paper, "Obstetric Care and Perinatal Mortality in Rural Northeast Brazil," has also been accepted by the Pan American Health Organization Bulletin.

In the coming months, we plan to conduct additional 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 programmatically useful 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.

V. FIELD DEVELOPMENT AND TRAINING

The Field Development and Training Division (FDT) has as its primary objective the development of strong reproductive health organizations and skilled investigators in priority developing countries through training and institutional development programs, the transfer of contraceptive technology, 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 these activities, FDT provides field support to the other research divisions. This includes the identification of new investigators and study sites, development of new projects, coordination of field negotiations, monitoring of studies as needed, and liaison with USAID missions and host country governments.

Activities during this reporting period cover the following areas: Institutional development; training and support for conferences, seminars, and expert meetings; contraceptive introduction; and information dissemination. During this reporting period, the new Associate Director for Contraceptive Introduction came on board and a large international conference on postpartum contraception was organized. Planning was initiated, in consultation with A.I.D. and other cooperating agencies, for FHI's role in the introduction of NORPLANT[R] in several countries. The staffing for information dissemination was completed with the addition of one writer, a new publications manager, and a training officer. The additional staffing enables FDT to provide increased support for media

dissemination of FHI work and to conduct related workshops, such as to train health journalists and to train investigators in scientific writing. Two journalist workshops were implemented during this past year.

A. Institutional Development

1. Family Health Research Centers (FHRCs)

Support to five maturing Family Health Research Centers (FHRCs) and several newer organizations remains a 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 countries.

FHI sponsors periodic meetings (every 18-30 months) of the FHRC Directors with relevant FHI staff to plan future development strategies and to exchange views on a wide range of topics of mutual interest, including research findings and directions, financial management systems, training, and protection of human subjects. These meetings have proved to be a valuable means to share information, and to plan for future collaboration. Although no formal FHRC Directors Meeting was held in FY 1990, several representatives of the FHRCs visited FHI headquarters for group and individual discussions immediately following their participation

in the Mexico Conference on Postpartum Contraception. The next FHRC Directors Meeting is scheduled tentatively for October 1991.

The following sections describe each FHRC program and the development activities underway with FHI support through core support subagreements, and summarize 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 trial 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 donors and research sponsors.

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 BFRP continued to monitor follow-up of women involved in pre-introductory NORPLANT[R] studies at three centers in Dhaka. These studies started in February 1985, and those women still continuing with the method began returning this year for removal of the implants. Some of them have opted to have a new set of implants inserted under the NORPLANT[R] Pre-Introductory Pilot Program (NPIPP).

The expanded NORPLANT[R] contraceptive implants program began in May 1988. This program has several components, including development of IEC 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. The BFRP continues to monitor the clinical trials associated with this expansion program and to implement the programmatic aspects of the project.

In February, 1990 the BFRP held its National Conference, a scientific meeting attended by 200 policymakers, researchers, and family planning physicians. In the same month, consultants from Deloitte & Touche visited the BFRP and installed a software program for managing financial accounts and generating monthly reports for review by management. The consultants also calculated the BFRP's overhead rate. This visit was followed up by technical assistance from FHI's Contracts and Grants Manager in July 1990. He helped solve some software problems, provided additional training in the concepts of overhead and direct and indirect costs, and set up a format for the BFRP to use in preparing an organizational budget.

and workshops. Projects were 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 training of a network of medical research collaborators; and to develop the EFCS administrative and financial management capacity to coordinate projects from multiple funding sources.

In December 1989, the EFCS hosted a highly successful workshop to identify national research needs in the area of human reproduction. The workshop, sponsored by WHO and attended by FHI and USAID, included Egyptian experts in all aspects of human reproduction. With assistance from FHI, the EFCS used the list of research needs produced at the workshop to develop a proposal for USAID/Cairo.

During this reporting period EFCS produced a final report on the 3-way IUD study (TCu 200 versus ML 250 versus Lippes Loop), to evaluate the long-term usage of the ML 250 IUD. The pregnancy rate among ML 250 users was lower (0.5%) than among users of the TCu 200 and the Loop (0.9% and 0.7% respectively). Acceptability of the ML 250 was high. Follow-up in the TCu 200 versus the TCu 380A study will continue through 24 months. Reporting is on hold until the new IUD-PS system is installed on the EFCS computers.

The EFCS librarian continued to update the library collection, including identifying missing editions of journals and ordering new publications. EFCS received a CD-ROM version of POPLINE during this reporting period.

The BFRP also held a Clinical Trials Research Methods Workshop in September 1990, funded with bilateral support. FHI provided two facilitators (one clinician and one biostatistician) to lead the workshop. Twenty persons attended, equally divided between BFRP professional staff and mid-level physicians, some of whom are current study investigators.

b. Egyptian Fertility Care Society (EFCS)

Founded in 1974, the Egyptian Fertility Care Society (EFCS) is a voluntary organization of over 260 medical specialists affiliated with the Egyptian Medical Association. EFCS enjoys an excellent reputation as the pre-eminent biomedical research organization in Egypt and has acted as the research arm of the National Population Council (NPC). Internationally, the EFCS has maintained working relationships with FHI, USAID, WHO, PIACT, AVSC, JHPIEGO, UNFPA, the Population Council, and the Ford Foundation, among other organizations. EFCS hopes to become a WHO Collaborating Center later in 1990.

FHI has supported the EFCS since 1980, both through centrally funded projects and since 1988 primarily through USAID/Cairo add-ons to FHI's Cooperative Agreement. FHI has worked with the EFCS on an institutional development/core support project; an IUD study (reported in the section on clinical trials); and a NORPLANT[R] project.

The last FHI/EFCS subagreement continued under a no-cost extension through September 1990. The subagreement focused on clinical trials, information dissemination, and institutional development through individual training

The EFCS continues to manage and coordinate the bilaterally-funded NORPLANT[R] project (see section on Contraceptive Introduction) begun in 1986. This project has given the EFCS experience in coordinating large multi-center research projects and has raised the national status of the organization. The project has increased the EFCS's funding base and improved staff and computer capabilities.

The NPC has recently decided that all biomedical research will be coordinated through the NPC. All A.I.D. funding for such research will be channeled through the NPC. The EFCS will send proposals to the NPC for further funding. FHI and EFCS are currently exploring alternative sources of funding for EFCS.

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 whose headquarters are located in Bandung, Indonesia. The BKS PENFIN is now composed of 15 member units: the Departments of Obstetrics and Gynecology at 13 Government University teaching hospitals, as well as those at Central Army Hospital and Harapan Kita Maternity Hospital. The BKS PENFIN was established to serve primarily the research needs of the national programs on family planning and family health. At the time the BKS PENFIN was established, no private research organization with a national scope existed in Indonesia to carry out research in human reproduction. 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 and has widely disseminated the results of the BKS PENFIN studies.

Core support to BKS PENFIN was completely phased out according to a long range plan in December 1988. Financial support is now provided to the BKS PENFIN on a project-by-project basis. In addition, much on-going technical assistance is provided by an assigned Program Officer and, as an FHRC, BKS PENFIN has been the recipient of occasional supplemental equipment support. As an example of the latter, a CD-ROM drive and POPLINE system was installed at BKS PENFIN's Head Office in December 1989. More significantly, a new IBM PS/2 PC and laser printer were provided in June 1990. This equipment, together with new SAS-based software developed by FHI, will facilitate the processing and analysis of BKS PENFIN's 3,000 case IUD study data. It will also serve to replace the aging Texas Instruments computer at BKS PENFIN.

In the past, one of BKS PENFIN's largest roles was as a coordinating center for multi-center clinical trials. That role is diminishing with the completion two FHI-sponsored studies: 1) a 3,000 case evaluation of the TCu 380A versus the Lippes Loop D versus the Multiload Cu 375 and 2) a 300 case study of the Filshie clip versus the tubal ring via laparoscopy. Final close-out visits were paid to the two Filshie clip study sites in January and February 1990. Also in January two FHI staff visited the BKS PENFIN's Head office to check on the status of the IUD data and to assist in the preparation of a preliminary report of the study results. BKS

PENFIN's ability to coordinate research conducted by its members centers has grown and developed but there is currently relatively little demand for large-scale clinical trials in Indonesia.

At the 1990 Annual Meeting of BKS PENFIN, held January 25-27 in Jakarta, members not only presented research results (including the preliminary IUD report noted above) but also discussed additional research needs and potential sources of funding. The latter is particularly difficult since so much of the funding for family planning research in Indonesia passes through the National Family Planning Coordinating Board (BKKBN) and all projects of a family planning nature require BKKBN's approval. In order to expand the possibilities for funding within Indonesia, the BKS PENFIN is targeting some of its efforts to broader health concerns. Recently they obtained a large grant from the Ministry of Health to survey hospitals in one part of Indonesia about equipment needs for obstetric, gynecological, and pediatric services.

The Annual Meeting is an important activity for the BKS PENFIN because it is the only time during the year that the BKS PENFIN's Head Office staff and at least two representatives from each center come together to discuss organizational issues. FHI provided only partial support to the meeting this year; additional support was provided by one pharmaceutical firm and by the small tuition charged to a large group of midwives invited to

attend one day's sessions. Accommodations were provided by the Harapan Kita Hospital (BKS PENFIN's newest center). BKS PENFIN would like FHI to continue to provide support for this meeting, given its importance to the identity and long-range planning of the organization.

Four training activities for BKS PENFIN members were funded by FHI during this reporting period: 1) a clinical trials workshop, 2) a data analysis workshop, 3) training in rapid survey methodology, and 4) PC training for researchers from eight BKS PENFIN centers.

The clinical trials workshop was held the week of October 23, 1989 for members from eight BKS PENFIN centers which had never been included in such training. This workshop was entirely organized and run by the BKS PENFIN. They requested FHI assistance for someone to help present lectures on data analysis. Given the amount of material already to be covered in the short workshop, it was decided that a separate workshop specifically on data analysis would be a more realistic goal.

Subsequently, a four-day data analysis workshop was held directly after the Annual Meeting, January 29 - February 1. One representative from each of BKS PENFIN's 15 centers was selected to attend and an FHI biostatistician led the course along with an Indonesian professor of statistics. Evaluations were positive and the materials developed for and distributed during the workshop should prove a lasting resource.

While FHI had considered conducting its own training on rapid survey methodology for the BKS PENFIN, USAID/Jakarta informed FHI of similar

training being planned for BKKBN by URC. Given that this training would be conducted in Bahasa Indonesia and provide an opportunity to foster BKS PENFIN and BKKBN collaboration, FHI agreed to cover travel and tuition costs for five BKS PENFIN representatives to attend the 10-day training course in Yogyakarta, Indonesia. It is hoped that the five participants will subsequently be able to train others and that BKS PENFIN will be better positioned to secure funding for the more marketable rapid surveys.

The final training planned for FY 1990 was a follow-on to similar PC training conducted in the previous fiscal year. Whereas in FY '89 a FHI staff member and consultant assisted BKS PENFIN in a 10-day PC training course for researchers from 7 of the 15 collaborating centers, the FY '90 training was conducted entirely by BKS PENFIN staff and consultants for researchers from the eight centers not previously trained. This second course was somewhat shorter (seven versus ten days) and omitted training in SPSS, but it took advantage of materials developed for the first workshop. As a network of collaborating centers, the BKS PENFIN Head Office had provided at least one PC to each center in 1989. This training completed a long-term commitment made by BKS PENFIN at the time that the PCs were provided.

A final important activity involving both the BKS PENFIN and FHI in FY 1990 was a review of their accounting procedures and organizational budget by FHI's Contract and Grants Manager and the Program Officer during a joint visit in June. Issues affecting all budgets, namely depreciation, office rent and the calculation of indirect costs were addressed. While BKS PENFIN has made significant progress over the years in their

accounting practices, indirect costs continue to prove a difficult principle for them to adopt--partly because many donors (and in particular the Indonesian government organizations) are unwilling to pay indirect costs and partly because auditing has consistently been slow so that later adjustments to their indirect rates would be difficult. In FY '91, we hope to provide some in-country fiscal accounting training (using in-country consultants) for the central office staff so they become more familiar and comfortable with a computerized accounting system. Ultimately, however, FHI's input into how BKS PENFIN presents their overall budget will diminish as our role in funding that budget also diminishes.

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, this FHRC was established within the Research and Evaluation wing of the FPA/SL in late 1983.

The unsettled political situation within Sri Lanka has, not surprisingly, had several detrimental impacts on the FPA/SL. One has been the inability to hire and retain qualified personnel. For example, despite many efforts, in the past year the FPA/SL was not able to locate a candidate they felt was suitable for the Director of the Evaluation Division. Two appointments were given for the post of Assistant Director but then,

within one month of accepting the offer, both persons received and accepted other appointments to work abroad. Likewise, three members of the computer staff left for jobs outside of the country as did the Financial Manager who was hired by IPPF.

As of January, the staffing situation has improved somewhat. An individual with previous experience in the Census Department accepted the position of Director of Evaluation, and additional computer staff, two with previous related work experience, have been employed.

Activities have also been affected by the civil unrest. The initiation of a small scale NORPLANT[R] study to introduce three physicians to the method specifically, and to clinical research in general, was postponed. It will be reconsidered as soon as terrorist activity--occasionally directed at family planning providers--declines. In the interim, however, the FPA/SL has maintained its own clinical trials activities. A study conducted with the Sri Lankan Association for Voluntary Sterilization on the no-scalpel method of vasectomy was completed. Follow-up continued in FHI-sponsored clinical trials of NORPLANT[R] as did a 1,000 case post-marketing surveillance study organized by the World Health Organization. The FPA/SL has also been assisting the government in introducing NORPLANT[R] slowly into the tea plantations.

In November, FHI's Associate Director of Scientific Support visited the FPA/SL in order to assess computer needs (hardware, software and training) as well as to install a CD-ROM drive.

Based on the FPA/SL's continuing need for computer capacity no longer met by the aging and increasingly unreliable Texas Instruments microcomputer previously provided by FHI, a decision was made to provide the FPA/SL with an IBM-PC and laser printer. This computer, the purchase of which was completed in September, will be used by the Association's accounting staff for financial record-keeping as well as by the computer staff for research needs.

One of the most impressive activities supported with the FPA/SL's core support funds in FY 1990, was a national seminar on "Family Planning Research and Emerging Issues for the Nineties", held in Colombo, June 15-17, 1990. This was the first large scale seminar in Sri Lanka dedicated to the dissemination of family planning research results (primarily from in-country research) and the variety of results presented--from comparisons of different pills to patterns of use of traditional methods and males' influence on the selection of female contraceptives--was as impressive as the presentations themselves. By placing the seminar back-to-back with a regional IPPF meeting, the Family Planning Association was also able to secure several international speakers in addition to the invited FHI staff who presented on new developments in hormonal contraception, research on misconceptions about the pill, and emerging issues.

The FPA/SL does not feel that a similar seminar would be useful on an annual basis and, given the small size of the country and the limited amount of research that is completed within any single year, this seems a valid assessment. Nonetheless, one role the FPA/SL can see itself

playing is to ensure a national forum, perhaps on a biannual basis, for the dissemination of family planning research results. As their Executive Director notes, such a forum would serve not only to increase the potential benefits of the research but also to encourage physicians and others to become involved in research efforts.

e. Thailand Fertility Research Association (TFRA)

The TFRA was established in 1979, with FHI assistance, 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 which operates within the administrative structure of the Ministry of Public Health (MOPH) in Bangkok and, therefore, enjoys a close relationship with the NFPP. As such, it is uniquely situated to enlist and coordinate capable researchers from both the private and public sectors, including MOPH 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 reach 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 contributed significant core support in the form of office space, transportation and personnel. The TFRA also has received limited

project support from private pharmaceutical companies and has initiated three major studies under separate contracts with FHI.

The first half of the year was a time of reflection and planning for the TFRA. It was determined that a senior social scientist was needed to bolster the technical skills of the staff. Dr. Napaporn Havanon, a faculty member of a local university and experienced researcher, was identified to serve in that role. She began working with the TFRA staff and FHI's Country Representative for Thailand to develop several study ideas, which will be initiated next fiscal year:

(1) Study of Provision of NORPLANT^R by Nurses. In this project, 12 nurses at district hospitals will be trained in NORPLANT^R insertion and removal procedures. They will then insert NORPLANT^R in at least 500 women who opt to adopt the method. Variables which will be examined include insertion-related complications and continuation rates, how contraceptive mix changes with the introduction of NORPLANT^R services, and the cost of providing the NORPLANT^R services. The survey will provide useful information to the Royal Thai Government in understanding the costs entailed in providing this service and the place of NORPLANT^R within the mix of available methods.

(2) Pill Compliance Study. In this study, 10 women at each of 20 pharmacies in a provincial center will be interviewed to determine their knowledge of correct oral contraceptive use, with special attention to cycle transition errors.

(3) Condom distribution at government health facilities. This study, to be funded by non-A.I.D. sources, will look at condom distribution patterns in relation to the spread of HIV in the country. Condom distribution has skyrocketed recently, many suspect that they are being used for disease prevention rather than for contraception. This study will examine the reasons for the increased use of condoms (for STD prevention, pregnancy prevention, or both), average consumption pattern, and condom compliance.

During this reporting period, the TFRA, along with the Ministry of Public Health, also cosponsored a seminar on the Integration of AIDS Prevention into the Family Planning Network. About 200 government officials, provincial chief medical officers, and chiefs of district hospital family planning units attended the seminar in Pattaya in July 1990. The seminar (which was conducted in the Thai language) was the first time many had attended a formal presentation on AIDS, and featured frank discussion of the issues and constraints for trying to involve family planning workers in AIDS prevention activities. FHI support for this seminar was channeled through the TFRA, with funding derived half from A.I.D. and half from private sources.

f. University of Nairobi (UON/Kenya)

A three-year institutional development project entitled "Reproductive Health Research/Institutional Development Project" (IDP) was initiated in December 1988 with the Department of Obstetrics and Gynecology of the University of Nairobi. Funding for this project is through an add-on from USAID/Kenya to FHI's cooperative agreement. The goal of the IDP is to

develop the Department's research capabilities in order to expand the Department's role in addressing the research needs of the Kenyan national family planning program.

In order to expand the Department's capabilities to process and analyze data, five microcomputers, a laptop computer, printers and various data entry, data analysis and project management software packages have been purchased. Updates of computer-aided teaching programs are being provided on a regular basis.

A CD-ROM system to provide access to medical and family planning information such as POPLINE and MEDLINE has been installed. The software package InMagic will be used for library data management. Approximately 500 citations of studies carried out in Kenya on reproductive health issues have been abstracted and will be input on InMagic. This compilation of studies will, for the first time, provide easy access to students and staff interested in a review of literature.

A research development workshop was held in August 1989. During FY 1990, researchers from the Department, with FHI technical assistance, have revised proposals to address four priority research areas: 1) reasons for contraceptive discontinuation, 2) barriers to contraceptive acceptance, 3) maternal mortality, and 4) male involvement in family planning. The first two proposals have been finalized, submitted to A.I.D., and approved for funding under the IDP. Site visits by Department staff involved in the development of the maternal mortality proposal have been made to determine

the feasibility of the proposed data gathering. A study proposal on male involvement is also under development.

A number of research studies are ongoing. A questionnaire was mailed to 900 physicians throughout the country to ascertain their knowledge, attitudes and practices concerning reproductive health and family planning. Responses were received from over 400 of them. The Department has completed data collection, entry and cleaning. Cross tabulations have been run and the final report will be finished by November 1990.

An acceptability study to look at contraceptive acceptance and reasons for discontinuation was begun in June 1990. Over 600 of the planned 1500 women have been recruited into the study. These are women who accept the pill, IUD or injectables for the first time. Women will be followed up for one year to determine side effects, continuation rates and reasons for discontinuation. Home visits are being made by clinic staff to women who do not return for the scheduled clinic visit. Five centers are involved in data collection, giving the Department experience in conducting a multi-center study. A data management system has been established to log data and track study progress. Data are being entered as they arrive in the Department and will be analyzed by Department staff.

The IDP Project Coordinator, Dr. Christine Kigondu, visited FHI at the end of November to plan activities for FY 1990, to better familiarize herself with FHI and its capabilities, and to meet non-traveling FHI staff who are involved with the Project. Mr. J.M. Nyagero, Assistant Project Coordinator, visited FHI at the end of April. During his visit, Mr.

Nyagero familiarized himself with FHI and learned the data entry and analysis package EPI INFO. Mr. Nyagero also attended a three-week workshop on "Needs Assessment for and Management of Family Planning and Health Programs" in Bangkok, Thailand.

Two workshops were planned for this fiscal year. A one-week workshop was held in May to provide an overview of different qualitative research methods with an emphasis on focus group discussions. Practical exercises gave participants the experience necessary to conduct focus groups as part of the Department's research projects. A workshop planned for August to review different analysis techniques for quantitative data was postponed to allow the Department to conduct a preliminary workshop on the use of computers. This provided 15 faculty and staff with practical skills in MS-DOS, EPI INFO, d-BASE, and Word Perfect. The data analysis workshop has been rescheduled for January, 1991. It will familiarize Department staff with different statistical techniques, when to use them, and each technique's advantages and limitations. These skills will make Department staff more critical readers of study results published in professional journals as well as enhance their own data analysis skills.

In addition to the Assistant Project Coordinator, three new full-time staff have been hired: 1) an administrative secretary, 2) a data entry clerk, and 3) a research nurse who will help in monitoring study centers involved in the various research projects. The Department has also advertised for a computer programmer, who should be hired by the end of 1990.

A heavy-duty photocopy machine and an electronic typewriter were purchased this year. A fax machine is on order.

FHI staff from the Program Evaluation, Field Development and Training and Biostatistics/Quality Assurance Divisions have provided technical assistance during the past six months. FHI's Corporate Medical Director was a presenter and participant in an IUD update seminar to discuss the appropriateness of the IUD for Kenyan women and allay fears about the discoloration of the TCu 380A IUD. He also presented at the annual Kenyan Obstetrics and Gynecology Society meeting and worked with Department staff on the utilization of various computer software.

2. Fiscal and Data Management Support Projects

a. Financial Management Assistance to the Family Health Research Centers (FHRCs)

FHI has utilized the accounting firm Deloitte, Haskins & Sells (DH&S), to provide concentrated technical assistance in financial management at three FHRCs: the BFRP, EFCS, and BKS PENFIN. Phase I of this project assessed needs and planned 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 to implement the new system. The third phase covered the development and implementation of an automated accounting and reporting system through use of a PC and commercially available software. During this reporting period, a site visit by DH&S personnel was made to the BFRP to automate

their system. The EFCS and BKS PENFIN had already received similar software and technical assistance, and have each established a continuing relationship with a local accounting firm to assist them further. Despite this technical assistance over a period of several years, some serious problems persist due to the unavoidable complexity of the system, staff turn-over or vacancies, and donor resistance to overhead payments. In some cases, the availability of bilateral USAID support has offset the phase-out of FHI core support, extending the period of concurrent and somewhat confusing grant funding and cost recovery funding. Continued technical assistance will be provided to FHRCs, to strengthen both accounting and fund raising capacity. During the months of June and July 1990, FHI's own Contract and Grants Manager made site visits to the BKS PENFIN and BFRP. These visits served to provide continued technical assistance in financial management systems in general and to resolve any specific FHI contractual issues at these FHRCs in particular.

b. Microcomputer Development and Training

(1) New Microcomputer Installations

IBM PS/2 microcomputer systems with 80386 CPUs and laser printers were provided to the BKS PENFIN, EFCS, and FPA/SL during this reporting period. In addition, a similar IBM-compatible system was chosen by the TFRA for purchase and installation in the near future. Competitive bids were obtained locally in each case, prior to final selection and submission for required A.I.D. approvals. The purpose of these new computer placements is to enable these FHRCs to begin phasing out reliance on the Texas

Instruments (TI) Business Systems Model 351 microcomputers which were provided by FHI 5-8 years ago and which are now nearing the end of their life expectancy. FHI is no longer capable of supporting these TI machines or the specialized software which was developed for them. FHI and the FHRCs have recognized the need to phase out the aging, non-compatible TI computers and to develop new approaches to software needs, with an emphasis on utilizing commercially available programs and statistical packages on IBM-compatible replacement hardware. While some of the FHRCs had already acquired IBM-compatible PCs (either with FHI funding or from other sources), these have not had sufficient memory and speed to handle relatively large clinical trials and other datasets.

A laptop computer, printer, and software were provided to the Malian Family Planning Association (AMPPF) as part of FHI's institutional development support. Installation and training assistance was obtained locally.

As reported previously, FHI has provided several desktop IBM-compatible PCs and one laptop computer to the University of Nairobi Department of Ob/Gyn, as part of the Institutional Development Project (IDP). FHI has begun soliciting equipment and price information in preparation for further enhancing the Department's computing capacity through provision of one additional, more powerful (80386 CPU) PC and at least one more laptop computer in FY 1991.

(2) CD-ROM Installations

Compact Disc-Read Only Memory (CD-ROM) technology allows storage of 500-600 megabytes of data (equivalent to 1,500 floppy discs or 200,000 pages of print) on one compact disc. This technology is ideally suited for databases, such as POPLINE which has been made available on CD-ROM by Johns Hopkins University with funding from UNFPA. During this reporting period, FHI provided CD-ROM drives and POPLINE to BKKBN, BKS PENFIN, TFRA, Siriraj Hospital (Bangkok), Chulalongkorn Hospital (Bangkok), FPA/SL, BFRP, and GIMIESAR. (CD-ROM drives were installed previously at EFCS and UON/Kenya.)

(3) Software Modifications

During this reporting period, work was initiated on the adaptation and transfer of certain specialized FHI software programs for use in the field on IBM-compatible microcomputers. To overcome problems detected in the IUDPS program (which was available to Texas Instruments BS users but not IBM-compatible microcomputer users), a new SAS-based program was developed, tested, and installed at BKS PENFIN and EFCS (where IUDPS studies are ongoing). Also under development is an adapted Maternity Care Monitoring (MCM) program for use on IBM-compatible PCs in the field. A modified form has been developed and field tested; and a data entry and analysis program utilizing EPI INFO is currently under development.

3. Other Institutional Development Activities

As resources permit and as local interest and absorptive capacities allow, FDT has initiated institutional development programs in other countries, notably in Mali, Niger, Gambia, Mexico, and Egypt. Progress in these programs during this reporting period is described below.

a. Technical Assistance to the Malian Family Planning Association (AMPPF)

Technical assistance by FHI to the Malian Family Planning Association (AMPPF) began in 1981. Broad-based assistance is continuing with the current two-year subagreement. A laptop computer and various software packages for word processing, data entry and data analysis have been provided to the AMPPF so that they will have the in-country capabilities to analyze their own data. Training on the operation of the computer is being done locally. Besides analysis of research data, the computer will also be used to computerize service statistics and financial reports. CERPOD is providing technical assistance to the Sahel region on computerization of service statistics, and they have offered to aid the AMPPF in developing this system. Likewise, the AMPPF has contacted other IPPF affiliates who have computers to determine what financial program software they are using.

The AMPPF is interested in encouraging a more diversified contraceptive method mix and in expanding the family planning program to non-clinic settings. Since health professionals greatly influence client decisions,

including method choice, data have been collected from 400 physicians and midwives as to their knowledge, attitudes and practices towards family planning and different contraceptive methods. A final report has been prepared and an information dissemination seminar of study results is being planned for January 1991. This seminar will present the study results and develop strategies on how to improve service delivery.

Data collection for a surveillance study of 220 IUD users was completed in March 1990. Women were followed for one year to determine side effects, expulsion and continuation rates. This is a repeat of an earlier IUD surveillance study to determine whether there has been an improvement in insertion techniques and continuation rates. A final report is being prepared.

A mandate of the AMPPF is to sensitize the public about the advantages of family planning and promote acceptance of family planning methods. The AMPPF has used several techniques to transmit the family planning message, the most recent is the training of different types of community development workers about family planning and how to incorporate family planning into their daily work schedules. The AMPPF has included the evaluation of this program in its current subagreement. Two hundred community workers have been interviewed to determine to what extent they have incorporated family planning into their daily program and what obstacles they have faced in doing so. Focus group discussions with men and women in selected communities where these agents work will determine how effectively they have transmitted the family planning message and the obstacles that the community faces to accept a family planning method.

Data collection has been completed and data entered on the AMPPF computer. FHI is providing technical assistance for analyzing the data and writing the final report. The results of this evaluation will provide information to IEC staff in the development of the next phase of the IEC program.

b. Niger: Technical Assistance to the Centre National de Sante Familiale (CNSF)

The Centre National de Sante Familiale (CNSF) is the principal government agency providing family planning services in Niger. The Niger Ministry of Social Affairs and Women's Status 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 FY 1989, FHI provided CSNF with a desk-top computer and printer, as well as data entry, analysis and text-processing software. During FY 1990, FHI staff provided training and assistance to two CNSF staff members in the coding and entry of completed questionnaires.

To determine the reasons for high drop-out rates at the CNSF, FHI and USAID/Niamey provided technical assistance and funding for a study entitled "Contraception Continuation Rates and Reasons for Discontinuation at the CNSF." Six hundred-fifty new clients accepting the pill, IUD or injectable were recruited into the study and were followed for six months to determine discontinuation rates and reasons for method switching and discontinuation. Home visits were made to all women not returning for their scheduled visits to determine why they did not return to the clinic. Regular site visits were made by an FHI staff member to provide related

computer training and to monitor the progress of the continuation study and data entry. Data collection was completed in May 1990 and the data were cleaned in Niger during a June visit by FHI staff. In August, the Nigerien investigator who began the study (and who is currently studying at Tulane University) visited FHI for two weeks to complete the data analysis and write a final report. Study results showed that the six month rate of contraceptive discontinuation was about 25 percent. Taken together, side effects and the fear of side effects proved to be the most common reason for abandoning contraception. The report is being finalized and will be distributed by the end of 1990.

The Niger Family Health and Demography Project (PSFD), USAID's population initiative in Niger, plans to use the results of this study to design new interventions and OR projects to improve family planning service provision. It is likely that FHI will be asked to evaluate these interventions.

c. Gambia: Contraceptive Continuation Rates and Reasons for Discontinuation

FHI is providing technical assistance to The Gambia Family Planning Association (GFPA) for a prospective study of contraceptive continuation rates and reasons for discontinuation at four GFPA clinics. The study was initiated in November 1988 with field costs provided by the International Development Research Center (IDRC). In addition to making regular visits to monitor the progress of the study, an FDT staff member has been providing computer training to GFPA research staff.

The GFPA has collected background data on more than five hundred new family planning acceptors in four clinics. These clients are currently being followed up six to eight months after entering the study to determine their reasons for continuing or discontinuing contraception. Home visits are being made to women who do not return for their regularly scheduled visits. Of particular interest to the GFPA are those factors, such as counseling, that can be influenced by the nature of the service delivery program. FHI staff traveled to The Gambia during FY 1990 to help local research staff with the data collection and entry, and will return in FY 1991 to complete the data analysis and final report.

d. GIMIESAR: Mexico

As an outgrowth of an FHI-supported epidemiology training program at the Instituto de Investigación Científica of the Universidad Juarez in Durango, Mexico, the Mexican Interuniversity Group for Epidemiologic Research in Reproductive Health (GIMIESAR) was formed in 1984. GIMIESAR, based in Durango, is made up of representatives from major Mexican universities and medical schools who have received training in the Epidemiologic Research Methods Workshop. There are currently seven GIMIESAR affiliates.

FHI began providing core support to GIMIESAR in FY 1989 and continued this support in FY 1990. FHI is continuing to provide basic institutional support to GIMIESAR and has provided technical assistance as they work to diversify their funding base. An FHI consultant traveled to GIMIESAR in

March, 1990 to assess their capabilities and future needs. This was followed by travel of FHI's Director of Development in August, to provide assistance in expanding sources of donor support. FHI's support provides the organization with funds necessary to permit periodic meetings to review ongoing projects, develop new research proposals, and plan for future efforts to obtain funds from the international donor community. In particular, GIMIESAR has developed a five-year institutional development plan which outlines the organization's plans for growth and increased self-sufficiency. The plan, developed in close collaboration with FHI, will be used to secure funding from the international donor community, including WHO and the Rockefeller Foundation.

The FHI support also will help GIMIESAR develop as a major epidemiologic research organization, a goal outlined in their five-year plan. GIMIESAR is currently developing several large-scale epidemiologic research projects to be submitted to various donor agencies for funding. FHI has also supported GIMIESAR in conducting Epidemiologic Research Methods Workshops, details of which are reported elsewhere in this document.

During this reporting period, GIMIESAR provided data analysis and processing support to its affiliates, including training in the SURVEY data processing package. A GIMIESAR staff member traveled in July, 1990 for training in the SPSS and survival analysis. GIMIESAR received a CD-ROM drive from FHI, which will enable them and their affiliates to conduct literature searches on POPLINE.

In addition, FHI provided a fellowship for a GIMIESAR affiliate investigator, who was a key instructor in the GIMIESAR Epidemiologic Research Methodology Workshops, to receive training at FHI while she pursues a doctorate in epidemiology at the University of North Carolina at Chapel Hill.

e. Egypt: Institutional Development Project (IDP)

FHI has worked with its subcontractor, E. Petrich and Associates since 1988, to assist Egypt's National Population Council (NPC) to enable it to function as the coordinating organization for population activities in Egypt. The IDP is working to strengthen both the technical secretariat and governorate level NPC offices.

A redesign of the IDP project in June 1989 shifted the focus for institutional development from national to governorate-level population councils. Institutional weaknesses in policy analysis and formulation, multiyear and annual planning, program and administrative management, including program monitoring and evaluation, have been identified as high priority areas to be addressed under the revised IDP. Under a subcontract with Ernest Petrich and Associates, a resident advisor for the IDP project is now working in Cairo. During this reporting period, a comprehensive implementation plan and a training plan for the IDP were developed and training took place in contraceptive technology. The NPC and the USAID/Cairo mission are now interested in developing an MIS system as a new component under the IDP.

In addition, an operations research (OR) component was designed to institutionalize the capability within the Egyptian implementing agencies to utilize operations research as a means of solving operational problems associated with family planning; and to design, carry out, and evaluate operations research studies. For this component, FHI is now represented by a resident research expert who works in FHI's Cairo office.
FHI has conducted two successful two-week family planning operations research workshops in February-March and in August-September of 1990, at which participants from the MOH, the Clinical Services Improvement Project (CSI), the Family of the Future (FOF), the Teaching Organization (THO), the Regional Center for Training (RCT) and the NPC developed proposals for OR studies. Professor Dr. Maher Mahran, Secretary General of the NPC, opened the workshops (the openings were covered on the evening news) and reiterated his interest in and commitment to the operations research program in Egypt.

FHI has worked with the MOH, CSI, and FOF from the first workshop to help them implement the proposed OR studies. Four studies are underway; and the FOF management just granted permission to their research department to conduct their OR study. Five studies designed at the second OR workshop will be implemented in FY 1991.

The IDP project is currently undergoing its fourth revision. The focus will extend to the NPC technical secretariat in addition to the governorate NPC offices.

B. Training

FDT has taken an active role in planning and managing research training programs for the field. This work has involved the development of specific curricula and translation of these curricula into French, Spanish, and Portuguese as needed; conducting workshops in the field; developing in-country capacity to conduct future workshops; and funding locally organized workshops.

1. Development of Training Curricula

FHI has developed curricula to train investigators in several key areas of scientific research including clinical trials, epidemiology research, data analysis, and research management. These curricula are designed to encourage interactive learning through a process involving practical exercises. The exercises, rather than lectures or lengthy readings, form the core of the curricula. During the workshops several facilitators discuss the materials and then work individually with participants and participant groups as they do exercises. This interactive process has proved to be extremely effective in transferring research skills to participants, and has the added advantage that the curricula can be readily adapted and used by in-country personnel.

a. Development of a Reproductive Epidemiology Manual

FHI is collaborating with the Centers for Disease Control (CDC) and the World Health Organization (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. CDC has field tested these materials in Mexico and plans to use them in another workshop in India early in 1991. Based on experience at these workshops, the curriculum will be revised, and it is hoped that WHO will then publish and distribute the manual as a joint publication of the three agencies involved. The manual also will be translated into French and Spanish.

b. Clinical Trials Research Methods

Regional and national clinical trials workshops are an important way to meet clinical trials training needs in the developing world. FHI's standardized clinical trials research methods curriculum has been implemented successfully in several workshops since 1985. The curriculum has been translated and utilized in Spanish and Portuguese (most recently in an August 1990 workshop in Curitiba, Brazil). A French version was used for the first time in a general research methodology workshop in Cameroon (September 1989), and FHI conducted a regional Francophone clinical trials methods workshop in Senegal in June 1990. FHI has been pleased to receive several third-party requests to use these materials. For example, the National Family Planning Coordinating Board (BKKBN) in Indonesia has reproduced the modules locally. Using these curricula, FHRCs in Egypt, Sri Lanka, and Indonesia are now able to conduct clinical

trials workshops with minimal technical assistance from FHI. For example, the BKS PENFIN conducted a local workshop for 9 of its 15 centers (those which did not participate in their first workshop) in October 1989, with funding support from FHI.

c. Clinical Trials Data Analysis

FHI has produced 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 their research assistants who want to do their own analysis. Investigators who have attended the basic clinical trials workshop and who desire a more complete understanding of the analysis process also would 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 five FHRCs in 1988. After some revision in both content and materials, this training was provided for BKS PENFIN staff and investigators in Indonesia, January-February, 1990. FHI's Biostatistics staff are in the process of further revising and finalizing this curriculum. It will be used in the January 1991 IDP workshop at the University of Nairobi.

2. Research Methods Workshops

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, FDT provided support for various research training workshops. During this funding period, the following training activities were implemented:

a. Senegal: Francophone Clinical Trials Workshop

The Field Development and Training Division conducted a workshop on Randomized Clinical Trials Methods for Contraceptive Research in Senegal, West Africa, June 3-10, 1990. This was FHI's first Francophone clinical trials workshop and was conducted in collaboration with the University Hospital of Dakar.

The objectives of the workshop were: a) to teach clinical trials research skills in order to improve the quality of current and future clinical trials undertaken by participants, and b) to strengthen FHI's research network of Francophone African investigators and research institutions in order to encourage future collaborative clinical trials research in Africa.

The six-day workshop was attended by investigators from Senegal, Cameroon, Mali, Niger and Burkina Faso.

b. Brazil: Clinical Trials Workshop

Following upon the successful 1988 Brazil workshop, FHI conducted a second workshop on Clinical Trials Research Methodology in collaboration with the Federal University of Paraná (FUP), in Curitiba, Brazil, August 13-17, 1990. Thirteen Brazilian physicians were trained. FHI provided technical assistance and partial support for the workshop. The team of trainers and researchers who participated in the first workshop conducted this workshop with reduced direct FHI involvement.

It is anticipated that the training will improve Brazilian clinicians' ability to conduct policy relevant clinical research. The affiliation with the FUP, in partnership with 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.

c. Mexico: Epidemiology Research Methods Workshop

FHI provided support to GIMIESAR to conduct two epidemiology research methods workshops in FY 1990: One regional workshop for 17 Latin American participants in May, and the other for GIMIESAR affiliates in September 1990.

These two-week workshops form part of a series of training activities carried out by GIMIESAR. The courses cover the theoretical basis of epidemiology methods, including research design, inferential statistics,

and data processing and analysis. In addition, participants develop a research protocol on a topic of interest during the second half of the workshop.

The workshops were 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-service basis. These workshops have generated several projects, including an FHI-funded study of vitamin B6 used to manage the side effects of OC use.

d. Cameroon: Applied Research Methodology Workshop

FHI, in collaboration with the University of Yaounde and the World Health Organization, conducted an Applied Research Methodology Workshop for Francophone Africa September 18-29, 1989 in Yaounde, Cameroon. Eighteen participants from seven Francophone African countries participated in this regional workshop. The workshop's main objective was to teach basic research skills and provide participants, including physicians, demographers and sociologists, with the knowledge necessary to develop viable research projects. Topics covered in the workshop included research priorities, development of research questions, basic epidemiology, protocol development, instrument development, coding, data entry and analysis.

FHI monies have been budgeted to fund several of the proposals developed during this workshop. One such study, a KAP survey of adolescent sexuality in Bamako, will be conducted by the Family Planning Association

of Mali (AMPPF). Another study to be funded is a KAP study of physicians' attitudes toward family planning in Cameroon. Proposed projects that fell outside of FHI's mandate are being proposed to other funding agencies for support.

e. Haiti Research Methodology Workshop

FHI, in collaboration with the Haitian Child Health Institute (CHI), conducted a two-week workshop on applied research methodology, November 6-17, 1989, at the Institute's headquarters in Port-au-Prince, Haiti. The objective of the workshop was to provide the skills necessary to develop viable research projects that address reproductive health issues in Haiti. Topics covered included research priorities, problem identification and definition, sampling methods, data collection, coding and analysis, and the development of study budgets and work plans. Ten participants developed concept proposals for six different research projects in reproductive health. Physicians and nurses from both the public and private sectors participated in the workshop. Proposals developed during the workshop will be presented to various funding agencies for support, including FHI.

f. Philippines: Research Utilization Workshop

FHI and the Commission on the Population Regional Office No. XI (POPCOM XI) collaborated on a Research Utilization Workshop in Davao, Philippines, April 26-27, 1990. The workshop was initially scheduled in September 1989, postponed until January 1990, and again rescheduled for April

because of logistical problems that hindered the arrival of workshop funds and materials from FHI to Davao.

The overall goal of the Research Utilization Workshop was to promote policies, based on research findings, that support the integration of population issues into planning of socioeconomic development activities by the Government and non-governmental agencies within the Region. It was attended by approximately 50 directors of agencies implementing family planning programs as well as local government leaders. The workshop followed a two-day Population Forum planned by POPCOM XI at which 200 representatives of the public and private sector discussed fertility control and the relationship between population and development.

POPCOM XI promotes research that can influence regional family planning policy. At the Davao workshop, researchers presented the results of several studies including a study of factors associated with the family planning practices of married women in agro-industrial companies in Region XI and the 1986 Contraceptive Prevalence Rate Survey in the Philippines and 13 Regions. Additionally, the FHI collaborator in the the comparative study of Triquilar versus Lo Ovral oral contraceptives discussed her experience as a clinical trial researcher. During the second day of the workshop, participants developed action plans based on the results of the three studies presented in the workshop.

3. Sharon Camp Fellowship Program

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. Although funds were budgeted in FY 1990 to accommodate one or two fellows, FHI's selection committee could not agree on a suitable candidate and no fellow was invited. No funds have been budgeted for this program in FY 1991 and its future is under review.

C. Support for Conferences, Seminars and Expert Meetings

Participation in selected regional and international meetings, conferences and seminars affords the opportunity to generate research ideas, discuss major issues, and share research findings. FDT provides limited support for key regional meetings and for our international colleagues to attend and participate in such meetings. Support provided during this reporting period is described below.

1. Institutional Support

a. Mexico: AIBIR/ALIRH Conference

FHI provided support to the Mexican Academy of Research in Reproductive Biology (AIBIR) for their fifteenth Annual Meeting held May 30 through

June 2, 1990. The 1990 meeting was attended by one FHI staff member. The AIBIR annual meeting is an important event which brings together scientists working in human reproduction in Mexico. FHI views its participation as an important aspect of its activities in Mexico. Specifically, these meetings provide an opportunity for FHI to discuss our research directions in reproductive health and contraceptive technology with our Mexican colleagues, as well as with other international health research organizations.

b. Mexico: PLACIHR Board of Directors Meeting

FHI participated in a seminar on "Regional Priorities of Research and Training in Reproductive Health in Latin America", sponsored by the Latin American Program of Research and Training in Human Reproduction (PLACIHR) held in Mexico City, March 28-29, 1990. During the seminar PLACIHR presented the preliminary results of an inventory of Latin America research, training, and human resource organizations, completed with support from FHI. A follow-up survey to augment this inventory is being conducted with further FHI support. FHI will also support the printing and dissemination of the inventory. PLACIHR is a new organization, with considerable Rockefeller Foundation support, formed by leading scientists working in the field of reproductive health in the Latin American region. The organization should become a major actor in research and training activities in human reproduction in the region, and it is anticipated that both PLACIHR and FHI will benefit greatly from a close working relationship.

c. Brazil International Symposium on Hormonal Therapy in Human Reproduction

FHI provided support for the International Symposium on Hormonal Therapy in Human Reproduction, hosted by the Maternidade Climério de Oliveira of the Federal University of Bahia, Brazil, on December 17-19, 1989. The Symposium brought together family planning experts from North and South America and Europe. The topics presented included hormonal contraception, the use of LH-RH analogs and hormonal therapy during menopause.

FHI's support for this event permitted a wide dissemination of theoretical, practical and research-oriented experience of the use of hormonal therapy among reproductive health scientists and family planning experts throughout Latin America. Many of the participants at the Symposium were long-time collaborators of FHI, and their presentations included results of research studies conducted with FHI.

d. Senegal: Colloquium on Laboratory Testing and Hormonal Contraception

In November 1988, researchers at the University of Dakar, Department of OB/GYN in collaboration with Family Health International, the regional office of the International Science and Technology Institute (ISTI) and the Family Health and Population Project (PSFP) carried out a prospective study to determine the percentage of women identified as poor risks for oral contraception (OC) by laboratory tests currently recommended in Senegal and to compare the results of laboratory tests with the results of clinical exams and medical histories. Five hundred first time oral

contraceptive acceptors were admitted into the study at three different family planning centers in Dakar. Analysis showed that required laboratory testing was not cost-effective. Its systematic use was extremely expensive and found very few contraindications (12/410, only one confirmed). Correlation between lab tests and clinical exams was poor.

The University of Dakar, ISTI, and FHI organized a colloquium to (1) disseminate the results of the Dakar study, (2) to invite colleagues from other West African countries to discuss hormonal contraception and laboratory testing in their respective countries, and (3) to develop a set of guidelines and a consensus agreement based on the research and papers presented. The International Colloquium on Laboratory Testing and Hormonal Contraception was held at the Foire International Conference Center in Dakar, February 21 - 23, 1990 and was attended by approximately 150 physicians, family planning providers, nurses and midwives from all over Senegal. The African countries of Benin, Togo, Burkina Faso, Cote d'Ivoire, Niger, Mali and Morocco were also represented. The conference received extended media coverage.

A consensus agreement entitled "The Dakar Resolution" was issued on the last day of the colloquium. Its two main recommendations were to eliminate systematic laboratory testing prior to OC prescription and to improve clinic screening procedures for all family planning methods. In April 1990, FHI will distribute a Final Report of the Laboratory Testing Study. The report will include copies of all the papers presented at the colloquium as well the consensus agreement. A shorter English version will be distributed shortly thereafter.

e. Pakistan: NRIFC 14th Annual Research Seminar

In early December 1990, the National Research Institute of Fertility Control (NRIFC) in Pakistan will hold its 14th Annual Research Seminar, with funding by FHI. Approvals were obtained and funds transferred during this reporting period in preparation for the seminar. NRIFC is responsible for the selection of technical papers and in-country logistics. Approximately 150 scholars from universities and colleges throughout Pakistan and employees of the Population Welfare Division and four Population Welfare Departments will be invited to attend.

Among other topics, during this seminar NRIFC will present the initial results of their 500-case NORPLANT[R] clinical trial, and a senior representative from FHI's Clinical Trial Division will speak on complications at NORPLANT[R] insertion sites. It is hoped that these presentations will encourage the Government of Pakistan to expand the current caseload and/or include the method in its Family Welfare Program.

2. Conference Travel (Non-FHI Staff)

FHI provided assistance for the following investigators to participate in conferences and workshops:

a. First National Congress on Gynaecology and Obstetrics, Acapulco, Mexico, October 22-27, 1989.

- Dra. Gloria Alvarado, Durango, Mexico.

b. Center for African Family Studies: "Family Planning Management Workshop," Mombasa, Kenya, September 18-October 26, 1990

- Mr. Falu Njie, Program Coordinator, The Gambian Family Planning Association, Banjul, The Gambia

D. Contraceptive Introduction

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

FHI's Contraceptive Introduction Program was launched early in FY 1990 with the addition of a new Associate Director responsible for developing and implementing a strategy to facilitate the introduction of contraceptive methods. The primary goal of the program is to expand the use of existing methods, introduce new technologies and strengthen appropriate service delivery systems to help integrate these methods into national family planning programs. A major component of the Contraceptive Introduction Program will address issues related to postpartum contraception and consider ways to promote wider usage of contraceptive methods during the postpartum period.

During this reporting period a strategy document was developed, outlining specific program activities, which include developing national strategies, sponsoring seminars aimed at providers and policymakers, developing information and education materials, strengthening provider training capabilities, establishing user registries and surveillance programs, and identifying programmatic and policy research needs. The focus of the introduction program over the next 1-2 years will be on NORPLANT[R] introduction and the use of methods during the postpartum period. However, in the future the program will help introduce new FHI methods, including NET-90 injectables, Annuelle[R] biodegradable implants and plastic condoms.

To carry out these activities, the introduction program will draw upon both in-house and out-of-house resources. In order to avoid interagency duplication of effort, the program will foster collaborative relationships with other international family planning organizations in order to support responsible introduction of new methods into selected countries.

Priority countries for the contraceptive introduction program include: Bangladesh, Egypt, Haiti, Kenya, Mexico, Nigeria, Pakistan, Senegal and Sri Lanka, although other countries may be considered, depending on FHI's organizational resources, Mission support and evolving local interests.

As part of the planning stage for widescale introduction of NORPLANT[R], FHI is participating in an A.I.D.-organized working group as one of the four lead agencies involved in NORPLANT[R] introduction. The first meeting

of the Core Working Group, composed of two representatives from each of the four participating Cooperating Agencies (CAs) plus A.I.D. Office of Population staff from three divisions, was held on August 28, 1990 in Washington, D.C. Country priorities were reviewed and agency responsibilities identified. FHI was identified as the lead or co-lead agency in seven of the 14 high-priority countries, and as such will work with the other CAs to develop country assistance strategies for NORPLANT[R] introduction in those countries. The A.I.D. Core Working Group will continue to meet regularly to coordinate activities and to develop implementation plans, utilizing individual CA strengths and expertise in areas of training, information and education, and research to facilitate introduction of NORPLANT[R].

In the area of postpartum contraception, FHI proposes to implement a broad range of activities to promote postpartum contraception among population policymakers and family planning service providers. A first step in this strategy was to host a one-day coordinating meeting on May 10, 1990 with A.I.D. staff and representatives of other CAs to review ongoing and planned projects in the field of postpartum contraception, coordinate interagency resources, and propose areas of possible collaboration. The meeting was attended by 25 participants and was useful both as an information-sharing activity and as a mechanism to open dialogue for collaboration among agencies on postpartum projects.

1. International Postpartum Contraception Conference

The single largest component of the postpartum strategy was an international conference, held September 17-20, 1990 in Mexico City, Mexico. FHI, in collaboration with other CAs, hosted the four-day event for 160 participants representing 48 countries from Asia, Africa, the Near East and Latin America. The purpose of the conference was to provide family planning policymakers and service providers with updated information and specific guidelines on appropriate methods of contraception for postpartum women. The program agenda included formal presentations on appropriate methods for postpartum use and the components of a successful postpartum program, as well as smaller working group sessions that addressed method-specific, regional and policy issues affecting the acceptance of postpartum contraception. The conference was well-received by the participants, and stimulated much discussion and interest in postpartum contraception.

Follow-up activities to the international conference include several regional meetings, identification of clinical and programmatic research needs, and provider training in postpartum programs and method-specific techniques. A major training activity involves strengthening national or regional postpartum training centers, for example the Mexican Social Security System (IMSS). Other appropriate institutions, particularly our FHRCs, will be approached to determine their interest in establishing postpartum training capabilities. The objective of these programs is to

provide the basis for implementing postpartum surveillance and introduction projects in specific countries.

2. Turkey: Developing a Postpartum Program

In January 1990 FHI sent five key physicians from Turkey to Mexico to learn about the IMSS postpartum contraceptive program. FHI worked with the IMSS to tailor a one-week program specifically for the Turkish physicians from the MOH, the Social Security Administration and Hacettepe University.

FHI will now work with the Turkish physicians to follow-up on progress made in developing a postpartum program in Turkey.

3. Haiti: Seminar on Appropriate Contraception for Breast-feeding Women

FHI, in collaboration with the Haitian Ministry of Health's Family Planning Division (MSPP) and the International Planned Parenthood Federation's Port-au-Prince Field Office, will conduct a two-day seminar to address the contraceptive needs of breast-feeding women. Development and planning for this activity have been completed, with implementation scheduled to take place October 22-23, 1990, in Port-au-Prince.

The objective of the seminar is to provide correct information to health personnel about appropriate contraceptive methods for breast-feeding women and to develop strategies on how to increase their contraceptive use. Participants will be MSPP policymakers, regional directors and health

professionals. After this initial seminar, three regional seminars will be held, with funding from other sources, in order to provide the latest information about contraceptive methods for breast-feeding women to regional health personnel.

4. Egypt: NORPLANT[R] Support (Long-Acting Contraceptive Steroids)

The three-year NORPLANT[R] research program is being coordinated in Egypt at five university teaching hospitals by the EFCS with assistance from FHI. In 1986, the EFCS was awarded a contract by the NPC to assume responsibility for management and implementation of this NORPLANT[R] project.

The project has several components: a large scale program of training and introduction designed to assess the performance of NORPLANT[R] 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 program of acceptability studies designed to indicate patterns of acceptability in various sectors; a cohort study to monitor rare adverse events; and, the development of informational materials for acceptors, counselors and physicians.

By October 1989, all 1528 cases had been enrolled and in February 1990, a report had been compiled on the first year of the clinical trial. The report has been submitted to the Supreme Organization of Pharmaceuticals (SOP) for use when considering registration of NORPLANT[R]. The EFCS is currently working on the second year report, also to be submitted to the

SOP. The acceptability study stages I and II have been completed, including the survey of 1351 (out of 1537) clinical trials cases. Focus group discussions have been completed and the field survey was pretested in Assiut. The cohort study, funded by WHO (with NORPLANT^R sets provided by USAID) was initiated in August. Training of the investigators took place in December 1989.

FHI has presented a proposal for planning for the introduction of NORPLANT^R in Egypt. FHI will work closely with the NPC and other agencies to facilitate a smooth introduction of the methods in Egypt once regulatory approval is received.

5. Senegal: NORPLANT^R Coordination and Management

In 1986 USAID/Dakar provided add-on funds to FHI for activities related to the introduction of NORPLANT^R. A pre-introductory clinical trial was initiated at Le Dantec Hospital in Dakar to provide information on the acceptability of NORPLANT^R among Senegalese women. Follow-up of this study is on-going. In February 1990, at the Colloquium on Laboratory Testing and Hormonal Contraception in Dakar, FHI supported a slide presentation of the results of the One Year NORPLANT^R Experience in Dakar, followed by a round table discussion. The presentation generated a great deal of discussion among midwives and other service providers unfamiliar with this method. Later, FHI staff distributed NORPLANT^R provider manuals in French to midwives and physicians who attended the meeting.

As a result of the interest generated at the February Colloquium and in order to make NORPLANT[R] services more accessible, a second center for NORPLANT[R] insertions has been initiated at the Senegalese Family Planning Association Clinic in Dakar. Also, preparations have begun to develop NORPLANT[R] user-oriented materials designed expressly for non-literate Senegalese women. We will also explore with USAID/Dakar the possibility of developing Senegalese physicians' manuals and counseling guides.

6. Bangladesh: NORPLANT[R] Introductory Activities

In 1986 the USAID/Dhaka Mission agreed to fund a variety of activities, most of which related to an expansion of NORPLANT[R] activities in Bangladesh. Most of the projects involve coordination with the Bangladesh Fertility Research Programme (BFRP) through a series of subcontracts. Add-on 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 analysis of data from the projects.

Several studies are underway using these add-on funds, and are described in more detail in other sections of this report. Included are a four-phase NORPLANT[R] Removal, Motivation, and Acceptability Study and a five-part expansion of NORPLANT[R] clinical trials, including training, educational materials, a registry/surveillance system, and the clinical trials themselves.

Phase One of the Removal, Motivation, and Acceptability study was a follow-up study of NORPLANT[R] removal clients, to identify problems in

obtaining implant removals. The study found that nearly 10% of clients had difficulty getting the physician to remove their implants. Two papers are being written from the data collected. Phase Two was a study of counseling of husbands as an intervention, to see if continuation rates were affected by counseling husbands about the method. Data analysis will begin in April 1991, after women have had at least one year of continuation. Phase Three will be a repeat of Phase One, with a new generation of acceptors.

Phase Four of this study began during this reporting period, and consists of a population-based comparative study of general health complaints of contracepting and non-contracepting women. Focus group discussions were carried out for development of the questionnaire and field work was completed in September, 1990.

The remaining add-on funds were used for a variety of study and institutional development purposes, including purchase of a new ALR Flexcache microcomputer, laser printer and UPS system. They also supported the financial management consultancy by Deloitte & Touche and the Clinical Trials Research Methods Workshop mentioned in the above section on the Bangladesh Fertility Research Programme.

7. Haiti: Introduction of NORPLANT^R Activities

On the basis of two-year data from the on-going pre-introductory trials, the Haitian Ministry of Public Health and Population approved NORPLANT^R to be integrated into the national Family Planning Program in July 1989.

This expanded program incorporates several FHI activities: a national registry, an IEC booklet for users, and the development of a training program to initiate NORPLANT[R] centers in both the private and public sectors.

a. National Registry

FHI has provided technical assistance to the Haitian Ministry of Public Health and Population (MSPP) and the Private Health Sector Association (AOPS) in the development of a NORPLANT[R] National Registry. The registry records data on NORPLANT[R] acceptors and is used as a record keeping system to follow up acceptors. A limited number of the first draft of the registry form (250 copies) was printed in October 1989, to be used and evaluated by NORPLANT[R] centers prior to finalizing the form. Changes to the form are under discussion.

b. IEC Booklet

The Haitian Public Health Institute (INHSAC), in collaboration with FHI, produced an IEC booklet for NORPLANT[R] acceptors in November 1989. This booklet, which is written in Creole, is being used as an educational tool to inform clients about NORPLANT[R]. It was also used during the NORPLANT[R] Counseling Training provided by INHSAC in July 1990.

c. NORPLANT[R] Training

INHSAC is also coordinating theoretical and practical NORPLANT[R] training sessions. Two theoretical and two practical training sessions were held, the first in October/November of 1989 and the second in April/May of 1990. A total of nine physicians was trained. Current plans are to hold four additional theoretical and practical training sessions by September 1991. Each session will train four physicians. Based on this schedule, there will be 27 operational NORPLANT[R] centers within Haiti by the end of FY 1991. This plan will be evaluated as it progresses, and modified as necessary to meet any changes in demand.

In addition, INHSAC provided a special training session on NORPLANT[R] counselling for the nurses and social workers involved in NORPLANT[R] service delivery in July 1990. It is usually the nurses and social workers (rather than the physicians who insert the implants) who counsel acceptors.

8. El Salvador: Postpartum IUD Introduction and Evaluation

Through a PIO/T funding mechanism with USAID/El Salvador, FHI has provided technical assistance to the Salvadorean Family Planning Program for the introduction and evaluation of a postpartum IUD program. Initiated in February 1987, the program has four components: information dissemination, training, clinical research and an evaluation. Specifically, the objectives of the project are to:

(1) inform the Salvadorean family planning community about the programmatic utility of a postpartum IUD program; (2) 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; (3) implement a 400 case non-comparative clinical trial of postpartum insertion of an IUD in El Salvador, with cases to be divided evenly between the Ministry of Health and the Social Security System; and (4) evaluate the program.

Admissions to the clinical trial have been completed and follow-up is ongoing. The initial phase of the evaluation has been completed, with the follow-up phase underway. Few differences among IUD users and controls were reported, although some differences by institution were apparent. The program is significant in its attempt to expand contraceptive alternatives in El Salvador, and also by its nature of cooperation between the Ministry of Health, the Social Security Institute, and the Salvadoran Demographic Association, which is coordinating project activities.

9. Mexico: Postpartum IUD Training Center

FHI initiated plans to provide support to the Mexican Social Security Institute (IMSS), through a contract with the Mexican Academy for Research in Medical Demography (AMIDEM), to strengthen IMSS's training capabilities in postpartum contraception and to train teams of clinicians from selected countries interested in postpartum contraception. FHI core support will

enable the IMSS to share their experience in postpartum contraception with interested clinicians throughout the developing world and will allow them to continue to develop systems and mechanisms for effective training.

The IMSS postpartum training program will be a valuable asset in the development of postpartum contraceptive programs worldwide. We anticipate that IMSS will make this resource available to government family planning programs, international family planning organizations and other cooperating agencies.

10. Contraceptive Technology Update Seminars

a. Uruguay: FLASOG Seminars

FHI will provide support for the XIII Latin American Congress of Obstetrics and Gynecology (FLASOG), scheduled to take place December 2-7, 1990, in Montevideo, Uruguay. The central theme of the Congress is Maternal and Child Mortality, with other official themes to include Contraception, Prenatal Care and Accessibility to Medical Assistance. FHI will sponsor two seminars during the Congress: 1) "Advances in Contraceptive Technology," which will include scientific presentations on research findings on oral contraceptives, IUDs and NORPLANT[R] and 2) "Symposium on Human Lactation." FHI's Director of Clinical Trials will participate in these seminars, and FHI will also sponsor the travel of several presenters from Latin American countries. Partial funding was advanced to FLASOG during this reporting period.

b. Philippines: Reproductive Health and Contraceptive Safety Seminar

Family Health International is providing financial and technical support of the 1990 Annual Convention of the Philippine Ob/Gyn Society, scheduled for November 24-26, 1990 in Manila. Approximately 1,500 members of this prestigious organization are expected to attend. FHI will sponsor a half-day session entitled "Women's Reproductive Health and Contraceptive Safety." FHI will provide international speakers on OC compliance, complications at NORPLANT[R] insertion sites, and breast feeding of high-risk infants. FHI will also prepare a country report on the two FHI-sponsored IUD studies recently completed and sponsor a panel discussion on NORPLANT[R].

c. Jordan: Contraceptive Technology Seminar

During this reporting period, FHI staff visited Jordan and initiated plans for FHI involvement to assist the Ministry of Health in the introduction and expansion of birth spacing methods, particularly in the public sector. Working primarily with the University of Jordan, in close consultation with the Ministry of Health, FHI developed plans to conduct a contraceptive technology update seminar in collaboration with the University's Center for Educational Development for Health Personnel (CED) in January 1991. Entitled "Birth Spacing and Family Health," the purpose of the seminar is to update physicians on the range of currently available spacing methods as well as new methods under development. The seminar will serve to provide factual, up-to-date information on relative risks and benefits of various contraceptive methods, to respond to particular

concerns and common misconceptions, and to explore Jordan's research and programmatic needs in the area of birth spacing and contraceptive introduction. The recent political events in the region have raised obvious questions about the feasibility of proceeding with these plans in January 1991, and we are currently seeking guidance from the A.I.D. Mission in Amman as well as from our Jordanian colleagues.

d. Thailand: No-Scalpel Vasectomy Symposium

In December 1989, FHI cosponsored with the Association for Voluntary Surgical Sterilization (AVSC) a 3-day meeting entitled the "International Symposium on the No-Scalpel Vasectomy Technique" in Bangkok. Organized by the Population and Community Development Association (PDA), the symposium was conducted in conjunction with the King's birthday vasectomy festival, an annual event at which time free vasectomies are provided to interested and qualified men.

The symposium was attended by 54 participants from 14 countries and seven international organizations. FHI funded four international participants and two FHI staff member. Participants were primarily physicians who had been trained in the technique, and papers were read about experiences with the method in various countries. FHI hosted one session on biomedical and programmatic research needs. Suggested research topics from that session are being evaluated within the appropriate divisions for suitability for funding.

E. Information Dissemination

FHI's information programs aim to disseminate information on research findings to family planning and reproductive health researchers, providers, policymakers, and fellow organizations, and to provide technical assistance in communications to the media and to FHRCs. Through these programs, FHI works to support regulatory and health policy changes; provide continuing education materials for better health service delivery; counteract misinformation on contraception; provide background knowledge for research planning, scientific paper writing and publication; and support training and health communications strategies.

This is done through the following means:

-- Regular publications

-- Placement of articles in the international media

-- Training of family health research centers in research utilization

-- Scientific paper writing workshops

-- Journalists workshops and related technical assistance

-- Providing POPLINE on CD-ROM and providing technical assistance in setting up libraries.

During this reporting period, FHI's information dissemination activities included the following:

1. network

Themes addressed in network in 1989-1990 included institutional development, HIV and breast-feeding, and postpartum contraception. network is distributed to 7,600 readers in 129 countries. The spring issue on HIV and breast-feeding was distributed in April 1990. The summer issue on postpartum contraception was used as background material for the Mexico Postpartum Conference. The fall issue will feature articles on NORPLANT[R]. Future issues will address AIDS and family planning and the role of men in contraception.

2. network in Spanish

Readership of network en español, FHI's Spanish-language newsletter, stands at 4,600. network en español Vol. 5, No. 1 was published in the summer. Vol. 5, No. 2, a translation of the issue on postpartum contraception, was published in September and distributed at the Mexico Postpartum Conference.

3. network in French

Readership of network en français includes almost 1,500 recipients. Following the same production schedule as network en español, issues on

hepatitis B and postpartum methods were published and distributed in the summer and fall of 1990.

4. Media Outreach

Press releases are sent to targeted media outlets with each issue of English, French and Spanish network. In addition, during FY 1990, the staff responded to numerous requests for information from the media, resulting in stories in newspapers, magazines, television and radio shows in the U.S. and abroad.

5. Journalists Workshops

In 1989, following FHI's successful 1988 Francophone Africa regional journalists workshop in Senegal, FHI received requests to train health journalists in Pakistan (regional), Indonesia, Turkey, Zambia, Bangladesh and Kenya (regional). These requests were followed in 1990 with additional requests from Sri Lanka, Tanzania and Malawi. The journalists workshops, part of a larger technical assistance program, are designed to address the need for accurate, up-to-date information on family health, particularly as new research findings add to the base of family health information. They aim to (1) increase health journalists' knowledge of reproductive health issues, (2) improve their journalism skills including a greater use of multiple sources and more investigative and feature reporting and (3) develop strategies for providing regular coverage of family planning and other important reproductive health issues.

a. Anglophone East and Southern Africa Journalists Workshop

FHI conducted a two-week regional workshop for 24 Anglophone East and Southern African print journalists in Kenya from June 25 - July 6, 1990. The African Council on Communication Education, with its expertise in communications and training and chapters in 33 countries, cosponsored the workshop and collaborated on the training needs assessment (conducted in January 1990), curriculum development, implementation and evaluation of the training. Regional representatives of the Pathfinder Fund also contributed to the needs assessment by reporting on the relations between the medical community and journalists in a number of the represented countries.

Through the needs assessment, a curriculum was developed to address specific problems which inhibit regular and accurate reporting of family planning and other reproductive health issues. The journalists, representing eight countries, participated in a workshop that employed a participatory, competency-based approach, requiring them to practice new skills and use new knowledge gained throughout the training. The primary training methodologies included presentations, discussion, role play, site visits, small group problem solving, individual writing and group critique of the participants' family planning articles. Additionally, three participants who are employed in journalism training institutions discussed the issues and approach to health journalism training presented in the workshop and made plans for replicating the training in their respective countries.

Participants demonstrated gains in family planning and reproductive health knowledge, as measured by pre and post tests, and in their research and writing skills, as shown in pre and post writing samples. Further, they expressed greater confidence in approaching members of the medical and research communities for information and a higher level of motivation to write about family planning and other family health issues. Follow-up plans include collaboration with several regional journalist trainers to monitor the family health articles written by participants and the coverage of health issues in the press in 4 of the countries represented at the workshop. Requests for training or technical assistance in 3 of the countries are being explored.

b. Indonesian Journalists Workshop

At the request of BKS PENFIN, FHI worked collaboratively with their staff and with PWI, the Indonesian Journalists Association, to develop a five-day health journalist workshop. The 21 participants represented the major Indonesian newspapers and magazines and were assigned by their publications to report on health. The workshop was held in Bandung, Indonesia, August 27-31, 1990. It was conducted in Bhasa Indonesia since this is the language used in all major Indonesian publications and since Indonesian journalists are, for the most part, not proficient in English.

A training needs assessment was collaboratively conducted in March, 1990 and was the basis of the curriculum, which employed participatory methods and a competency-based design. Knowledge of family planning, STDs, AIDS and safe motherhood increased, as did the accuracy and readability of

articles written about these topics, as evidenced by a comparative evaluation of the first article and its revision and pre and post test results. Over 20 articles about family planning and safe motherhood appeared in the local papers within days of the workshop, demonstrating the potential for a wider dissemination and understanding of research findings.

Due to the country-specific nature of this workshop, the training was also able to promote the building of relationships between the medical and research communities and the journalists and to open a dialogue between the two groups to a greater degree than had previously existed. The geographical areas represented by the journalists coincide with BKS PENFIN center locales, making it more feasible for them to stay informed about current research in family planning and safe motherhood. These participants, like their counterparts in Africa, also expressed an increased confidence and motivation for reporting on health issues.

6. Special Publications

a. Indonesia: Maternal and Child Health Monograph

For many years BKS PENFIN's centers collected information on obstetric care and infant outcomes, utilizing FHI's maternity care monitoring forms and local data processing capacity. While a few articles were published on some of the data, a simple comprehensive treatment of the major findings was lacking. During the past year, the BKS PENFIN--with assistance from FHI--completed an Indonesian language monograph on the

data. The final product is highly graphic and pictorial, drawing on the chartbook format.

FHI funded the printing and distribution of 1,000 copies to BKKBN, the Ministry of Women's Affairs, Ministry of Health and targeted health providers. If there is sufficient demand, BKS PENFIN intends to print additional copies and sell them to individuals or organizations upon request.

7. Special Meetings

FHI organized a conference November 16-17, 1989 in Washington, D.C. to explore the implications for funding family planning services in the 1990s. On the first day, about 30 academics examined findings from a recent study showing the beneficial socioeconomic effects of fertility decline in Thailand. The study was begun in 1987 by the Institute for Population Studies of Chulalongkorn University in Bangkok, with support from FHI and UNFPA.

On the second day, a larger group discussed both the Thailand findings and a recent FHI study of family planning service costs in a sampling of developing countries in the three world regions. Estimates were given of the funding needed to support family planning activities in order to attain moderate population growth in the 1990s. About 67 persons attended the second day, including representatives from A.I.D., donor agencies, Congressional staffs and the media.

8. International Journal of Gynecology & Obstetrics (IJGO)

FHI is providing 300 IJGO subscriptions to overseas colleagues this year. A thorough review was conducted to ensure distribution of the Journal to those persons in the field who have the greatest need. Comments received from recipients indicate that the Journal continues to be a vitally important source of up-to-date information. IJGO is the only journal of its kind that is geared toward a Third World audience.

9. Translation Program

FHI has completed the second year of its Scientific Articles Translation Program. A total of 22 articles and papers were translated into French and/or Spanish, and distributed to 1,000 readers in Latin America and Francophone Africa. These include 15 articles (six in Spanish and nine in French) on postpartum contraception, which were also distributed at FHI's International Conference on Postpartum Contraception in Mexico City in September.

10. Library and Information Services

Two of the most important objectives of FHI's information dissemination program are (1) to disseminate information on reproductive health topics, especially controversial topics, such as breast cancer and OCs, to policymakers, health care providers and journalists, and (2) to develop and transfer the technology to provide access to research literature to FHI staff and collaborating investigators.

In this reporting period, the library staff have worked toward these objectives by carrying out the activities described below.

a. Dissemination of Duplicate Books

The library shipped duplicate journals and books to Chile and to the Asia Foundation for distribution to developing country institutions. Others were distributed through the Association of Population/Family Planning Libraries and Information Centers-International Duplicate Books program.

b. Dissemination of Current Awareness

Current Awareness, the FHI library publication containing the tables of contents of the major journals received in the library is being distributed to 15 individuals at FHI and elsewhere. An abridged version covering 37 titles is being sent to nine Family Health Research Centers throughout the world.

c. Operations Research Collection Created

Special files in Operations Research, country information, and organization information were organized and made available to the staff.

d. FHI Scientific Articles Reprint Series

The FHI reprint mailing list grew to 1100 names; the AIDSTECH-supported AIDS information packet mailing of English material grew to 900 names and the French AIDS mailing to 250 names.

VI. MATERIALS TECHNOLOGY DIVISION

The various projects in the Materials Technology Division (MTD) are organized under two broad programs, development of a plastic condom and quality surveillance of latex condoms. In the plastic condom program, FHI is seeking to demonstrate the technical and economic feasibility of producing inexpensive condoms, of novel design, that will resist deterioration during storage, provide adequate safety and efficacy, and offer the necessary aesthetic qualities to assure widespread consumer acceptance. FHI has found that heat-sealed polyurethane films offer the most promise for meeting these requirements. Diverse activities relating to this product are conducted in the MTD and in other divisions as well.

The quality surveillance program consists of a range of projects that not only include the retrieval and physical testing of condoms from sites overseas, but also involve research activities that are intended to validate the relevancy of current physical test methods, and to investigate the deterioration of latex condoms under various conditions. A series of human use studies designed to correlate condom breakage in use with results from physical tests also is a part of this program. Activities in other FHI divisions relating to these programs are coordinated with MTD.

A. DEVELOPMENT OF A PLASTIC CONDOM

Major efforts are being devoted to process development, machinery design and construction, condom fabrication, and product testing and evaluation. Earlier in the year, condoms were fabricated on moderate-volume production machinery at Guard Associates, Inc., of Denver, Co., and were used in laboratory and functionality testing. More recently, a small, semi-automatic heat-sealing machine was constructed locally and is now used at FHI to make prototypes for further testing. In addition, refinements of the product are still in progress. Because of some comments offered by users participating in expanded consumer preference studies last spring, softer materials, new processing conditions, and design modifications have been incorporated into the program.

1. Materials and Research Development

The characterization and evaluation of polyurethane films have encompassed a major portion of activities in this area. Films of Elastollan^R 1185A have been obtained from a new source to replace the expensive premium products that were used initially. In addition, a softer grade of Elastollan^R, other polyurethanes, and some novel blends of polymers have been produced. All are softer than the earlier Elastollan^R films. The uniformity of the new films has been assessed by capacitance measurements, both laterally (across the film), and longitudinally (in the machine direction). Condoms made from these products have been evaluated in airburst tests. The results show that most of these films form strong heat seals. The airburst volumes or pressures generally equaled or exceeded the values obtained for condoms made from earlier versions of Elastollan^R.

In addition to the work on the new films, a second design also is under investigation. This design is a "roll-on" condom that has some novel features to it. The condom undergoes an additional processing step that makes the plastic film thinner and softer. This new prototype is the subject of two patent applications that will be filed in late 1990.

2. Process Research and Development

The process research and development aspect of the project includes work on "debugging" and refining the heat sealing process. It lays the foundation for, and provides a transition to, the large-scale manufacturing process.

Considerable work was done to determine the need for supporting material for the polyurethane as it goes through the heat-sealing process. Release liners of various compositions and thicknesses were studied for this purpose. It was demonstrated that at low speeds, unsupported film can be heat-sealed successfully to make condoms. The ability to do this at high speed remains unproven, but will be investigated when appropriate equipment is available.

Process research and development also included work on refining the flanged condom design. Two problems have been encountered during the production of flanged condoms. The centering of the aperture at moderate speeds has proven to be a challenge and preventing the two flanges from sealing together during the manufacturing process has been difficult. Considerable progress in the first area was achieved when it was shown that a "one-strike" die that cuts and seals the condoms in one step could be used. With regard to the flange, however, considerable work remains to

be done. Studies on the temporary insertion of inert materials between the flanges during the sealing process are in progress. Many different materials have been tried, including silicone coated papers, aluminum foil, wax paper, and polyester film. Work in this area continues.
As mentioned above, a small, semi-automatic heat-sealing machine has been purchased by FHI. This provides the capacity to conveniently produce samples for physical testing, and consumer preference studies.
Furthermore, a pilot study on the various parameters that might affect the strength of heat seals has been completed. Elastollan^R condoms were heat-sealed under different die temperatures, pressures, and duration of contact. Although there are optimum sealing conditions, small variations in the process had little effect on the air-burst volumes or air-burst pressures of these condoms. Thus, the heat-sealing of Elastollan^R films is a robust process that is not affected by minor variations in the sealing conditions.

3. **Packaging**

Nine packaging material candidates were tested for resistance to heat, humidity, and solvents. These include various forms of metallized and non-metallized polyethylene, polyester/polyethylene, polyester/EVA, and polyester/polyolefin. The preferred material is a metallized polyester/polyethylene laminate, providing the best balance of properties, with the possible exception of cost. Other materials are being investigated. The following is a compilation of the packaging films investigated, listing the packaging films, their respective manufacturers, composition and acceptability.

Packaging Material	Composition	Acceptability
Elkay "zip-lock"	polyethylene	-very difficult to open -unattractive
Commercial	polyethylene	+excellent heat-seal and barrier properties +medical grade -poor tearability
Packaging Ind. Inc.	metallized polyester/ adhesive/EVA	+excellent heat-sealing and tearability +medical grade -lubricant diffuses through EVA causing delamination
Packaging Ind. Inc.#17820	metallized polyester gold ink/2 part adhesive/ polyethylene	+excellent heat-sealing and tearability +medical grade -water causes delamination
Packaging Ind. Inc.#17670	metallized polyester co-extruded polyethylene gold ink/primer	+excellent heat-sealing and tearability +medical grade -water can attack primer -minor delamination
Riley & Greer #N502-305	polyester/adhesive vacuum deposited metallized black olefin	+high heat-seal +excellent tearability +very tough under all tests +medical grade
WebTech Inc.	polyester with anti-static additive/ polyethylene	+excellent seal and tearability +aesthetic appeal -not FDA or medical grade
American Can E-16022-90 A	metallized polyester LDPE based sealant	+excellent seal +resistant to high heat humidity, etc.
E-16022-90B	" " " "	+food grade +quantity available ~reasonable tearability

For the construction of packages, a die was fabricated to make three-side-sealed pouches. After condoms are inserted, and lubricant is added, the packages are closed with a bag sealer and notched for easy opening.

Various forms of the package itself were considered, including rigid cases, tear apart wrappers, pop open pouches, packages which become donning aids, and tearnotch packs, the latter being the preferred configuration. In addition, concepts were explored for using the package material as a carrier/flange-separator in the manufacturing process to save costs.

Various methods/configurations for forming or otherwise compressing the condoms to fit within suitable packages have been explored. Packaging machinery to form and insert the condoms into these various package designs has been conceived, prototyped, and evaluated. Rolling flat, rolling in conventional condom fashion around a ring, random folding, and zigzag fan folding have been considered. The latter approach is now preferred, with the simplest form of packaging apparatus being "stuffing box" devices. The apparatus has been demonstrated and is now available in hand-powered and pneumatic powered versions. We plan to add film roll feed/seal/die-cut features in order to produce a semiautomatic packager.

4. Physical Testing

The standard physical test methods for latex condoms are inappropriate for plastic condoms. For example, the plastic condoms will not hold 300 ml of water as required for the leakage test, their elongation at break and volume at burst fall far below the requirements for latex, and their

pressure at burst is several times greater than that for latex. The task then is to show that the data outside the normal range of values for latex still are meaningful for predicting reliable performance in use. The standard physical tests are being conducted with plastic condoms of various thicknesses, and the data from the stress-strain curves are being analyzed in various ways in an effort to derive meaning.

One of the standard tests for latex condoms is the standard ASTM test for tensile strength. Polyurethane films perform quite well in this test relative to latex. This test, however, is inappropriate for the FHI plastic condom because it requires cutting a ring specimen out of the condom which compromises the integrity of the heat seal. Plastic condoms tested in this manner tear at the seal. Preliminary studies of a new test, referred to as the "frontal burst test", indicate that the intact, heat-sealed plastic condom is as strong or stronger than the latex condoms. In this test, a mandrel is pushed into the condom with increasing force until it breaks through the closed end. The condoms typically do not break at the seams. This test is considered by MTD to be a suitable, and perhaps more relevant, substitute for the standard tensile test.

Plastic condoms have been subjected to the air burst test. As expected, the data show that plastic condoms do not hold nearly as much air as latex condoms (approximately 6 vs. 25 liters) but will withstand much higher air pressures before bursting (approximately 5 vs. 2 kPa).

In collaboration with Research Triangle Institute, FHI has developed a water-burst test, in which water rather than air is used to inflate a condom. This is not intended as a substitute for the air burst test as a quality assurance test, but rather as a research tool to elucidate how various defects may affect condom breakage.

The measurement of the number and sizes of pores is of paramount importance within the physical testing area. A project was undertaken at Research Triangle Institute that used airborne particles as condensation nuclei for pore-size measurement. Because of an artifact caused by a shortcoming in the test apparatus, the data produced are equivocal. In April, representatives of FHI and CONRAD visited the Mariposa Foundation and met with the Physical Testing labs of the Food and Drug Administration to learn more about their work using fluorescent polystyrene beads. Based upon this meeting and subsequent discussions, Dr. Bruce Voeller of the Mariposa Foundation has written a protocol for porosity testing. It is currently being modified and will be implemented in late 1990.

5. Preclinical Biocompatibility and Safety Testing

Condoms made from Elastollan[R] 1185A were sent to North American Scientific Associates (NAmSA) for preclinical biocompatibility and safety testing. Where appropriate, all tests are performed under Good Laboratory Practices. The following list show the tests that are completed:

Physico-Chemical Tests	Completed
Mutagenicity, Ames Test	Completed
USP Systemic Toxicity	Completed

USP Intracutaneous Toxicity	Completed
Sensitization Patch (Buehler)	Completed
USP Muscle Implant (90 Days)	Completed
Vaginal Irritation with Histopathology	Completed

The above represent the complete battery of tests necessary to satisfy FDA requirements for preclinical safety tests. The condoms have passed all completed tests.

B. QUALITY ASSURANCE OF LATEX CONDOMS

The efforts of the MTD in surveying and assuring the quality of USAID latex condoms have increased substantially over the past year. In addition to hiring new staff and expanding our own internal testing capabilities, MTD has moved several large studies forward to the point where they will be implemented in early Fiscal Year 1991.

1. Field Evaluations

FHI embarked on an aggressive plan for 1990 in which field surveys were performed in Jamaica, Egypt, Nepal, Tanzania, Mexico, Guatemala, and Kenya.

Condom distribution systems and storage conditions vary considerably and continue to be of major concern. In many systems, shipments are not properly inventoried to FIFO standards, which inhibits proper distribution according to age. Shipping cases sometimes are damaged during transit which often ultimately affects the product when stored for long periods under sub-standard conditions.

Complaints from the field have steadily increased, prompting numerous requests for special sampling and testing to support stock management efforts. Reports of prolonged storage in customs warehouses or of adverse storage with direct exposure to the elements have prompted the testing of condom stocks before their acceptance into distribution programs. Because of FHI's growing presence in the testing area, our services are more in demand. The table below summarizes FHI's work in this area during Fiscal Year 1990.

COUNTRY	DATE SAMPLED	AGE	#LOTS	#DEFECTIVE
Zaire	Sept. '89	3-90	12	1
Jamaica	Nov. '89	4-64	27	13
Egypt	Jan. '90	4-32	15	2
Nepal	Feb. '90	6-60	15	6
Barbados	Mar. '90	16-57	10	5
Zambia	Apr. '90	6-45	13	4
Tanzania	May '90	9-11	3	0
Mexico	Aug. '90	6-42	5	0
Guatemala	Aug. '90	7-35	7	3
Kenya	Sept. '90	6-15	7	1

The result of these evaluations has led to the establishment of guidelines for future assessment and disposition of potentially defective stocks. These guidelines are intended to limit many of the programmatic problems that may result from condom stock rejections. The Condom Quality Index (CQI), developed by PATH, is now being used to determine the level of condom acceptability.

2. Research and Development

Several projects have been undertaken to enhance the understanding of condom use and testing. Two projects worthy of note are the development of a Waterburst Test that may more closely simulate actual use conditions than the airburst test, and the development of an Artificial Accelerated Aging method using gamma radiation.

FHI has collaborated with Research Triangle Institute in the design of a water burst apparatus that will evaluate condoms in a moist environment where conditions similar to actual use conditions can be controlled (ie: temperature and pH). The apparatus consists of a constant temperature water bath in which the condom is inflated to burst with water at a constant flow. Pressure and volume measurements are taken continuously during the inflation cycle. The preliminary results indicate that the pressure experienced by the condom during water inflation may be more indicative of product quality than volume measurements generated in the airburst test. Although this is not intended to be a quality assurance test, these data will be compared with airburst and tensile test data and all will be considered relative to actual use conditions.

FHI, in collaboration with Ansell, has completed a second trial of artificially aging condoms by gamma irradiation. The study involved exposure of condoms to radiation dosages ranging from 10 to 40 megarads to determine the level at which appreciable degradation of the latex

structure becomes apparent. The study revealed, in comparison with base-line data, dramatic lowering of mean tensile and elongation values beginning with the 20 megarad level and decreasing as the dosages intensified.

Presently, the irradiated samples are being tested by infrared spectrophotometry to evaluate chemical bond changes which have occurred during each exposure level. During natural aging, the molecular structure of condoms is altered by disrupting the normal latex structure, making it weak and less elastic. If similar changes are evident in the irradiated samples, this method could be useful in providing samples of target "ages", and could lead to studies that would determine the critical point(s) in the life cycle when condoms become unacceptable for normal use. For comparative purposes, the standard ASTM oven aging method also is being performed.

3. Natural Aging of Condoms

In a prospective study to examine the natural aging of condoms, new condoms will be placed in specific climatic and storage conditions in Mexico for a five year period. Three U.S. manufacturers' formulations will be included, consisting of samples lubricated with either silicone or non-aqueous N-9, and packaged in either plastic or foil. Samples will be withdrawn periodically for laboratory testing to determine the rate of deterioration and for human use studies to help relate the physical data to the breakage-in-use data. The protocol for the study has the approval of HIMA which represents the participating manufacturers. Shipment of the condoms to the study sites will take place in October, 1990.

4. Production Surveillance

The information that has been gathered through our field surveys and complaint evaluations has increased the importance of assuring the quality of the product coming from the producers. The possibility that condoms are adversely affected during shipping or temporary storage in customs warehouses also needs to be addressed. Beginning in Fiscal Year '91, FHI will conduct monthly quality audits of production at Ansell and Aladan manufacturing sites and will implement a monitoring program for shipping.

In preparation for implementation of a production surveillance program, a referee laboratory that would be acceptable to both the manufacturers and FHI had to be identified. This was accomplished through an extensive four month inter-laboratory study designed to assure comparability in test results. Akron Rubber and Development Laboratory was accepted as the referee laboratory.

Although the quantity of testing necessary to verify compliance to contract requirements initially was of concern to both USAID and the manufacturers, it was felt that the inconveniences of cost and time lost were appropriate and necessary to properly address the quality issues surrounding condom distribution. USAID decided that between 5% and 10% of the lots produced will be examined monthly for compliance testing. In addition, test data on all lots produced may be used for dissemination to the field for use in effectively monitoring stocks.

5. Condom Breakage During Human Usage

During the past year, a pilot study of condom breakage during human use was initiated. This study was intended to provide preliminary data on the correlation of physical laboratory and breakage-in-use data. The table below provides an interim analysis. The airburst volume data on the three lots of condoms are represented by the Condom Quality Index (CQI). CQI values normally range from 0-100, with values below 20 being considered as unacceptable.

BREAKAGE OF CONDOMS DURING VAGINAL INTERCOURSE

LOT NO.	CQI	PERCENT BREAKING[a]
1	16	16
2	<1	28
3	21	12

[a] Data from 111 couples each using 2 condoms of each lot.

These data suggest that the cut off for unacceptable airburst values may be higher than originally thought.

The expanded follow-up study in which 300 couples will be recruited to use condoms from 20 different lots will be initiated in October, 1990. Each couple will use one condom from each of the lots. Lots were chosen based upon their CQI and span the entire range of possible values. Most were recovered from warehouses overseas and fall in the mid-range of CQI values of 20-60.

FUTURE PLANS

All aspects of the plastic condom project will be active in Fiscal Year '91. It is anticipated that a softer second generation material for the flange condom will be chosen by January. At that time, if results are encouraging, a large-scale consumer preference study will be initiated. The problems encountered in manufacture will continue to be studied.

Work will continue on the roll-on design as well. The softening process will be refined and a prototype machine to accomplish this task will be built.

Lubricants and packaging materials will be selected and the packaging method will be refined for both designs. In addition, studies on the biocompatibility/safety testing will be completed in February 1991. Studies on the porosity of the polyurethanes will be initiated early in Fiscal Year '91.

In the quality assurance of latex condoms, future plans encompass work in all five areas of the program. Surveys of condom stocks will be directed to problem areas where stocks are not well maintained and condom usage is not well defined. Special emphasis will be placed on the establishment of in-country quality monitoring programs in countries with qualified personnel and testing facilities. Bilateral funds for this work will be sought whenever possible. The Production Surveillance Program will begin in October, 1990, and will provide assurances that USAID is providing quality condoms to the developing world. This program will enable FHI to assess the level of condom quality at the point of manufacturing as well as any changes that may occur during transit, or in storage overseas.

The continued testing of condoms for breakage during vaginal intercourse represents an important component of the program. The large study described above will correlate physical test results and CQIs with breakage in use. Of particular importance is the clinical performance of those condom lots that pass or fail standard tests by marginal levels. More troublesome, however, are lots that fail one test method, but pass another. Future studies will examine baseline data on condom breakage under ideal conditions and also will examine the effects of different lubricants on breakage during human use.

The Prospective Aging Study of condoms placed in Mexico will be initiated in early Fiscal Year 91. Activities for the rest of the year on this project will involve two trips to gather samples for physical testing.

Research and development projects will continue work on the water burst phenomenon and on gamma irradiated condoms. In addition, development of simple physical tests of condoms that can be used in the field will be explored.

VII. Regulatory Affairs

The development and investigation process for new drugs and devices is regulated by the U.S. FDA and other regulatory agencies worldwide. The Regulatory Affairs Division of FHI oversees and ensures FHI's compliance with its regulatory obligations throughout this process.

To this end, guidance is provided to all FHI divisions regarding their responsibilities in complying with current Good Clinical Practices (GCP), Good Laboratory Practices (GLP), and Good Manufacturing Practices (GMP). Other specific activities of the Regulatory Affairs Division include assembling and maintaining the various regulatory instruments used for: 1) securing approval to evaluate investigational new drugs and devices, 2) securing U.S. and foreign import and export approvals for drugs and devices, and 3) securing U.S. and foreign marketing approval for drugs and devices evaluated in clinical trials.

FHI currently holds the following seven Investigational New Drug Applications (INDs) and three Investigational Device Exemptions (IDEs) filed with the U.S. FDA:

- Iodine Formulation (IND #29,626)
- Norethindrone 90-Day Microspheres (IND #18,592)
- Subdermal Norethindrone Pellets (IND #17,452)
- D-Propranolol (IND #30,380)
- Quinacrine Pellets (IND #19,163)
- Norinyl 1+35 (IND #24,871)
- Gyne-T™ Postpartum IUD (IND #29,046)

- LEA's SHIELD (IDE #G860182)
- IUD String Retriever (IDE #G850227/AL)
- WPC-333 Vaginal Pouch (IDE #G890203)

These products are in various stages of clinical development. The clinical trials conducted by FHI with these products, as well as clinical trials conducted by FHI for the NORPLANT[R] Contraceptive Implant System (developed under an IND held by the Population Council) and the Filshie Clip, have been performed according to current Good Clinical Practices.

No clinical trials have been initiated under the IND for Iodine and FHI has contracted a laboratory to develop a new formulation of Iodine. It is expected that the new formulation will be more stable than the original formulation with a longer shelf-life. For the FDA to keep an IND on active status, clinical trials must commence within a certain time period. On July 27, 1990, FHI requested that the FDA place the IND for Iodine on inactive status. By placing the IND on inactive status instead of withdrawing the IND, FHI can proceed with the reformulation, file pertinent documentation with the FDA regarding the formulation, and request activation of the IND when clinical trials are imminent without having to resubmit the entire filing.

In consultation with the U.S. FDA, work is proceeding with the Filshie Clip to submit a Premarketing Approval Application (PMA) in 1991. This product approval application is unique in that it will be the "first-ever" PMA submitted to the FDA without prior submission of an IDE and the only PMA ever submitted to the FDA based solely on foreign data. All clinical trials of the Filshie Clip (which is currently marketed in England) were performed overseas. Approval of

this PMA by the U.S. FDA would be a landmark in device development and will set a precedent for future application approvals.

U.S. FDA regulations specify that all life-threatening or fatal adverse experiences and adverse experiences considered serious and unexpected that are related to the product under investigation must be reported in writing to the U.S. FDA and all participating investigators within 10 working days of notification. During the past three months, the Regulatory Affairs adverse experience data base on PC was transferred to a VAX-system data base. The establishment of this data base has expanded the capabilities of the previous system. At the same time, a new position was created in the Executive Office, a PHSC Administrative Assistant. This position reports directly to the Corporate Director of Medical Affairs. One of the functions of the PHSC Administrative Assistant is to maintain the VAX-system data base. The read and report-generation facilities of the new data base can be accessed by other divisions within FHI.

The Regulatory Affairs Division has recently expanded its scope of responsibility by interfacing with and directly supporting CONRAD in meeting regulatory responsibilities. CONRAD and FHI are cooperating to conduct a clinical trial with the WPC-333 vaginal pouch (Reality^{R} Female Condom/Wisconsin Pharmacal) under an IDE filed by FHI. The Regulatory Affairs Division of FHI is handling all regulatory matters with regard to this study. In the future, generally all regulatory matters concerning CONRAD projects will be managed through FHI's Regulatory Affairs Division.

Other divisions within FHI rely on the Regulatory Affairs Division to train and

update their staff on the current regulations and their obligations in respect to those regulations. A workshop on basic drug law is being developed by the Regulatory Affairs Division for all staff involved in conducting regulatory controlled clinical trials. Clinical trial protocols, consent forms, and other supporting documentation are reviewed routinely by the Regulatory Affairs Division. Monthly team meetings are conducted by the Regulatory Affairs Division to guide the development of NDAs for the norethindrone products and the PMA for the Filshie Clip.

Attitudes, interpretations, and regulations concerning drug and device development evolve as the body of available scientific information expands. A major factor influencing the product development atmosphere today is the emergence of the European Community (EC) and the harmonization of drug and medicinal device regulations within the EC by 1992. Worldwide changes are taking place as the U.S. FDA and Japan collaborate with the EC to harmonize their regulations. Since it takes an average of 12 years to develop a product from inception to approval, it is imperative that staff responsible for guiding a product's development keep current with this ever-changing environment. The staff of the Regulatory Affairs Division attends FDA Advisory Committee meetings and other appropriate domestic and international meetings and seminars to maintain professional contacts and to ensure their current understanding of the product development environment and regulations worldwide. This takes on even more importance as the future direction of FHI's Regulatory Affairs Division focuses on obtaining regulatory marketing approvals for products (e.g., Reality[R] Female Condom, male plastic condom) in European and developing countries.

VIII. MANAGEMENT

PROTECTION OF HUMAN SUBJECTS COMMITTEE

Four meetings of the Protection of Human Subjects Committee (PHSC) were held at FHI on November 3, 1989; February 23, 1990; June 1, 1990; and August 24, 1990 to review 65 research proposals, inclusive of amendments and those for expedited review.

Three members rotated off at the end of the calendar year: Dr. John Reed (social scientist and committee chairman for three years), Ms. Rose De Buysscher (FHI staff representative), and Dr. Betty Dennis (public health representative and former committee chair of four years).

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

Susan G. Dull, MA, Legislative Aide to Senator Joseph V. Gartland, Jr. (Fairfax, Virginia) and the Virginia Coordinator of the Chesapeake Bay Commission.

Vanessa P. Haygood, MD, private practice as an obstetrician/gynecologist in Greensboro and Medical Director of Maternity and Family Planning Services of the Guilford County Health Department.

Three new members were appointed for three-year terms:

John Gulick, PhD, Professor Emeritus of Anthropology and Fellow, Carolina Population Center, University of North Carolina, Chapel Hill. He received his Bachelor, Master and PhD (anthropology) degrees from Harvard University. Through teaching, lecturing, and field research projects (Lebanon, Iraq, Iran, Egypt and North Carolina), he has achieved a notable career in the field of anthropology. Having published extensively, he is a noted scholar and author in his field.

Susan L. McIntyre, MSW, MPH, Program Officer, Field Development & Training Division of Family Health International. She received her Bachelor of Arts degree (sociology) from Franklin and Marshall College; her Masters of Social Work and Public Health from the University of North Carolina at Chapel Hill. She travels frequently to the Asian Region as part of her management duties. As one of the first participants in the University of Michigan's Population Service Fellowship Program, she was assigned to an Indonesian foundation as Program Development Manager from 1985-86.

Donald E. Maynard, PhD (Ex-officio/non-voting), Director, Regulatory Affairs of Clinical Research International, Durham. He received his Master of Science (chemistry) degree from the University of Kentucky and his PhD (biochemistry) from Ohio State University. His 25 years of experience in the pharmaceutical industry include former affiliations with Glaxo, Incorporated, the Revlon Health Care Group, and Hoffman-La Roche. Through his experience with the pharmaceutical industry, he has gained considerable knowledge in regulatory matters.

Appointed as Chair and Vice Chair of the Committee, respectively, were Drs. Dennis Campbell and Vanessa Haygood.

Mr. Steven Shaber of the Committee and Carol Connell of the Regulatory Affairs Division attended the PRIM&R (Public Responsibility in Medicine & Research) Conference, Whither IRBs in the 1990s?: New Directions and New Decisions, held October 12/13, 1989 in Boston, Massachusetts. The primary purpose for attending this conference was to obtain regulatory updates from the National Institutes of Health, the Office for Protection from Research Risks, and the FDA concerning the Final Rule for dealing with and reporting scientific misconduct allegations, pending guidelines on conflict of interest, and the new Federal policy or Common Rule for the protection of human subjects.

Ms. Susan McIntyre of the Committee (FHI staff representative) attended the NIH/FDA Regional Workshop on Protection of Human Subjects - Bioethical Issues, held July 19/20, 1990 in St. Louis, Missouri.

The Committee adopted a Declaration Statement regarding Conflicts of Interest, prepared by FHI's Corporate Attorney, which will be submitted annually to the committee members for signature.

EXPERT MEETING: ORAL CONTRACEPTIVE COMPLIANCE

The oral contraceptive (OC) has been used by millions of women worldwide for 30 years. While the pill has the lowest failure rate of any reversible method of contraception when taken as prescribed, the non-compliance rates are frequently high, especially in developing countries where little is known about how the pill is used. The Program Evaluation Division organized an expert meeting on Oral Contraceptive Compliance, held July 18, 1990, aimed toward identifying gaps, setting priorities and recommending designs for research on OC compliance. Among the 13 participants were representatives from the AID/Office of Population (Dorflinger), US/Food & Drug Administration (Corfman), two members of FHI's Technical Advisory Committee (Droegemueller and Shain) and two members of FHI's Board of Directors (Klein and Senanayake). The priorities designated by the assembly were:

- Standardizing pill-use instructions;

- Behavioral research focused on the specific errors of OC consumers.

The FDA's Supervisory Medical Officer for Fertility and Maternal Health Drugs applauded FHI's vision and efforts in this area, offering to schedule a public meeting of the Fertility & Maternal Health Advisory Committee on standard labeling for OCs, which was confirmed by letter on July 23, 1990. FHI was asked to assume the lead in organizing the presentations and working with the FDA's Supervisory Medical Officer for Fertility & Maternal Health Drugs in developing the agenda.

TECHNICAL ADVISORY COMMITTEE

The Technical Advisory Committee (TAC) held its annual meeting at FHI on Thursday, July 19, 1990. Seven of the eight committee members were present.

Ten observers attended the 1990 TAC meeting:

Dr. Jose Barzelatto, Ford Foundation;

Dr. Gabriel Bialy, Contraceptive Development Branch, National Institute of Child Health & Human Development;

Dr. Arthur Christakos, Department of Obstetrics/Gynecology, Duke University Medical Center, who represented FHI's Board of Directors;

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

Dr. Mahmoud Fathalla, Special Programme of Research, Development and Research Training in Human Reproduction, World Health Organization;

Dr. Henry Gabelnick, Extramural Programs, CONRAD Program;

Dr. Luella Klein, Department of Gynecology/Obstetrics, Emory University School of Medicine, who represented FHI's Board of Directors;

Dr. Carolyn Makinson, Mellon Foundation;

Dr. Pramilla Senanayake, International Planned Parenthood Federation, who represented FHI's Board of Directors;

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

Drs. Deborah Anderson and Jorge Martinez Manautou have been reappointed to the Committee for three-year terms (1990-93).

BOARD OF DIRECTORS

The Board of Directors held two meetings:

Spring meeting, April 29/30, 1990 (Colorado Springs, Colorado);

Annual meeting, September 21-24, 1990 (FHI and Research Triangle Park, North Carolina).

Six incumbent Directors were re-elected:

Gen. Alexander B. Andrews - Attorney-at-law and US Air Force (ret.), Raleigh, NC;

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

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

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

Roger Short, ScD, FRS - Professor, Department of Physiology, Monash University; Clayton, Victoria, Australia;

R. Peyton Woodson, III - Woodson Associates, Raleigh, NC.

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

David W. Barry, MD - Vice President of Research, Development & Medical, The Wellcome Research Laboratories, Burroughs Wellcome Company, Research Triangle Park, NC;

American Ambassador Nancy Ostrander - Former Ambassador for Population Affairs (retired), Indianapolis, IN.

The two new Directors filled two vacant seats left by the resignation of Dr. Halfdan Mahler and the decision of Dr. William Hubbard, Jr. to step down following nine years of service. All 15 seats on FHI's Board have been filled.

A new vice presidential corporate office, Vice President of Product Management, was established.

Appointed as Corporate Officers were the following:

Dr. Torrey Brown, Chair

Dr. Pramilla Senanayake, Vice Chair

Dr. Malcolm Potts, President/COO

Mr. William Schellstede, Senior Vice President

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

Dr. Howard Miller, Vice President of Product Management

Mrs. JoAnn H. Lewis, Vice President of Programs

Dr. Arthur Christakos, Secretary

Mrs. Marie F. Porter, Assistant Secretary

Mr. Peyton Woodson, III, Treasurer.

The following Directors were appointed as observers (1990/91) to FHI's external advisory committees:

Dr. Arthur Christakos - Protection of Human Subjects Committee

Dr. Pramilla Senanayake - Technical Advisory Committee

Dr. Luella Klein - Latin American Advisory Committee

The Board of Directors voted to charter a satellite Foundation, controlled by its own Board of Trustees (seven Trustees of which five will represent FHI's Board of Directors) for the sole purpose of increasing funds for FHI.

A. PUBLICATIONS LIST

FAMILY HEALTH INTERNATIONAL

Annual Publications Listing
October 1, 1989 - September 30, 1990

89-34 R Rivera, JR Gaitan, R Ruiz, DP Hurley, M Arenas, C Flores, AB Hernandez. **Menstrual Patterns and Progesterone Circulating Levels Following Different Procedures of Tubal Occlusion.** Contraception 40(2):157, 1989.

89-35 T Khan, KI Kennedy, A Kazi, M Steiner. **A Study of Breastfeeding and the Return of Menses and Pregnancy in Karachi, Pakistan.** Contraception 40(3):365, 1989.

89-36 NE Williamson. **Breastfeeding Trends and Patterns.** Int J Gynecol Obstet, Suppl. 1, p. 145, 1989.

89-37 G Savina, KI Kennedy. **The Effect of a Breastfeeding Education Program on Lactational Amenorrhea in the Philippines.** Stud Fam Plann 20(4):203, 1989.

89-38 HW Perera, M Steiner, KI Kennedy, R Snowden. **Perspectives of Physicians in Sri Lanka on Periodic Abstinence.** Ceylon Med J 34(2):87, 1989.

89-39 GS Grubb, A Coker. **Re: Condylona and the Intraepithelial Neoplasia of the Uterine Cervix: A Case-Control Study.** Am J Epidemiol 130(2):427, 1989.

89-40 V Orense, M Steiner, KI Kennedy, R Snowden. **Perspectives of Physicians in the Philippines on Periodic Abstinence Methods of Family Planning.** J Philippine Med Assoc 65(2):216, 1989.

89-41 M Potts. RU-486: **Termination of a Pregnancy in the Privacy of One's Home.** NCMJ 50(10:531, 1989.

89-42 I Chi, LR Wilkens, DS Gates, PR Lamptey, T Petrick. **Tubal Ligation at Cesarean Delivery in Five Asian Centers: A Comparison with Tubal Ligation Soon After Vaginal Delivery.** Int J Gynecol Obstet 30(3):257, 1989.

89-43 RD Retherford, MK Choe S Thapa, BB Gubhaju. **To What Extent Does Breastfeeding Explain Birth-Interval Effects on Early Childhood Mortality?** Demography 26(3):439, 1989.

89-44 I Chi, LR Wilkens, CB Champion, RE Machemer, R Rivera. **Insertional Pain and Other IUD Insertion-Related Rare Events for Breastfeeding and Non-breastfeeding Women--A Decade's Experience in Developing Countries.** Adv Contracept 5(2):101, 1989.

89-45 M Potts, RV Short. **Condoms for the Prevention of HIV Transmission: Cultural Dimensions.** AIDS 3(Suppl 1):S259, 1989.

89-46 JA Fortney. **Contraception for Women Over Forty.** In: Menopause: Evaluation, Treatment, and Health Concerns, CB Hammond, FP Haseltine, I Schiff, Eds., (New York: Liss, 1989), p. 41.

89-47 H Mahler. **AIDS Battle Must Be Waged.** Med Tribune, October 26, 1989, p. 20.

89-48 M Potts, S McIntyre. **Efficacy of Barrier Methods in Contraception.** In: Adv Gynecol Obstet: Proceedings of the 12th World Congress of Gynecology and Obstetrics, Rio de Janeiro, October, 1988, Vol. 1, Fertility, Sterility and Contraception,
P Belfort, JA Pinotti, TKAB Eskes, Eds., p. 279.

89-49 MF McCann, AV Moggia, JE Higgins, M Potts, C Becker. **The Effects of a Progestin-Only Oral Contraceptive (Levonorgestrel 0.03 mg) on Breast-feeding.** Contraception 40(6):635, 1989.

89-50 B Kass-Annese, KI Kennedy, K Forrest, H Danzer, A Reading, H Hughes. **A Study of the Vaginal Contraceptive Sponge Used With and Without the Fertility Awareness Method.** Contraception 40(6):701, 1989.

89-51 B Israngkura, KI Kennedy, B Leelapatana, HS Cohen. **Breastfeeding and Return to Ovulation in Bangkok.** Int J Gynecol Obstet 30(4):335, 1989.

89-52 R Guzman-Serani, G Rosa. **Evaluation of the Femtest Device Pre- and Post-Sterilization.** Contraception 40(1):49, 1989.

89-53 NT Raoof, RM Pearson, P Turner. **Lithium Inhibits Human Sperm Motility In Vitro.** Br J Clin Pharmacol 28:715, 1989.

89-54 AE Omu, S Weir, B Janowitz, DL Covington, PR Lamptey, NN Burton. **The Effect of Counseling on Sterilization Accceptance by High-Parity Women in Nigeria.** Int Fam Plann Perspect 15(2):66, 1989.

89-55 B-ML Harris, G Eklund, O Meirik, LE Rutqvist, K Wiklund. **Risk of Cancer of the Breast after Legal Abortion During First Trimester: A Swedish Register Study.** BMJ 299:1430, 1989.

89-56 PJ Feldblum, MJ Rosenberg. **A Historical Perspective on Condoms.** In: Condoms in the Prevention of Sexually Transmitted Diseases, Proceedings of a Conference, Atlanta, Georgia, February 1987, (Research Triangle Park, NC: American Social Health Association, 1989), p. 1.

89-57 M Potts. **Using Controversy to Promote Condoms.** In: Condoms in the Prevention of Sexually Transmitted Diseases, Proceedings of a Conference, Atlanta, Georgia, February 1987, (Research Triangle Park, NC: American Social Health Association, 1989), p. 57.

89-58 A Tsui, S Thapa, D Hamill, V de Silva. **Contraceptive Method Change Among Rural Sri Lankan Women.** J Biosoc Sci Suppl 11:133, 1989.

89-59 JR Kahn, S Thapa, KHW Gaminiratne. **Sociodemographic Determinants of Contraceptive Method Choice in Sri Lanka: 1975-82.** J Biosoc Sci Suppl 11:41, 1989.

89-60 S Thapa, V de Silva, MG Farr. **Potential Acceptors of NORPLANT Implants in Comparison with Recently Sterilized Women in Sri Lanka.** Adv Contracept 5(3):147, 1989.

89-61 I Chi, MG Farr. **Review Article: Postpartum IUD Contraception--A Review of an International Experience.** Adv Contracept 5(3):127, 1989.

89-62 RD Retherford, S Thapa V de Silva. **Strength of Fertility Motivation: Its Effects on Contraceptive Use in Rural Sri Lanka.** Asia-Pacific Popul J 4(4):21, 1989.

89-63 A Tsui, V de Silva, S Thapa. **The Dynamics of Traditional Contraceptive Use: The Role of Fertility Awareness and Coital Behavior.** In: Proceedings of the International Population Conference, New Delhi, September 20-27, 1989, Vol. 1 (Belgium: International Union for the Scientific Study of Population, 1989), p. 255.
89-61 I Chi, MG Farr. **Review Article: Postpartum IUD Contraception--A Review of an International Experience.** Adv Contracept 5(3):127, 1989.

89-64 P Pitaktepsombati, B Janowitz. **Contraceptive Sterilization in Thailand.** In: Thailand: Health and Population Studies Based on the 1987 Thailand Demographic and Health Survey (Columbia, MD: Demographic and Health Survey, Institute for Resource Development/Macro Systems, Inc, 1989), p. 149.

90-01 SL Klavon, GS Grubb. **Insertion Site Complications During the First Year of NORPLANT Use.** Contraception 41(1):27, 1990.

90-02 S Koetsawang, DS Gates, S Suwanichati, S Jivasak-Apimas, N-A Leckyim, D Cilenti. **Long-Term Follow-up of Laparoscopic Sterilizations by Electrocoagulation, the Hulka Clip and the Tubal Ring.** Contraception 41(1):9, 1990.

90-03 M Potts, PJ Feldblum. **Changing Behavior: Barrier Methods in High-Risk Populations.** In: Heterosexual Transmission of AIDS, NJ Alexander, HL Gabelnick, JF Spieler, Eds. (New York: Alan R. Liss, 1990), p. 69.

90-04 PR Lamptey. **Barrier Contraceptives and the Interaction Between HIV and Other Sexually Transmitted Diseases.** In: Heterosexual Transmission of AIDS, NJ Alexander, HL Gabelnick, JF Spieler, Eds. (New York: Alan R. Liss, 1990), p. 255.

90-05 R Foldesy, MG Farr, DC Thompson, DN Catotti. **Design of Clinical Studies of Spermicides for Prophylaxis Against Sexually Transmitted Diseases.** In: Heterosexual Transmission of AIDS, NJ Alexander, HL Gabelnick, JF Spieler, Eds. (New York: Alan R. Liss, 1990), p. 291.

90-06 AC Tanquary, JH Witte. **Condoms: Overview of Technology, Materials, and Development.** In: Heterosexual Transmission of AIDS, NJ Alexander, HL Gabelnick, JF Spieler, Eds. (New York: Alan R. Liss, 1990), p. 339.

90-07 V Hull, S Thapa, H Pratomo. **Breast-feeding in the Modern Health Sector in Indonesia: The Mother's Perspective.** Soc Sci Med 30(5):615, 1990.

90-08 I Chi, CB Champion, MG Farr, M Potts. **Two Clinical Trials Designed to Evaluate the Prevention of Pelvic Inflammatory Disease in IUD Users.** Infect Med Dis Let Obstet Gynecol 12(1):3, 1990.

90-09 I Chi, MG Farr, RC Dominik, N Robinson. **Do Retroverted Uteri Adversely Affect Insertions and Performance of IUDs?** Contaception 41(5):495, 1990.

90-10 NE Williamson. **Breastfeeding Trends and the Breastfeeding Promotion Program in the Philippines.** Int J Gynecol Obstet 31 (Suppl 1):35, 1990.

90-11 I Chi, UR Ko, LR Wilkens, HK Chang, JJ Nam. **Vasectomy and Non-fatal Acute Myocardial Infarction: A Hospital-Based Case-Control Study in Seoul, Korea.** Int J Epidemiol 19(1):32, 1990.

90-12 **A Penny a Day.** Family Health International, 1990.

90-13 TJ Petrick. **Ethics and the Reproductive Process.** Ginecol Obstet Mexico 58 (Suppl 1):35, 1990.

90-14 KI Kennedy. **Lactation and Contraception.** Ginecol Obstet Mexico 58 (Suppl 1):25, 1990.

90-15 ET Robinson. **Disseminating Information on Family Planning: FHI's Experience Reaching Health Personnel and the Media in Developing Countries.** In: Proceedings of the 22nd Annual Conference, APLIC International, J Vanderlin, W Barrows, Eds., Baltimore, Maryland, March 27-30, 1989 (New York: Association for Population/Family Planning Libraries and Information Centers, International, 1990), p. 19.

90-16 BP Mulhall, S Fieldhouse, S Clark, L Carter, L Harrison, RV Short. **Anti-Sperm Antibodies in Homosexual Men: Prevalence and Correlation with Sexual Behavior.** Genitourin Med 66:5, 1990.

90-17 M Potts. **Pakistan: Safe Motherhood.** Lancet 335(8694):903, 1990.

90-18 Family Health International. **Vote with Conscience** (editorial). Lancet 335(8695):943, 1990.

90-19 Family Health International. **No Regrets.** Lancet 335(8699):1188, 1990.

90-20 C Sakondhavat, L Potter. **Further Testing of Female Condoms** (letter). Brit J Fam Plann 15(4):129, 1990.

90-21 I Chi. **Vasectomy and Testicular Cancer** (letter). Brit Med J 300(6729):944, 1990.

90-22 MM Shaaban, KI Kennedy, GH Sayed, SA Ghaneimah, AM Abdel-Aleem. **The Recovery of Fertility During Breast-feeding in Assiut, Egypt.** J Biosoc Sci 22(1):19, 1990.

90-23 K Kanchanasinith, P Piyapinyo, P Pitaktepsombati, S Vibulsresth, DS Gates, B Janowitz, M Robbins. **Postpartum Sterilization by Nurse-Midwives in Thailand.** Int Fam Plann Perspect 16(2):55, 1990.

90-24 P Bailey, AO Tsui, B Janowitz, R Dominik, L Araujo. **A Study of Infant Mortality and Causes of Death in a Rural North-East Brazilian Community.** J Biosoc Sci 22(3):349, 1990.

90-25 TC de Cetina, LP Teyes, LV Gamboa, TR Dunson, AJ Rowan, C Waszak, MB Weaver. **A Comparative Clinical Trial of Norinyl 1+35 Versus Norinyl 1+50 in Merida, Yucatan, Mexico.** Adv Contracept 6(2):125, 1990.

90-26 TT Kane, MG Farr, B Janowitz. **Initial Acceptability of Contraceptive Implants in Four Developing Countries.** Int Fam Plann Perspect 16(2):49, 1990.

90-27 I Chi, MG Farr, K Thompson, M Acosta, G Alvarado, R Rivera, J Bandaragoda, JD Betancourt. **Is the Copper T 380A Device Associated with an Increased Risk of Removal due to Bleeding and/or Pain? -- An Analysis.** Contraception 42(2):159, 1990.

90-28 JA Fortney. **Oral Contraceptives for Older Women.** IPPF Med Bull 24(3):3, 1990.

90-29 Cellular and Molecular Events in Spermiogenesis, Proceedings of a Symposium Held at Oaxtepec, Mexico, 11-13 March, 1987, DW Hamilton, GMH Waites, Eds. (New York: Cambridge University Press, 1990).

90-30 K Singh, OAC Viegas, SS Ratnam. **A Three-Year Clinical Evaluation of NORPLANT in Singaporean Acceptors.** Adv Contracept 6(1):1, 1990.

90-31 K Singh, OAC Viegas, SS Ratnam. **A Three-Year Evaluation of Metabolic Changes in Singaporean NORPLANT Acceptors.** Adv Contracept 6(1):11, 1990.

90-32 K Singh, OAC Viegas, SS Ratnam. **A Three-Year Evaluation of Hemostatic Function in Singaporean NORPLANT Acceptors.** Adv Contracept 6(1):23, 1990.

90-33 Barriers and Boundaries (editorial). Lancet 335(8704):1497, 1990.

90-34 Nothing is Unthinkable (editorial). Lancet 336((8716):659, 1990.

90-35 M Potts. **The Challenge of the 1990s.** In: Proceedings of the Seminar: Public Health and Family Planning: Strategies for the Future, Canberra, November 30 - December 1, 1989 (Canberra: Australian National University, 1990), p. 5.

90-36 B Janowitz, JH Bratt, DB Fried. Investing in the Future: A Report on the Cost of Family Planning in the Year 2000, 1990.

90-37 M Potts, S Thapa. Child Survival: The Role of Family Planning, 1990.

90-38 M Potts. **The Origin of the Attitudes.** Healthright 9(3):29, 1990. Also in Proceedings of the Seminar: Public Health and Family Planning: Strategies for the Future, Canberra, November 30 - December 1, 1989 (Canberra: Australian National University, 1990), p. 49.

B. CONSULTANT REPORTS

CR LISTING (Fiscal Year '90)

CR#	Title	Prepared for	Date	Center #	Study #	Author
636	A Study of a Progestogen-Only Oral Contraceptive for Lactating Women in Fortaleza, Brazil	Dra. Sylvia Bomfim	11/89	843	8875	McMullen
637	Comparative Study of Loestrin vs. Lo-Femenal in Mexico City, Mexico	Dr. Gregorio Perez-Palacios	6/90	8594	8820	McMullen/ Dunson
638	A Study of a Progestogen-Only Oral Contraceptive for Lactating Women in Accra, Ghana	Dr. Cecil Klufio	10/89	0044	8876	Dunson
641	A Study of a Progestogen-Only Oral Contraceptive for Lactating Women in Lima, Peru	Cesar Guzman	3/90	0102	8875	Dunson/ Trottier
642	A comparative study of the Filshie Clip & Pomeroy Methods of Tubal Occlusion as used for Post Partum Sterilization.	Suporn Koetsawang	11/89	0075	6260	Burdan/Bunce
643	A comparative study of TCu 380A & the TCu 220 IUD in the Philippines	Lydia Alfonso	11/89	0061	0532	Burdan

CR#	Title	Prepared for	Date	Center #	Study #	Author
644	Evaluation of Consumer Preference, Attitudes, and Acceptance of a New Vaginal Contraceptive Device and its Potential Function at 2 US Sites	Dr. R. Blackwell, Dr. Arbogast, Carter/Wallace	12/89	0931, 0928	7807	Thompson/Alam
645	A Comparative Study of Femenal vs. Lo-Femenal in Bamako, Mali	Malian Family Planning Assoc.	2/90	0441	8890	Dunson
646	A Study of a Progestogen-Only Oral Contraceptive for Lactating Women in Jos, Nigeria	Dr. E. A. Wright	3/90	0453	8875	McLaurin
647	A Study of a Progestogen-Only Oral Contraceptive for Lactating Woman in Dakar, Senegal	Salif Ndiaye	3/90	0483	8875	McLaurin
648	A Comparative Study of the TCu 380A & the TCu 220 IUD in Manilla, Philippines	Manuel David	1/90	0060	0532	Burdan
649* (TAR)	A Comparative Study of Triquilar vs. Lo-Gentrol in Davao City, Philippines	Emilia Cruz	2/90	0613	8841	McLaurin

CR#	Title	Prepared for	Date	Center #	Study #	Author
650	A Comparative Study of the Progestogen-Only Oral Contraceptive Ovrette vs. Non-Hormonal Methods in Lactating Women in Buenos Aires, Argentina	Dr. Angel Victor Moggia	2/90	0871	0877	Harris
651	A Comparative Study of the Progestogen-Only Oral Contraceptive, Ovrette vs. Non-Hormonal Methods in Lactating Women in Buenos Aires, Argentina	Dr. Angel Victor Moggia	2/90	0871	0878	Harris
653	A Study of a Progestogen-Only Oral Contraceptive for Lactating Women in Bamako, Mali	Dr. Rakie Samake	3/90	0460	8876	McLaurin
654	A Study of Progestogen-Only Oral Contraceptive for Lactating Women in Londrina, Brazil	Dr. Jose Luis de Oliviera Camargo	3/90	8056	8875	Lamprecht
655	A Study of Progestogen-Only Oral Contraceptive for Lactating Women in Sauta Maria Rio Grande Do Sur, Brazil	Dr. Luis C. Russi Barbosa	3/90	0865	8875	McLaurin

CR#	Title	Prepared for	Date	Center #	Study #	Author
656	A Study of a Progestogen-Only Oral Contraceptive for Lactating Women in Tabasco, Mexico	Dr. Jose Delgado Betancourt	3/90	0084	8875	Lamprecht
657	A Comparative Study of Triquilar vs. Lol-Ovral in Manilla, Philippines	Dr.Lazarito Villamar	3/90	6000	8841	McLaurin
658*(TAR)	A Surveillance Study of a Low-Dose vs. a Standard-Dose Oral Contraceptive in Niamey, Republic of Niger	Dr. Halima Maidouka	3/90	0463	8890	Dunson
659	A Comparative Study of Loestrin vs. Lo-Femeral in Alor Setar, Malaysia, and Sungai Petani	Dr. Ranu Mukherjee	6/90	0076	8820	Harris
660	A Noncomparative Study of the Filshie Clip Method of Tubal Occlusion	Dr. Luis Uribe	4/90	0864	6249	Burdan
661	A Clinical Comparison of Two Progestogen-Only Contraceptives in Zimbabwe	Zimbabwe National Family Planning Council	5/90	4011 4012 4013	8877	McLaurin
662	A Comparative Study of the TCu 380A IUD and the TCu 220 IUD in Cebu City, Philippines	Dr. Emilia Dacalos	5/90	0066	0532	Burdan

CR#	Title	Prepared for	Date	Center #	Study #	Author
663*(TAR)	A Descriptive Summary of a Crossover Study of Oral Contraceptives, Noriday 1/50 and Lo-Femenal in Songkla, Thailand.	Dr. Kanchana Kanchanasinith	5/90	0112	8845	Harris
664	A Comparative Study of the TCu 380A IUD and the Nova T IUD in Caracas, Venezuela.	Dr. Itic Zighelboim	5/90	100	0536	Burdan
665	A Comparative Study of Oral Contraceptives: Triquilar vs. Lo-Femenal in Sudan.	The Sudan Fertility Control Association	8/90	400	8840	McLaurin
666	Clinical Acceptability of Delfen Foam and Profam Suppositories for Women at High Risk of Contracting Sexually Transmitted Diseases in Santo Domingo, Dominican Republic	Dr. Milton Cordero	6/90	8044	0799	Alam
667	A Non-Comparative Study of an Oral Contraceptive Lo-Femenal in Jakarta, Indonesia	Dr. Firman Lubis	6/90	683	8822	McLaurin
668	A Compartive Study of Triquilar vs. Lo-Femenal in Quito, Equador	Dr. Eduardo Leon Aguayo	8/90	0964	8840	Dunson/ Monteith

CR#	Title	Prepared for	Date	Center #	Study #	Author
669	Condom Usage Among U.S. Military Personnel Attending a Sexually Transmitted Disease Clinic at a U.S. Military Base	Dr. Charles Magruder	7/90	0028	7801	Farr
670	A Comparative Study of Loestrin vs. Lo-Femenal in Bangkok, Thailand	Dr. Boonsri Israngkura	8/90	679	8820	Harris
671	A Comparative Study of the Filshie Clip and Wolf Clip Methods of Tubal Occlusion by Minilaparotomy	Dr. Milton Cordero	10/89	8044	6266	Bunce

C. STUDY STATUS LISTS

Gates

STUDY STATUS LIST
FEMALE STERILIZATION STUDY

October 1990

Description of Study: Retrospective Filshie Clip

Study Number: 6240

Total Number of Cases: 800

Total Number of Studies: 1

Proposal Number: 637

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed ADM	1mo FU	6mo FU	LTFU	Date Last Shipment	Date Last Site Visit	Status/ Comments
747	Arshat/ Malaysia	FS 86/009	9/86	1/87	6/88	800	641	130	344	219	1/27/89	9/88 DG	Closing

*Forms received/not processed

STUDY STATUS LIST
FEMALE STERILIZATION

October 1990

Description of Study: Laparoscopy - Filshie Clip
Study Number: 6249
Total Number of Cases: 1795
Total Number of Studies: 11

Proposal Number: 631-2

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Date Last Adm.	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADM	1mo FU	6mo FU	12mo FU	24+mo FU			
284	Yuzpe/Canada	FS 85/007	6/85	7/85	5/24/88	250	216	184	156	150	26	9/13/89	9/89 KK	Closing
285	O'Brien/ England	FS 85/020	10/85	1/86	1/06/88	100	79	68	54	35	7	3/20/89	8/89 DG	Closing
224	Condie/ England	Subcontract	10/85	8/87	9/21/87	50	10	9	8	8	4	6/07/89	8/89 DG	Closing
286	Newton/ England	Subcontract	10/85	4/86	6/23/88	250	283	254	241	219	224	10/16/89	8/89 DG	Closing
293	Pogmore/ England	Subcontract	10/85	10/86	4/20/88	150	65	51	46	47	48	7/11/89	8/89 DG	Closing
201	Campbell/ England	FS 86/006	04/86	8/86	4/27/88	200	216	161	120	56	161	2/07/90	8/89 DG	Closing
200	Baird/ Scotland	FS 86/007	04/86	7/86	10/28/87	220	220	167	239	196	2	8/23/89	8/89 DG	Closing

STUDY STATUS LIST
FEMALE STERILIZATION

October 1990

Description of Study: Laparoscopy - Filshie Clip (continued)

Study Number: 6249

Total Number of Cases: 1795

Total Number of Studies: 11

Proposal Number: 631-2

Center	Investigator/ Countr·	Index Number	Date Initiated	Date Active	Date Last Adm.	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADM	1mo FU	6mo FU	12mo FU	24mo FU			
283	Gomel/Canada	FS 85/009	2/86	7/86	12/12/88	75	80	53	68	42	6	9/13/89	9/89 KK	Closing
274	Milne/Canada	FS 86/005	5/86	12/86	6/14/88	200	54	50	39	26	X	9/13/89	9/89 KK	Closing
268	Fugere/Canada	FS 87/005	1/87	5/867	6/15/88	200	152	118	119	119	7	9/13/89	9/89 KK	Closing
864	Uribe/Mexico	FS87/009	11/87	2/88	6/21/88	100	108	107	94	24	X	8/07/89	8/89 CEC	CR in Review

*Forms received/not processed

STUDY STATUS LIST
FEMALE STERILIZATION

October 1990

Description of Study: Minilaparotomy - Filshie Clip vs. Secuclip (Studies cancelled)
Study Number: 6258
Total Number of Cases: 200
Total Number of Studies: 2

Proposal Number: 600-3

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Date last Adm.	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADM	1mo FU	6mo FU	12mo FU	24mo FU			
865	Bossemeyer/ Brazil	FS 84/004	8/84	8/84	7/25/85	100	83	69	80	70	47	01/04/88	3/87 DB	Closed
836	Nagahata/ Peru	FS 84/005	8/84	8/84	4/28/84	100	75	75	74	73	70	08/28/85	10/87 DB	Closed

STUDY STATUS LIST
FEMALE STERILIZATION

October 1990

Description of Study: Minilaparotomy - Filshie Clip vs Pomeroy
Study Number: 6260
Total Number of Cases: 1400
Total Number of Studies: 4

Proposal Number: 600-3

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Date last Adm	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADM	1mo FU	6mo FU	12mo FU	24+mo FU			
075	Suporn/ Thailand	FS 85/017	9/85	12/85	11/12/86	300	300	312	138	152	211	6/27/89	4/89 DG	Closed
600	Apelo/ Philippines	FS 83/009	4/84	4/84	12/06/84	300	300	214	140	148	243	11/07/88	3/89 SMc	Closed
781	Yan/ Taiwan	FS 84/003	4/84	4/84	6/20/86	200	200	180	186	161	141	8/03/88	4/89 DG	Closing
832	Lasso de-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	Closed
				12/86	9/11/87	300	300	285	291	274	185	8/28/89	2/88 CEC	Closing

*Forms received/not processed

STUDY STATUS LIST
FEMALE STERILIZATION

October 1990

Description of Study: Minilaparotomy - Filshie Clip vs. Tubal Ring
Study Number: 6264
Total Number of Cases: 940
Total Number of Studies: 6

Proposal Number: 625

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Date last Adm	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADM	1mo FU	6mo FU	12mo FU	24mo FU			
083	Contreras/ Panama	FS 84/019	7/84	10/84	11/29/85	300	300	284	283	299	17	03/26/87	7/86 CEC	Closed
451	Githiari/ Kenya	FS 86/004	2/86	10/86	10/21/87	140	118	115	108	39	18	09/07/89	3/89 MR	Closing
836	Nagahata/ Peru	FS 84/011	12/84	3/85	3/25/86	200	200	200	166	167	1	09/23/87	9/87 DB	Closed
865	Bossemeyer/ Brazil	FS 84/022	9/85	11/85	5/13/86	100	100	66	60	37	24	03/27/89	3/87 DB	Closing
8594	Perez-Palacios Mexico	FS 87/007	8/87	12/87	6/24/88	200	183	162	139	157	14	09/27/89	8/89 CEC	Closing

*Forms received/not processed

STUDY STATUS LIST
FEMALE STERILIZATION

October 1990

Description of Study: Laparoscopy - Filshie Clip vs. Tubal Ring
Study Number: 6265
Total Number of Cases: 2020
Total Number of Studies: 8

Proposal Number: 624

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Date last Adm	Proposed No. of Cases	Forms Processed ADM	1mo FU	6mo FU	12mo FU	24mo FU	Date Last Shipment	Date Last Site Visit	Status/ Comments
075	Suporn/ Thailand	FS 84/015 Subgrant	10/84	10/84	3/24/86	300	301	299	269	253	44	12/28/88	4/89 DG	Closing
081	Moreno/ 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/ Indonesia	FS 85/018	11/85	6/86	11/11/87	150	150	141	138	141	139	6/23/89	1/90 SM	Closing
741	Kobchitt/ Thailand	FS 84/023 Subgrant	6/85	8/85	10/27/86	300	158	123	100	101	X	5/27/87	12/89 VL	Closing
				4/86	02/26/88	300	300	276	261	213	67	12/19/89	12/89 VL	Closing
759	Moeloek/ Indonesia	FS 85/019	11/85	7/86	9/30/87	150	144	126	117	125	70	11/03/89	2/90 DG	Closing
892	Ortiz-Mariscal/Mexico	FS 85/012	7/85	5/86	1/26/88	220	219	183	126	134	X	2/02/89	2/89 CEC	Closing
8044	Cordero/ Dominican Republic	FS 85/011	8/85	3/87	6/30/85	300	255	243	244	212	X	9/05/89	6/89 CEC	Closing

*Forms received/not processed

STUDY STATUS LIST
FEMALE STERILIZATION

October 1990

Description of Study: Minilaparotomy - Filshie Clip vs. Wolf Clip
Study Number: 6266
Total Number of Cases: 1150
Total Number of Studies: 4

Proposal Number: 629

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Date last Adm	Proposed No. of Cases	Forms Processed ADM	1mo FU	6mo FU	12mo FU	Date Last Shipment	Date Last Site Visit	Status/ Comments
832	Lasso de-la Vega/Panama	FS 85/013	8/85	9/85	5/28/86	300	300	289	288	279	5/18/87	6/87 CEC	Closed
8044	Cordero/ Dominican Republic	FS 85/014	8/85	10/85	2/25/87	300	302	260	213	193	7/18/88	8/88 CEC	Closed
684	Thambu/ Malaysia	FS 85/024	9/86	12/86	4/25/88	150	106	76	95	33	9/28/88	2/90 SM	Closing
8593	Remes/ Mexico	FS 87/006	8/87	9/87	10/10/88	300	164	149	57	8	8/28/89	8/89 CEC	Closing
685	Lim/ Malaysia	FS 85/024	9/86	12/86	12/01/86	100	5	5	5	4	2/28/90	9/88 DG	Closing

*Forms received/not processed

STUDY STATUS LIST
FEMALE STERILIZATION

October 1990

Description of Study: Laparoscopy - Filshie Clip vs. Wolf Clip
Study Number: 6267
Total Number of Cases: 1300
Total Number of Studies: 4

Proposal Number: 628-1

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Date last Adm	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADM	1mo FU	6mo FU	12mo FU	24mo			
841	Santiso/ Guatemala	FS 85/010	2/86	2/86	7/30/86	300	288	237	255	211	22	5/27/88	3/89 CEC	CR in Progress
8009	Louissaint/ Haiti	FS 85/016	8/85	9/85	9/30/86	300	237	215	131	116	X	10/20/87	4/87 SB	Closed
864	Uribe/Mexico	FS 85/022	11/85	1/86	6/29/88	400	400	396	350	250	138	8/07/89	8/89 CEC	Closing
100	Zighelboim/ Venezuela	FS 86/001	12/85	1/86	5/22/87	300	300	271	195	146	157	7/10/89	1/89 CEC	Closing

*Forms received/not processed

STUDY STATUS LIST
FEMALE STERILIZATION STUDY

October 1990

Description of Study: Bipolar Electrocautery vs. Filshie Clip
Study Number: 6269
Total Number of Cases: 1075
Total Number of Studies: 5

Proposal Number: 636

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Date last Adm	Proposed No. of Cases	Forms Processed ADM	1mo FU	6mo FU	12mo FU	Date Last Shipment	Date Last Site Visit	Status/ Comments
029	Kauppila/ Finland	FS 87/002	12/86	2/87	2/14/88	200	199	191	193	192	10/16/89	8/89 DG	Closing
750	Kwak/Korea	FS 87/004	3/87	6/87	9/10/87	300	300	290	298	276	11/16/88	8/89 DG	Closing
781	Yan/Taiwan	FS 86/015	9/86	3/87	11/28/87	75	75	64	38	9	8/01/89	4/89 DG	Closing
231	Leodolter/ Austria	FS 86/014	9/86	3/87	03/28/88	300	200	192	183	179	9/13/89	9/89 DG	Closing
260	Wagenbichler/ Austria	FS 87/001	12/86	6/87	11/26/87	200	200	200	178	136	2/07/89	9/89 DG	Closing

*Forms received/not processed

STUDY STATUS LIST
FEMALE STERILIZATION STUDY

October 1990

Description of Study: Minilaparotomy and Laparoscopy - Filshie Clip
Study Number: 6700
Total Number of Cases: 200
Total Number of Studies: 1

Proposal Number: 632

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADM	1mo FU	6mo FU	12mo FU	24mo FU			
8063	Abdala/ Brazil	FS 85/015	6/85	7/85	3/87	200	198	197	197			4/21/87	4/86DB	Closed
					Corrected forms		200	140	145	150	10			

STUDY STATUS LIST
MALE STERILIZATION STUDY

October 1990

Description of Study: Standard Incision vs. Puncture Method of Vasectomy
Study Number: 704
Total Number of Cases: 1200
Total Number of Studies: 4

Proposal Numbe: 707

Center	Investigator/ Country	Index Number	Date Initiated	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed			Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADM	Early	10 Wks			
733	Beligaswatte/ Sri Lanka	MS88/002	3/88	8/88	8/88	300	300	244	262	12/21/89	5/89 SMC	CR in Progress
698	Apichart/ Thailand	MS88/001	3/88	4/88	10/88	300	300	269	251	2/06/89	9/88 DG	CR in Revision
858	de Castro/ Brazil	MS89/002	4/90	4/90		300	32	27	10	8/30/90	8/90 DT	Active
841	Santiso/ Guatemala	MS89/001	4/88	6/89	12/89	300	294	226	288	8/29/90	3/90 DC	Active
Multi	Azrul/ Indonesia	MS90/002				400					10/90 SMC	Under Development

Gaston Farr

STUDY STATUS LIST
INVESTIGATOR NETWORK NEEDS
FCO 3114
ACTIVE STUDIES

October 1990

Description of Study: TCU 380A VS TCU 200

Study Number: 5550

Total Number of Cases: 800

Total Number of Studies: 3

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
						ADM	1 mo FU	3 mo FU	6 mo FU	12 mo FU			
079	Shrestha/Nepal	IUD 87/001	11/87	10/91	200	200	204	170	193	201	9/05/90	2/90 SB	FU only*
875	Arboleda/Colombia	IUD 87/005	9/87	4/89	400	394	354	311	286	166	8/01/89	9/87 DC	Closed Data Cleaning
424	Kagone/Burkina Faso	IUD 89/001	7/89	7/91	200	43	11	6	1		7/11/90	2/90 KJ	Active

*conducting 36 month follow-up visits

Gaston Farr

STUDY STATUS LIST
INVESTIGATOR NETWORK NEEDS
FCO 3114
ACTIVE STUDIES

October 1990

Description of Study: FS SURVEILLANCE
Study Number: 6900
Total Number of Cases: 200
Total Number of Studies: 1

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active		Expiration Date	Proposed No. of Cases	Forms Processed					Date Last Shipment	Date Last Site Visit	Status/ Comments
							ADM	1 mo FU	3 mo FU	6 mo FU	12 mo FU			
040	Otolorin/Nigeria	FS 86/003	6/86	9/86	2/88	200	204	184	X	79	43	8/88	6/89 SB	Closing

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STUDY STATUS LIST
IUD

October 1990

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/ COUNTRY	INDEX NUMBER	DATE INITIATED	EXPIRATION DATE	PROPOSED NO. OF CASES	FORMS PROCESSED					DATE LAST SHIPMENT	DATE LAST SITE VISIT	STATUS/ COMMENTS
						ADM	1MO FU	3MO FU	6MO FU	12MO+ FU			
823	GUIDOS/EL SALVADOR	88/002	5/88	3/91	200	161	118	91	83	48	8/14/90	9/90 CR	FU Only
824	ZAVALETA/EL SALVADOR	88/003	5/88	3/91	200	125	53	65	40	29	8/14/90	9/90 CR	FU Only

STUDY STATUS LIST
IUD

October 1990

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	35/008	7/85	6/87	300	300	260	269	288	282	12/08/87	5/87 CEC	CLOSED Data Cleaning
060	DAVID/PHILIPPINES	86/004	7/87	1/88	200	200	164	149	162	156	10/10/89	9/89 SM BT	CR # 648
061	ALFONSO/PHILIPPINES	86/006	7/87	5/88	200	201	192	184	180	173	05/15/89	9/89 SM BT	CR # 643
066	DACALOS/PHILIPPINES	86/007	7/87	5/88	200	195	189	177	164	111	10/10/89	9/89 SM BT	CR # 662

STUDY STATUS LIST
IUD

Octobor 1990

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 ADM	FU 1MO	FU 3MO	FU 6MO	FU 12MO+	DATE LAST SHIPMENT	DATE LAST SITE VISIT	STATUS/ COMMENTS
342	EFCS/EGYPT	86/008 SUB 3151-4	9/87	9/88	1000	989	837	791	812	3020	N/A	9/90 GF	FU ONLY
						NO IN-HOUSE DATA							
363	TOPPOZADA/EGYPT	85/005	6/85	6/87	200	199	113	112	106	92	10/25/88	10/88 PG	CLOSING
401	MUAKTAR/SUDAN	85/14	10/85	2/89	100	26	20	15	5		9/03/86	3/87 PG	CLOSED No CR Planned

STUDY STATUS LIST
IUD

October 1990

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 ADM	FU 1MO	FU 3MO	FU 6MO	FU 12MO+	DATE LAST SHIPMENT	DATE LAST SITE VISIT	STATUS/ COMMENTS
452	DOH/CAMEROON	86/012	6/86	6/88	300	278	206	169	149	199	11/20/89	9/89 RD/ JS	CR IN PROGRESS
680	HUSAIN/PAKISTAN	85/15	3/86	11/87	300	299	207	175	215	212	6/13/89	2/88 SB	CR IN PROGRESS
821	HENRIQUEZ EL SALVADOR	85/17	1/86	11/87	300	300	261	220	213	220	7/18/88	5/88 DC	CR #635
825	ALVARADO/MEXICO	85/12	8/85	9/87	300	300	257	253	245	237	9/ 8/87	5/87 CEC	CR IN PROGRESS
854	BELTRAN/CHILE	86/009	6/86	1/88	300	300	288	282	284	180	11/16/87	10/87 CEC	CLOSED PAPER PENDING Data Cleaning

STUDY STATUS LIST
IUD

October 1990

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 ADM	FU 1MO	FU 3MO	FU 6MO	FU 12MO+	DATE LAST SHIPMENT	DATE LAST SITE VISIT	STATUS/ COMMENTS
8020	AGUINAGA/BRAZIL	85/011	10/85	1/88	300	300	217	163	142	92	4/12/88	11/87 DB	CLOSED Data Cleaning
8052	IHSS/HONDURAS	86/010	6/86	6/88	300	295	236	177	131	250	10/10/88	9/88 DC	CLOSED Data Cleaning
8065	FERNANDEZ/ COSTA RICA	86/011	3/87	6/88	200	74	65	55	11	-	9/28/87	6/88 CEC	CLOSED NO CR PLANNED

STUDY STATUS LIST
IUD

October 1990

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 ADM	FU 1MO	FU 3MO	FU 6MO	FU 12MO+	DATE LAST SHIPMENT	DATE LAST SITE VISIT	STATUS/ COMMENTS
042	EKWEMPU/NIGERIA	86/013	6/86	7/88	300	300	261	210	199	165	11/17/88	6/89 SB	CLOSED
101	ACOSTA/PERU	85/16	12/85	5/88	300	297	240	227	234	233	09/02/88	6/88 CEC	CR IN PROGRESS
304	KISNISCI/TURKEY	85/002	7/86	6/87	200	170	110	69	66	84	04/21/88	2/88 PG	CLOSED Data Cleaning

STUDY STATUS LIST
IUD

October 1990

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 ADM	FU 1MO	FU 3MO	FU 6MO	FU 12MO+	DATE LAST SHIPMENT	DATE LAST SITE VISIT	STATUS/ COMMENTS
703	BANDARAGODA SRI LANKA	86/002	2/86	1/88	300	300	299	288	278	270	5/18/88	2/88 SM	CLOSED PAPER WRITTEN
741	DAMRONG/THAILAND	85/009 SUB 3151-1	5/85	9/88	1400	1396	1260	1154	1099	2234	10/15/90	7/90 JM	FU ONLY
779	GUNASEKERA SRI LANKA	86/003	2/86	1/88	300	300	273	264	264	261	7/25/88	7/88 SM	CR 634
780	CHOONG MALAYSIA	86/001	1/86	2/88	150	149	144	127	130	117	7/06/89	7/88 SM	CLOSED

STUDY STATUS LIST
IUD

October 1990

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 ADM	FU 1MO	FU 3MO	FU 6MO	FU 12MO	FU 24MO	DATE LAST SHIPMENT	DATE LAST SITE VISIT	STATUS/ COMMENTS
BKS PENFIN	INDONESIA	85/18 SUB 3151-3	5/86	9/88	3000	2992	2966	2864	2757	2680	2372	N/A	1/90 GF	CLOSED Final Report Pending
						NO IN-HOUSE DATA								

STUDY STATUS LIST
IUD

October 1990

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 ADM	FU 1MO	FU 3MO	FU 6MO	FU 12MO	DATE LAST SHIPMENT	DATE LAST SITE VISIT	STATUS/ COMMENTS
441	SANGARET/MALI	88/001	5/88	6/90	300	232	232	221	212	188	5/16/90	2/90 KJ	CLOSED DATA CLEANING

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 ADM	FU 1MO	FU 3MO	FU 6MO	FU 12MO+	DATE LAST SHIPMENT	DATE LAST SITE VISIT	STATUS/ COMMENTS
698	APICHART/THAILAND	85/007	5/85	7/87	200	172	137	105	103	91	03/31/89	2/88 JM	CLOSED DATA CLEANING

STUDY STATUS LIST
IUD

October 1990

Description of Study: Post C-Section IUD Insertion

Study Number: 564

Total Number of Cases: 1000

Total Number of Studies: 1

FCO: 3155

CENTER NUMBER	INVESTIGATOR/ COUNTRY	INDEX NUMBER	DATE INITIATED	EXPIRATION DATE	PROPOSED NO. OF CASES	FORMS PROCESSED ADM	1MO FU	3MO FU	6MO FU	12MO+ FU	DATE LAST SHIPMENT	DATE LAST SITE VISIT	STATUS/ COMMENTS
868	AZNAR/MEXICO	85/015	8/86	4/88	1800	2418	2209	1275			N/A	3/88 MW	CLOSED
										NO FORMS IN-HOUSE			

Study Status List: Phase 3 NET Microspheres October 1990

All centers have been closed

			Number of Follow-up Visits (by months)						
Site	Investigator	ADM	3	6	9	12	15	18	21
0223	Hanson	97	85	53	16				
0225	Poindexter	100	93	83	50	1			
0226	Yon	42	30	9	6				
0798	Ratnam	80	76	63	38	13	5		
0850	Guzman-Serani	100	100	99	93	89	64	43	13
0920	Darney	51	45	25	6				
8067	Alvarado	98	96	77	60	39	11	1	
0908	Archer	100	96	82	66	49	39	1	
0912	Shoupe	30	25	9	2				
0952	Singh	100	97	79	40	3			
0961	Groff	19	19						
0025	Boyd	89	76	53	20				
0085	Bassol	99	98	81	56	39	17	12	3
0923	Pasquale	16	12	3	1				
0075	Suporn	18	18	14	7	5	1		

TOTALS:	65mg	100mg	Total
Admissions	337	702	1039

STUDY STATUS LIST
NONSURGICAL FEMALE STERILIZATION
QUINACRINE

OCTOBER 1990

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

Study Number: 640 FCO: 3164* PHSC Proposal Number: 607

Total Number of Cases: 200

Total Number of Centers: 1

Center	Investigator/ Country	Index Number	Date Active	Expiration Date	Proposed No. of Cases	Forms Processed ADM	Instillations 1	2	3	Follow-ups 1yr	2yr	3yr	4yr	5yr	Date Last Shipment	Date Last Site Visit	Status/ Comments
088	Zipper/Chile	77/288	4/77	9/91	200	166	166	165	153	143	126	124	112	109	9/90	12/88 AR	Active

Long Term Follow-up

6yr	7yr	8yr	9yr	10yr
108	108	108	99	88

*until October 1, 1990

STUDY STATUS LIST
NONSURGICAL FEMALE STERILIZATION
QUINACRINE

OCTOBER 1990

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

Study Number: 643 FCO: 3164 PHSC Proposal Number: 607-1

Total Number of Cases: 500

Total Number of Centers: 3

Center	Investigator/ Country	Index Number	Date Actv	Expiration Date	Proposed No. of Cases	Forms Processed ADM	Instillations 1	2	3	Follow-ups 1yr	2yr	3yr	4yr	5yr	Date Last Shipment	Date Site Site Visit	Status/ Comments
088	Zipper/Chile	78/020	10/79	9/91	200	143	143	141	128	108	78	115	111	107	9/90	12/88 AR	Active
850	Guzman-Serani/ Chile	78/021	5/79	8/88	150	151	151	151	150	145	137	147	145	143	10/88	12/88 AR	Closed
058	Bhatt/India	78/016	10/79	2/82	150	84	84	84	82	77	5	81	81	0	11/83	-	Closed

	6yr	7yr	8yr	9yr	10yr
Long-term Zipper	102	94	73	36	12
Long-term Guzman-Serani	142	129	112	73	

*until October 1, 1990

STUDY STATUS LIST
NON-SURGICAL FEMALE STERILIZATION
QUINACRINE

OCTOBER 1990

Description of Study: Quinacrine Pellets, 100 Minute Release Rate, 250 mg, 2 Insertions

Study Number: 0646 FCO: 0605 PHSC Proposal Number: 622

Total Number of Cases: 100

Total Number of Centers: 1

Center	Investigator/ Country	Index Number	Date Actv	Expiration Date	Proposed No. of Cases	ADM	Proced 2	Forms Processed 6mo FU	12mo FU	24mo FU	36mo FU	48mo FU	Date Last Shipment	Date Last Site Visit	Status/ Comments
0088	Zipper/Chile	84/018	7/82	9/91	100	112	107	90	89	94	92	87	9/90	12/88 AR	Active

STUDY STATUS LIST

NORPLANT Implant Studies

DATE: OCTOBER 1990

Description of Study: NORPLANT IMPLANTS - Pre-introductory Clinical Trials
Project Manager: M. Forgione
Study Number: 866
Total Number of Admissions: 5407
Total Number of Studies: 36

Center Number	Investigator/ Country	Index Number	Date Initiated	Expiration Date	Proposed No. of Cases	Forms Processed ADM	FU Slot 1	FU Slot 6	FU Slot 12	FU Slot 18	FU Slot 24	FU Slot 36	Date Last Shipment	Date Last Monitor Visit
040	O. LADIPO NIGERIA	NOR 85/014	10/11/85	3/92	370	247	175	70	128	91	69	39	9/17/90	12/89
041	A. COLLISON GHANA	NOR 85/012	10/16/85	8/87	100	4	5	1			1		10/11/88	6/05/87
042	C. EKWEMPU NIGERIA	NOR 85/013	10/10/85	9/91	355	113	104	90	77	60	45	32	6/19/90	12/89
435	O. FAKEYE NIGERIA	NOR 86/004	1/13/86	6/91	355	119	103	95	110	59	59	35	9/11/90	12/89
437	E. OKPERE NIGERIA	NOR 85/015	10/09/85	6/91	355	138	110	97	70	54	52	20	1/19/90	12/89
453	J. OTUBU NIGERIA	NOR 86/005	11/08/85	12/91	350	186	158	140	98	88	76	29	7/25/90	12/89
468	J. MANTEY GHANA	NOR 87/007	6/08/87	9/93	100	100	81	21	64	38	56		9/17/90	6/27/90
482	M. GUEYE-BA SENEGAL	NOR 87/002	12/10/86	3/91	300	138	104	79	48	42	40	5	3/07/90	2/23/90
600	R. RAMOS PHILIPPINES	NOR 85/005	2/07/85	4/91	50	50	48	51	41	11	47	24	8/06/90	5/02/90
600	R. RAMOS PHILIPPINES	NOR 86/007	9/27/85	9/92	100	100	95	102	98	81	79	40	8/06/90	5/03/90

Center Number	Investigator/ 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 PHILIPPINES	NOR 85/006	2/07/85	3/91	50	50	44	59	58	36	34	32	9/04/90	5/03/90
602	I. BENITEZ PHILIPPINES	NOR 86/008	6/27/86	6/93	100	100	95	102	98	81	79	44	9/04/90	5/03/90
674	N. ATAULLAH PAKISTAN	NOR 88/005	9/13/88	9/90	100	136	146	115	63	22	1		9/10/90	11/22/89
675	Z. KAZI PAKISTAN	NOR 88/006	7/20/88	9/90	100	120	238	167	89	44	4		9/10/90	11/15/89
676	A. ZIA PAKISTAN	NOR 88/007	8/03/88	9/90	100	30	29	19	13	2	1		9/10/90	11/26/89
677	Z. AKHTAR PAKISTAN	NOR 88/008	9/10/88	9/90	100	108	111	134	108	13			9/10/90	11/18/89
678	M. HAMAYOUN PAKISTAN	NOR 88/009	8/17/88	9/90	100	121	102	121	67	22			9/10/90	11/20/89
703	S. BASNAYAKE SRI LANKA	NOR 85/010	5/14/85	1/91	275	275	294	285	295	285	266	201	8/16/90	6/19/90
704	K. BEGUM BANGLADESH	NOR 85/001	2/17/85	5/91	200	230	225	226	220	195	162	118	9/18/90	3/24/90
718	T. CHOWDHURY BANGLADESH	NOR 85/002	2/20/85	5/91	200	225	219	207	206	168	129	85	9/18/90	3/22/90
721	S. RAHMAN BANGLADESH	NOR 85/003	2/19/85	5/91	200	226	227	223	220	201	173	125	9/17/90	3/23/90

Center Number	Investigator/ Country	Index Number	Date Initiated	Expiration Date	Proposed No. of Cases	Forms Processed ADM	FU Slot 1	FU Slot 6	FU Slot 12	FU Slot 18	FU Slot 24	FU Slot 36	Date Last Shipment	Date Last Monitor Visit
729	H. LAMA NEPAL	NOR 85/004	2/14/85	9/91	300	307	304	282	256	188	172	257	9/13/90	2/13/90
731	A. BHATTA NEPAL	NOR 85/008	5/09/85	9/91	100	100	71	86	87	62	39	42	9/24/90	2/12/90
735	K. MALLA NEPAL	NOR 87/003	2/18/87	9/92	200	200	184	143	127	112	80	2	6/18/90	2/10/90
736	J. GIRI NEPAL	NOR 87/004	2/21/87	9/92	200	196	191	158	109	86	39		9/25/90	2/09/90
742	K.P. YADAV NEPAL	NOR 87/005	2/17/87	9/92	200	200	200	194	182	108	77	14	9/25/90	8/02/90
749	S. CHINNATAMBY SRI LANKA	NOR 85/009	5/16/85	9/91	200	200	153	212	209	169	149	96	9/20/90	6/19/90
758	I. VINITHARATNE SRI LANKA	NOR 85/011	5/17/85	1/91	200	200	200	193	194	183	149	104	8/16/90	6/18/90
798	S. RATNAM SINGAPORE	NOR 85/007	2/04/85	9/91	100	100	104	99	103	95	84	68	5/08/90	6/20/89
800	M.A. SALAZAR EL SALVADOR	NOR 88/003	2/01/88	9/90	50	49	46	48	55	18	9		9/20/90	5/02/89
821	S. CASTRO EL SALVADOR	NOR 88/001	2/05/88	9/90	100	99	107	102	101	53	27		9/20/90	5/02/89
823	R. VASQUEZ EL SALVADOR	NOR 88/002	2/04/88	9/90	150	150	141	151	144	46	22		9/20/90	5/03/89
824	M. HERNANDEZ EL SALVADOR	NOR 88/004	2/04/88	9/90	100	103	75	73	68	37	18		9/20/90	5/04/89

Center Number	Investigator/ 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		
8017	R. BOULOS HAITI	NOR 86/001	11/11/85	3/91	250	242	218	200	159	124	125	62	6/11/90	6/05/90
8331	G. THEODORE HAITI	NOR 86/003	11/14/85	9/93	400	395	350	233	234	126	114	62	6/11/90	11/09/89
8332	F. LOLAGNE HAITI	NOR 86/002	11/16/85	9/91	50	50	50	36	40	31	20	9	5/22/89	12/08/88

STUDY STATUS LIST
NORPLANT Expansion Studies

DATE: OCTOBER 1990

Description of Study: NORPLANT IMPLANTS - Expanded Clinical Trials
Project Manager: M. FORGIONE
Study Number: 1866
Total Number of Admissions: 2584
Total Number of Studies: 9

Center Number	Investigator/ Country	Index Number	Date Initiated	Expiration Date	Proposed No. of Cases	Forms Processed ADM	FU Slot 1	FU Slot 6	FU Slot 12	FU Slot 18	FU Slot 24	FU Slot 36	Date Last Shipment	Date Last Monitor Visit
166	M.A. SATTAR BANGLADESH	NOR 88/015	6/05/88	9/90	200	269	260	227	185	14	8		9/17/90	1/14/89
167	M.L. RAHMAN BANGLADESH	NOR 88/016	7/04/88	9/90	400	204	190	173	125	10			9/18/90	3/23/90
703	S. BASNAYAKE SRI LANKA	NOR 86/009	6/06/86	1/91	80	80	81	83	82	77	71	43	8/16/90	6/19/90
704	K. BEGUM BANGLADESH	NOR 88/010	4/13/88	9/90	500	498	464	342	163	2	10		9/18/90	3/24/90
718	T.A. CHOWDHURY BANGLADESH	NOR 88/011	4/05/88	9/90	500	346	268	217	174	18	13		9/18/90	3/22/90
721	S. RAHMAN BANGLADESH	NOR 88/012	5/04/88	9/90	500	452	426	263	145	1	31		9/17/90	3/23/90
722	M.A. QUADER BANGLADESH	NOR 88/013	4/06/88	9/90	200	277	262	207	143	4	6		9/18/90	8/08/89
729	H. LAMA NEPAL	NOR 87/006	2/24/87	9/92	200	200	191	168	169	122	115	51	9/13/90	2/13/90
766	M. MOSHARRAF BANGLADESH	NOR 88/014	4/10/88	9/90	300	258	239	203	144	22	4		9/17/90	3/24/90

STUDY STATUS LIST
NORPLANT-2 Implant Studies

DATE: OCTOBER 1990

Description of Study: NORPLANT-2 IMPLANTS - Pre-introductory Clinical Trial
Project Manager: M. FORGIONE
Study Number: 872
Total Number of Admissions: 12
Total Number of Studies: 1

Center Number	Investigator/ Country	Index Number	Date Initiated	Expiration Date	Proposed No. of Cases	Forms Processed ADM	FU Slot 1	FU Slot 6	FU Slot 12	FU Slot 18	FU Slot 24	FU Slot 36	Date Last Shipment	Date Last Monitor Visit
798	S. S. RATNAM SINGAPORE	NOR 86/010	6/01/87	9/90	100	12	11	12	11	12	10		7/23/89	6/20/89

User Name: RTAYLOR
Folder: NORPLANT
Title: STUDY STATUS LISTS

STUDY STATUS LIST
SYSTEMICS

RESEARCH ANALYST: RANDY DUNSON
OCTOBER 1990

Description of Study: Crossover - Noriday 1/50 to Lo-Femenal; Lo-Femenal to Noriday 1/50
Study Number: 8845 FCO: 3139
Total Number of Cases: 1200
Total Number of Studies: 4

Center	Investigator/ Country	Index Number	Date Init	Date Actv	Expiration Date	Proposed No. of Cases	Forms Processed ADM	1mo FU	3mo FU	4mo FU	6mo FU	Date Last Shipment	Date Last Site Visit	Status/ Comments
023	Breznik/Maribor, Yugoslavia	85/008	6/85	11/85	12/86	300	295	293	277	245	232	3/12/87	4/87JB	CR604
112	Kanchanasinith TFRA/Thailand	88/002	3/88	6/88	5/90	300	24	14	11	7	6	3/29/89	3/88JM	TAR663
602+	Benitez/ Metro Manila, Philippines	85/009	9/85	2/86	6/88	300	293	270	246	228	205	10/16/87	4/90BT	Closed Data analysis in progress
8593** ++	Remes/Veracruz, Mexico	86/019	9/86	10/86	11/88	300	296	239	179	132	112	4/11/89	1/88DC	Closed Data analysis in progress

TOTALS ON THIS LIST REPRESENT THE NUMBER OF FORMS LOADED INTO THE COMPUTER.
**Norminest instead of Noriday. Femenal instead of Lo-femenal.
+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.

STUDY STATUS LIST
SYSTEMICS

OCTOBER 1990

Description of Study: Triquilar vs Lo-Femenal
Study Number: 8840 FCO: 3138
Total Number of Cases: 1500
Total Number of Studies: 6

Center	Investigator/ Country	Index Number	Date Init	Date Actv	Expiration Date	Proposed No. of Cases	ADM	Forms Processed 1mo FU	4mo FU	8mo FU	12mo FU	Date Last Shipment	Date Last Site Visit	Status/ Comments
400+	Gerais/Khartoum, Sudan	86/002	2/86	8/86	9/88	300	299	276	253	233	39	2/3/88	3/87KHC	CR 665
703	Basnayake/Colombo, Sri Lanka	86/004	2/86	4/86	9/88	300	299	273	263	239	223	7/25/88	3/88SM	Closed NO CR to be written Publication on file
850	Guzman-Serani/ Valdivia, Chile	86/005	3/86	4/86	3/88	300	299	294	291	259	222	1/15/88	10/87CC	CR 634
964+	Aguayo/Quito, Ecuador	86/024	1/87	4/87	3/89	150	103	69	53	39	30	8/25/89	3/88DT	CR 668
8057+	Calventi/ Santo Domingo, Dominican Republic	86/003	6/86	3/87	12/89	150	93	35	13	3	0	9/7/88	8/88CC	Closed Final tables sent No CR to be written
8058	Andrade/Curitiba Brazil	86/018	7/89	7/89	11/91	150	25	13	6	2	0	4/25/90	8/90DT	Active

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

STUDY STATUS LIST
SYSTEMICS

OCTOBER 1990

Description of Study: Loestrin vs Lo-Femenal
Study Number: 8820 FCO: 3134
Total Number of Cases: 1500
Total Number of Studies: 5

Center	Investigator/ Country	Index Number	Date Init	Date Actv	Expiration Date	Proposed No. of Cases/ Lab	Forms Processed ADM/ Lab	1mo FU	4mo FU/ Lab	8mo FU/ Lab	12mo FU	Date Last Shipment	Date Last Site Visit	Status/ Comments
076	Mukherjee/ Malaysia	86/023	2/87	4/87	2/89	300	298	295	282	256	236	2/13/89	7/88SM	CR 659
314	Saleh/Cairo, Egypt	86/014	7/86	10/86	6/88	300/ 20	300/ 99	299/ 0	267/ 98	222/ 99	201/ 1	9/30/88	10/88PG	CR 632
679	Boonsri/Bangkok, Thailand	87/004	11/87	12/87	11/89	300	145	116	120	110	90	11/13/89	1/89JM	CR 670
683	Lubis/Jakarta, Indonesia	86/016	9/86	1/87	8/88	300	19	8	5			6/12/87	3/87MR	Closed No CR to be written
8594	Perez-Palacios/ Mexico City, Mexico	86/011	5/86	6/86	1/89	150/ 150	148/ 41	142/ 5	128/ 35	111/ 21	75/ 11	8/07/89	2/89DC	CR 637

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 1990

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

Study Number: 877, 878 FCO: 3133

Total Number of Cases: 800

Total Number of Studies: 3

Center	Investigator/ Country	Index Number	Date Init./	Date Active	Expiration Date	Proposed No. of Cases	ADM	Forms Processed 1mo FU	2mo FU	3mo FU	4mo FU	5mo FU	6mo FU	7mo FU	Date Last Shipment	Date Last Site Visit	Status/ Comments
340	Etman/Mehalla-Kubra, Egypt	85/005	10/85	6/86	1/89	300	296	221	225	224	221	224	222		10/25/88	10/88KHC	Closed Data analysis continuing
871	Moggia/Buenos Aires, Argentina	85/004	10/85	10/85	4/87	300	300	250	210	231	219	221	246		3/9/87	4/87CC	CR650
871	Moggia/Buenos Aires, Argentina	86/001	8/86	11/86	4/88	200	196	158	136	151	131	142	163		1/15/88	10/87CC	CR651

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

STUDY STATUS LIST
SYSTEMICS

OCTOBER 1990

Description of Study: Progestogen-Oral Contraceptives in Lactating Women
Study Number: 8875 FCO: 3142
Total Number of Cases: 4000
Total Number of Studies: 20

Center	Investigator/ Country	Index Number	Date Init Actv	Date Expiration Date	Proposed No. of Cases	Forms Processed ADM	2 mo FU	6 mo FU	12 mo FU	PT FU	Date Last Shipment	Date Last Site Visit	Status/ Comments
084	Delgado/Mexico Villahermosa	84/034	11/84	11/87	200	199	198	195	192		12/9/87	5/87 DC	CR 656
102	Guzman/Peru Lima	84/018	7/84	11/87	200	199	148	112	75		11/4/87	1/87 DT	CR 641
110	Nagahata/Peru Lima	84/014	3/84	9/87	200	193	191	187	190		1/15/87	1/87 CC	CR 597
400	Gerais/Sudan Khartoum	85/002	2/85	2/87	200	200	200	186	174		5/21/86	3/87 PG	CR 596
422	Broquet/Rwanda Gisenyi	84/004	6/85	3/87	200	18	11	1			5/20/86	5/86 JS	Closed No CR to be written
452	Doh/Cameroon Yaounde	84/030	12/84	1/87	200	228	128	98	91		1/6/87	2/87 RD	CR 587
453	Wright/Nigeria Jos	84/035	3/86	7/88	100	101	82	58	43		6/28/88	6/87 JC	CR 646
483	Ndiaye/Senegal Dakar	84/004	11/84	10/88	200	140	115	84	61		4/5/88	9/87 JS	CR 647
831	Aranda/CostaRica San Jose	84/019	9/84	9/86	200	169	115	71	53		2/19/86	1/86 CC	CR 578
840	FEMAP/Mexico Cuidad Juarez	84/029	10/84	9/86	200	200	164	134	59	63	5/7/86	12/85 CC	CR 620

Center	Investigator/ Country	Index Number	Date Init	Date Actv	Expiration Date	Proposed No. of Cases	ADM	2mo FU	Forms Processed 6 mo FU	12 mo FU	PT FU	Date Last Shipment	Date Last Site Visit	Status/ Comments
841	Santiso/Guatemala Guatemala City	84/031	12/84		10/86	200	199	192	162	148		11/11/86	3/87 CC	CR 606
843	Bomfim/Brazil Fortaleza	84/036	12/84		4/87	200	196	163	113	68	74	5/18/87	4/87 DB	CR 636
865	Barbosa/Brazil Santa Maria	84/038	2/85		7/88	200	197	132	82	44	25	3/8/88	4/87 DT	CR 655
869	Cetina/Mexico Merida	84/015	7/84		6/86	200	200	185	146	93		6/11/86	12/85 CC	CR 588
871	Moggia/Argentina Buenos Aires	84/020	8/84		9/86	200	200	162	1	130		4/21/86	4/86 CC	CR 579
893	Czeresnia/Brazil Sao Paulo	84/037	2/85		12/87	200	147	132	77	36	49	7/14/87	4/87 DB	CR 630
8014	Lecoin/Haiti 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 Londrina	84/039	2/85		4/87	200	196	158	92	46	18	4/14/87	8/86 DT	CR 654
8058	Andrade/Brazil Curitiba	84/041	5/85		4/87	200	205	158	97	44	54	5/5/87	4/87 DB	CR 618
8059	Nunes/Brazil Porto Alegre	84/040	2/85		4/87	200	200	195	177	126	43	1/20/87	4/87 DB	CR 609

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

STUDY STATUS LIST
SYSTEMICS

OCTOBER 1990

Description of Study: Expanded Strategy for Progestogen-only pills (either several centers per country or through CBD programs)
Study Number: 8876 FCO: 3142
Total Number of Cases: 1200
Total Number of Studies:

Center	Investigator/ Country	Index Number	Date Init	Date Actv	Expiration Date	Proposed No. of Cases	ADM	Forms Processed 2 mo FU	6 mo FU	12 mo FU	PT FU	Date Last Shipment	Date Last Site Visit	Status/ Comments
043	Gardiner/Ghana Accra	85/001	10/85		11/87	200	200	196	163	174		7/7/87	9/87 SW	CR 623
044	Klufio/Ghana Accra	84/003	10/85		7/87	200	199	191	185	168		6/22/87	6/86 JS	CR 638
440	Doucoure/Traore Bamako/Mali	83/031	1/85		7/87	100	99	79	58	37		5/5/87	10/87 KJ	CR 629
457	Toure/Traore Kayes/Mali	84/002	9/85		4/87	200	76	22				7/7/87	8/86 KJ	Closed No CR to be written
460	Samake/Traore Bamako/Mali	85/003	9/85		9/88	200	196	155	66	42		9/28/88	12/87 KJ	CR 653
8060	Russowsky/Brazil Porto Alegre	84/001	3/85		12/86	300	149	101	51	28		5/5/87	4/87 DT	Closed No CR to be written

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

STEIN
OCTOBER 1990

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 Centers: 1

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	FB Forms Loaded					Date Last Shipment	Date Last Site Visit	Status/ Comments
						ADM	1 mo FU	3 mo FU	6 mo FU	12+ mo FU			
298	Guillebaud/England	85/004	9/84 / 9/85	9/90	432	207	196	200	151	79	08/22/90	DG 8/89	Active

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OCTOBER 1990

STUDY STATUS LIST
VAGINAL CONTRACEPTION
3171

Description of Study: NEOSAMPOON VS. CONCEPTROL (OVT-N) FOAMING VAGINAL CONTRACEPTIVE TABLETS

Study Number: 7805

Total Number of Cases: 200

Total Number of Centers: 10

Center	Investigator/ Country	Index Number	Date Active	Expiration Date	Proposed No. of Cases	BC Forms Loaded								Date Last Shipment	Date Last Site Visit	Status/ Comments
						ADM	FU W/O ADM*	UNSCHED. FU**	1M FU	3M FU	6M FU	9M FU	12+Mo FU			
090	Kazi/Pakistan	BCS/89/001	7/89	2/91	20	15	0	2	9	5	1	0	0	05/18/90	BT 05/90	Active
091	Kazi/Pakistan	BCS/89/001	7/89	2/91	20	18	0	4	9	10	5	2	0	08/14/90	BT 05/90	Active
092	Kazi/Pakistan	BCS/89/001	7/89	2/91	20	13	0	0	10	4	3	0	0	08/14/90	BT 05/90	Active
095	Kazi/Pakistan	BCS/89/001	7/89	2/91	20	7	2	0	7	4	1	0	0	08/14/90	XX/XX	Active
096	Kazi/Pakistan	BCS/89/001	7/89	2/91	20	4	1	0	2	3	0	0	0	08/14/90	BT 05/90	Active

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OCTOBER 1990

STUDY STATUS LIST
VAGINAL CONTRACEPTION
3171

CONTINUATION:
Description of Study: NEOSAMPOON VS. CONCEPTROL (OVT-N) FOAMING VAGINAL CONTRACEPTIVE TABLETS

Study Number: 7805

Total Number of Cases: 200

Total Number of Centers: 10

Center	Investigator/ Country	Index Number	Date Active	Expiration Date	Proposed No. of Cases	EC Forms Loaded								Date Last Shipment	Date Last Site Visit	Status/ Comments
						ADM	FU W/O ADM*	UNSCHED. FU**	1M FU	3M FU	6M FU	9M FU	12+Mo FU			
097	Kazi/Pakistan	BCS/89/001	7/89	2/91	20	X	X	X	X	X	X	X	X	XX/XX/XX	XX/XX	Active Awaiting Forms
674	Kazi/Pakistan	BCS/89/001	7/89	2/91	20	14	0	0	13	12	0	0	0	08/14/90	BT 05/90	Active
675	Kazi/Pakistan	BCS/89/001	7/89	2/91	20	13	0	0	6	7	5	0	0	08/14/90	BT 11/89	Active
676	Kazi/Pakistan	BCS/89/001	7/89	2/91	20	7	0	1	1	3	1	0	0	08/14/90	BT 11/89	Active
680	Kazi/Pakistan	BCS/89/001	7/89	2/91	20	14	0	0	10	7	4	0	0	05/18/90	BT 11/89	Active

*These FU forms cannot be slotted until admission data is loaded.
**These FU visits do not fall within the specified FU intervals.

STEIN
OCTOBER 1990

STUDY STATUS LIST
VAGINAL CONTRACEPTION
3170

Description of Study: USE OF CONDOMS AND SPERMICIDE (PROFAM OVULE) BY WOMEN AT RISK OF CONTRACTING STD'S

Study Number: 7806

Total Number of Cases: 200

Total Number of Centers: 1

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	Forms Loaded*							Date Last Shipment	Date Last Site Visit	Status/ Comments
						ADM	ADM LAB	2 Wk CSFU	1 mo CSFU	2 mo CSFU	3 mo CSFU	3 mo LAB			
867	Acosta/Colombia	BC/90/001	5/90 / 6/90	XX/90	200	xxx	xxx	xxx	xxx	xxx	xxx	xxx	xx/xx/xx	5/90 Training	Planned

*CSFU unique to study 7806.

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OCTOBER 1990

STUDY STATUS LIST
VAGINAL CONTRACEPTION
3813

Description of Study: CONDOM BREAKAGE IN HUMAN USE

Study Number: 7808

Total Number of Cases: 160 couples

Total Number of Centers: 6

Center	Investigator/ Country	Index Number / Subcontract	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	Forms Loaded*		Date Last Shipment	Date Last Site Visit	Status/ Comments
						Condom Quest.	Condom Form			
010	Hatcher/GA	3813-1	4/90 / 5/90	8/90	25			09/18/90	Not Visited	Enrollment Complete
921	Pasquale/NJ	3813-3	4/90 / 5/90	8/90	25			08/10/90	Not Visited	Enrollment Complete
934	Forrest/CA (SC)	3813-4	4/90 / 5/90	8/90	30	14	84	08/07/90	Not Visited	Active
935	Brookshire/NC	3813-2	4/90 / 4/90	8/90	25	25	147	06/06/90	DC,GG 4/90	Enrollment Complete

*Forms are unique to Study 7808.

STEIN
OCTOBER 1990

STUDY STATUS LIST
VAGINAL CONTRACEPTION
3813

Description of Study: CONDOM BREAKAGE IN HUMAN USE

Study Number: 7808

Total Number of Cases: 160 couples

Total Number of Centers: 6

Center	Investigator/ Country	Index Number / Subcontract	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	Forms Loaded*		Date Last Shipment	Date Last Site Visit	Status/ Comments
						Condom Quest.	Condom Form			
225	Poindexter/TX	3813-6	6/90 / 7/90	10/90	25				Not Visited	Planned
990	Forrest/CA (SM)	3813-5	6/90 / 6/90	10/90	30	16	88	09/24/90	Not Visited	Active

*Forms are unique to Study 7808.

STEIN
OCTOBER 1990

STUDY STATUS LIST
VAGINAL CONTRACEPTION
3170

Description of Study: EFFICACY TRIAL OF REALITY VAGINAL POUCH (FEMALE CONDOM)

Study Number: 7809

Total Number of Cases: 370

Total Number of Centers: 9

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	BC Forms Loaded*					Date Last Shipment	Date Last Site Visit	Status/ Comments
						ADM	1 mo FU	3 mo FU	6 mo FU	6 mo Survey F / M			
211	F. Stewart/CA	CONRAD	1/90 / 6/90	06/91	40							1/90**	Active Awaiting Forms
825	Alvarado/Mexico	BC/90/002	5/90 / 6/90	06/91	40	18	2				08/21/90	KK,CR 8/90	Active
908	Archer/VA	CONRAD	1/90 / 5/90	05/91	40	8	4	0	0	0	09/11/90	KK 7/90	Active
921	Sinofsky/NJ	BC/90/003	1/90 / 6/90	06/91	50							1/90**	Active Awaiting Forms

*FCPQ=Survey forms unique to Study 7809. **Investigator's Meeting

153

STEIN
OCTOBER 1990

STUDY STATUS LIST
VAGINAL CONTRACEPTION
3170

CONTINUATION:
Description of Study: EFFICACY TRIAL OF REALITY VAGINAL POUCH (FEMALE CONDOM)

Study Number: 7809

Total Number of Cases: 370

Total Number of Centers: 9

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	BC Forms Loaded*					Date Last Shipment	Date Last Site Visit	Status/ Comments
						ADM	1 mo FU	3 mo FU	6 mo FU	6 mo Survey F/M			
925	Moghissi/MI	CONRAD	1/90 / 6/90	06/91	40							1/90**	Active Awaiting Forms
933	Heine/AZ	CONRAD	1/90 / 6/90	06/91	40							1/90**	Active Awaiting Forms
934	K. Forrest/CA	CONRAD	1/90 / 7/90	07/91	40							1/90**	Active Awaiting Forms
8044	Cordero/DR	BC/90/004	5/90 / 6/90	06/91	40	4	0	0	0	0	08/14/90	5/90**	Active
8593	Remes/Mexico	BC/90/007	5/90 / 6/90	06/91	40	8	2				08/21/90	KK,CR 8/90	Active

STEIN
OCTOBER 1990

STUDY STATUS LIST
VAGINAL CONTRACEPTION
3605

Description of Study: PHASE I D-PROPRANOLOL VS. NONOXYNOL-9 CONCEPTROL GEL

Study Number: 7811

Total Number of Cases: 20

Total Number of Centers: 1

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	Forms Loaded*								Date Last Shipment	Date Last Site Visit	Status/ Comments
						ADM	BC ADM LAB	ADM L1	ADM L7	1 mo FU	2 mo FU	3 mo FU	4 mo FU			
921	Blackwell/AL	BC/90/006			20											Planned

*L1 = SMAC, L7 = Urinalysis

STEIN
OCTOBER 1990

STUDY STATUS LIST
VAGINAL CONTRACEPTION
3608

Description of Study: PHASE I COMPARATIVE STUDY OF THE LEA'S SHIELD (WITHOUT SPERMICIDE) VS. THE PRENTIF CERVICAL CAP (WITH SPERMICIDE) FOR SAFETY, SHORT TERM TOLERANCE, AND POST-COITAL TESTING

Study Number: 7812

Total Number of Cases: 10

Total Number of Centers: 1

Center	Investigator/ Country	Index Number	Date Initiated/ Date Active	Expiration Date	Proposed No. of Cases	Forms Loaded*					Date Last Shipment	Date Last Site Visit	Status/ Comments
						BC ADM	BC LAB	BC FU	COLP	SURVEY M/F			
908	ARCHER/VA				10								Planned

*LKPQ = Survey unique to Study 7812, Colp = Colposcopy

D. EXPENDITURES

APPENDIX D

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

Expenditures By Type

1 October 1989 - 30 September 1990

Salaries and Fringe Benefits	$ 3,727,189
Service Centers	500,435
Consultant, Professional Fees, Contracted Labor	234,929
Travel - Domestic	216,757
Travel - Foreign	1,019,410
Supplies - Office	76,137
Supplies - Medical	150,320
Printing and Reprints	115,506
Office/Medical Equipment, Maintenance and Repair	129,256
Freight	39,812
Dues, Registration Fees, Training Grant	52,651
Subscriptions, Publications	32,705
IJGO Royalties	<2,645>
Other Purchased Services	668,746
Keypunching	22,488
Other Expenses and Bank Services Charges	51,864
Data Purchases	35,233
Subcontracts	2,061,736
Transfer to AID/DPE-3041-A-00-0043-00	<30,242>
General and Administrative Costs	2,223,015
TOTAL:	$11,325,302