

PN-ACA-626

FAMILY HEALTH INTERNATIONAL

Technical Advisory Committee

June 29/30, 1994

Research Triangle Park, North Carolina

SCHEDULE

Wednesday, June 29

9:00 am - 5:30 pm

Annual Meeting
Technical Advisory Committee
Radisson Governors Inn
Rooms F & G, Third Floor
Research Triangle Park, NC

6:15 pm

Social/barbecue dinner
Family Health International
Headquarters Park
Durham, NC

Thursday, June 30

8:30 - 11:55 am

Annual Meeting
Technical Advisory Committee
Radisson Governors Inn
Rooms F & G, Third Floor
Research Triangle Park, NC

12:00 noon

Lunch at the Radisson Governors Inn
Room H, Third Floor

TAC ROSTER AND ROTATION SCHEDULE

Family Health International
Technical Advisory Committee
for
Contraceptive Technology and Family Planning Research

1993 - 1994 Roster

Physiology

1995 Linda E. Atkinson, PhD (Chair)
 Senior Scientist
 Product Registration Manager
 Alza Corporation
 950 Page Mill Road
 Palo Alto, CA 94303-0802

415/494-5689

**Obstetrics-Gynecology/
 Reproductive Biology**

1996 Deborah J. Anderson, PhD
 Associate Professor
 Obstetrics, Gynecology &
 Reproductive Biology
 Harvard Medical School
 Director, Fearing Research
 Laboratory
 250 Longwood Avenue-SGMB 204
 Boston, MA 02115

617/432-0841; 617/432-2190
 FAX: 617/432-0359

**Epidemiology/Internal &
 Preventive Medicine**

1995 Willard Cates, Jr., MD, MPH
 Director, Division of Training
 Centers for Disease Control (C08)
 Atlanta, GA 30333

404/639-3071; FAX: 404/639-2222

Obstetrics-Gynecology

1995 William Droegemueller, MD
 Chairman, Department of Ob/Gyn
 University of North Carolina
 School of Medicine
 CB# 7570, MacNider Bldg.
 Chapel Hill, NC 27599-7570

919/966-5281

Reproductive Biology

1994 Michael John Kennedy Harper, PhD, ScD
 Department of Ob/Gyn
 Baylor College of Medicine
 6550 Fanning Street, Suite 821A
 Houston, TX 77030

713/790-3640 (B)
 FAX: 713/798-7564

Endocrinology/Reproductive Biology

1996 Gregorio Pérez-Palacios, MD
 Director General
 Dirección General de Planificación Familiar
 Secretaría de Salud
 Insurgentes Sur 1397, 6to Piso
 Col. Insurgentes Mixcoac
 03920 México, DF, México

52-5-598-5617 or 5182; FAX: 598-6528

Epidemiology

1994 Judith P. Rooks, CNM, MS, MPH
 Independent Consultant
 2706 SW English Court
 Portland, OR 97201

503/243-2253 (R)

Social Science

1994 Rochelle N. Shain, PhD
 Professor, Department of Ob/Gyn
 The University of Texas
 Health Science Center
 7703 Floyd Curl Drive
 San Antonio, TX 78284

210/567-5051

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FAMILY HEALTH INTERNATIONAL

TECHNICAL ADVISORY COMMITTEE

Rotation Schedule

To serve until 1994

Michael JK Harper
Judith Rooks
Rochelle Shain

To serve until 1995

Linda Atkinson
Willard Cates, Jr.
William Droegemueller

To serve until 1996

Deborah Anderson
Gregorio Perez-Palacios

Fhi

Headquarters:
P.O. Box 13950
Research Triangle Park, NC 27709 USA
Telephone: 919-544-7040
Telex: 579442 . Fax: 919-544-7261

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2101 Wilson Boulevard, Suite 700
Arlington, VA 22201
Telephone: 703-516-9779 . Fax: 703-516-9781
Voice Mail: 703-516-0460

Family Health International Technical Advisory Committee

June 29/30, 1994

Radisson Governors Inn
Research Triangle Park, NC

AGENDA

Linda Atkinson, Chairperson

Wednesday, June 29, 1994, 9:00-5:30

- | | | |
|----------|--|----------------------------|
| 9:00 am | 1. Introduction | |
| | a. Welcome/introductions | Theodore King |
| | b. Minutes/summaries of 1993/94 meetings | |
| * | 1) Minutes of annual TAC meeting, July 1, 1993 | |
| | 2) Minutes of Reproductive Biology Centers Meeting,
November 7-9, 1993 (independent document) | |
| * | 3) Minutes of Experts' Meeting to Plan Future Toxicologic
Studies with Quinacrine Hydrochloride Pellets as a
Method of Nonsurgical Female Sterilization, April 5, 1994 | |
| 9:30 am | 2. Technical Issues | |
| | a. Nonsurgical female sterilization | |
| | Discussants: William Droegemueller and Judith Rooks | |
| | Moderator: Michael Harper | |
| | 1) Introduction | Theodore King |
| * | 2) Progress report on the iodine studies | Diane Campen |
| 10:30 am | Break | |
| 10:45 am | * | |
| | 3) Quinacrine | |
| | • Previous FHI work | David Sokal |
| | • Current activities | Cindy Waszak/Carol Connell |
| 11:30 am | 4) Discussion | |
| 12:30 pm | Lunch | |
| 2:00 pm | b. Improving provider practices | |
| | Discussant: Gregorio Pérez-Palacios | |
| | Moderator: Rochelle Shain | |
| * | 1) Progress report | Roberto Rivera |
| * | 2) Risk/benefit model | Pamela Schwingl |
| * | 3) Case study in Mexico | David Hubacher |
| 3:00 pm | 4) Discussion | |
| 3:30 pm | Break | |
| 3:45 pm | c. Progress reports of research and program initiatives | |
| * | 1) Filshie Clip | Diane Campen |
| * | 2) NET products (injectable and pellets) | Elizabeth Raymond |
| * | 3) The timing of onset of contraceptive effectiveness in NORPLANT®
implant users as determined by changes in cervical mucus | Randy Dunson |
| * | 4) Mellon-sponsored projects | Roberto Rivera |
| 4:30 pm | 3. General Review of Program | |
| * | • Contraceptive Technology/Family Planning Research | Theodore King |
| | • AIDSCAP | Theodore King |
| | • International AIDS/HIV Vaccine Efficacy Trials Master Contract | Carol Connell |
| | • Women's Studies | Nancy Williamson |
| 5:30 pm | 4. Recess | |
| 6:15 pm | Social/barbecue dinner at FHI | |
| * | Accompanying materials | |

**Family Health International
Technical Advisory Committee**

June 29/30, 1994

Radisson Governors Inn
Research Triangle Park, NC

Thursday, June 30, 1994, 8:30-11:55

- | | | |
|-----------------|--|-----------------|
| 8:30 am | 5. Call to Order | |
| | 6. Technical Issue | |
| | a. Barrier methods and spermicides | |
| | Discussant: Rochelle Shain | |
| | Moderator: Willard Cates, Jr. | |
| | * 1) Introduction and FHI History | Paul Feldblum |
| | 2) Male Condoms | |
| | * a) Progress report on condom R & D and quality assurance | Howard Price |
| | * b) Progress report on condom breakage studies | Carol Joanis |
| | * c) Design of a new study on latex condom lab parameters and human use performance | Howard Price |
| | d) Discussion | |
| 9:20 am | 3) New Product Development | |
| | * a) Regulatory framework for approval of new products | Diane Campen |
| | * b) Measurement of efficacy | Rosalie Dominik |
| | * c) Contraceptive effectiveness of latex vs. plastic condoms: proposed study design | David Sokal |
| | d) Discussion | |
| 10:30 am | Break | |
| 10:45 am | 4) Spermicides and microbicides | |
| | * a) Progress report on barrier use and STDs | Paul Feldblum |
| | * b) N-9 and iodine vaginal products: recent developments | Gaston Farr |
| | c) Discussion | |
| 11:45 am | 7. Proposed Expert Meetings | |
| | * 8. Date/Site of 1995 Meeting | |
| 11:55 am | 9. Adjournment | |
| 12:00 n | Lunch | |
| | * Accompanying materials | |

Technical Advisory Committee (1993/94)

Dr. Linda E. Atkinson, Chairperson
Dr. Deborah J. Anderson
Dr. Willard Cates, Jr.
Dr. William Droegemueller

Dr. Michael JK Harper
Dr. Gregorio Perez-Palacios
Ms. Judith P. Rooks
Dr. Rochelle N. Shain

Representatives/Agency for International Development

Dr. James Shelton
Dr. Mihira Karra
Dr. Judith Manning
Dr. Erin McNeill
Mr. Mark Rilling

Representatives/Cooperating Agencies

Dr. Nancy Alexander, NIH (NICHD)
Dr. Susan Allen, CONRAD Program
Dr. Robert Fischer, NIH (NIAID)
Ms. Judy Norsigian, Boston Women's
Health Book Collective
Dr. Rosemarie Thau, Population Council
Dr. Francis Webb, WHO/HRP

Representative/FDA

Dr. Philip Corfman

Representative/FHI Board of Directors

Dr. Ursula Lachnit-Fixson

Representative(s)/Foundations

Dr. Carolyn Makinson, Mellon

Representative/South to South

Cooperation in Reproductive Health
Dr. O.A. Ladipo

FHI Staff

Dr. Theodore King, President/Chief Operating Officer
Dr. Diane Campen, Director, Regulatory Affairs/Quality Assurance
Ms. Lynda Cole, Director, Field Operations
Ms. Carol Connell, Director, Clinical Applications
Ms. Rosalie Dominik, Director, Biostatistics
Dr. Laneta Dorflinger, Director, Clinical Trials
Dr. Judith Fortney, Corporate Director/Scientific Affairs
Dr. Barbara Janowitz, Director, Service Delivery Research
Ms. JoAnn Lewis, Senior Vice President/Reproductive Health Programs
Dr. Arlene McKay, Director, Development
Dr. Howard Miller, Senior Vice President/Research & Development
Dr. Douglas Nichols, Acting Director, Contraceptive Use & Epidemiology
Ms. Susan Palmore, Director, Policy & Research Utilization
Dr. Howard Price, Director, Materials Technology
Dr. Roberto Rivera, Corporate Director/International Affairs
Dr. Nancy Williamson, Director, Women's Studies

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Agenda Item 1 (b-1)

Draft Minutes
of
TAC Meeting

July 1, 1993

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FAMILY HEALTH INTERNATIONAL
TECHNICAL ADVISORY COMMITTEE

Minutes
Annual Meeting
July 1, 1993

FHI Office
Durham, NC

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PARTICIPANTS

TAC Representatives

Linda Atkinson, PhD (Chairperson)
Deborah Anderson, PhD
Willard Cates, Jr., MD, MPH
William Droegemueller, MD

Michael Harper, PhD, ScD
Jorge Martinez Manautou, MD
Judith Rooks, CNM, MS, MPH
Rochelle Shain, PhD

AID/W Representatives

James D. Shelton, MD
Judith Manning, PhD
Erin McNeill, PhD

FDA Representative

Philip Corfman, MD

Foundation Representatives

Jose Barzelatto, MD (Ford Fdn.)
Carolyn Makinson, PhD (Mellon Fdn.)

Cooperating Agency Representatives

Claude Aguilhaume, MD/George Brown, PhD/
Ann Robbins, PhD (The Population
Council)
Nancy Alexander, PhD (NIH)
Douglas Colvard, PhD (CONRAD Program)
Jitendra Khanna (WHO)

FHI Board of Directors Representatives

Arthur Christakos, MD
John Ganley
Pramilla Senanayake, MD

South to South Cooperation in
Reproductive Health Representative

O.A. Ladipo, MD

FHI Staff

Theodore King, President/COO
Howard Miller, Senior Vice President/Contraceptive Research & Development
Judith Fortney, Corporate Director/Scientific Affairs
Thomas Petrick, Corporate Director/Medical Affairs
Roberto Rivera, Corporate Director/International Medical Affairs
Carol Connell, Director, Clinical Trials
Laneta Dorflinger, Director, Regulatory Affairs/Quality Assurance
Gaston Farr, Associate Director, Clinical Trials
Anita Flick, Associate Medical Director, Clinical Trials
Karen Hardee, Senior Research Associate, Service Delivery Research
Arlene McKay, Director of Development
Charles Morrison, Epidemiologist, Contraceptive Use & Epidemiology
Susan Palmore, Director, Policy & Research Utilization
Howard Price, Director, Materials Technology
Ronald Roddy, Senior Epidemiologist, Contraceptive Use & Epidemiology
David Sokal, Associate Medical Director, Clinical Trials
Nancy Williamson (sabbatical leave)

1. Introduction

a. Welcome/introductions

The meeting was convened at 8:30 am, July 1, 1993, by the Chairperson,
Dr. Atkinson.

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Dr. King welcomed the Committee and the observers, who were introduced:

Drs. Claude Aguiillaume, George Brown and Ann Robbins, The Population Council;

Dr. Nancy Alexander, Chief, Contraceptive Development Branch, National Institute of Child Health & Human Development (NICHD);

Dr. Jose Barzelatto, Ford Foundation;

Dr. Arthur Christakos (retired from Duke University), Mr. John Ganley (retired from Clinical Research International), and Dr. Pramilla Senanayake (Assistant Secretary General, International Planned Parenthood Federation), who represented FHI's Board of Directors;

Dr. Douglas Colvard, The CONRAD Program;

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

Mr. Jitendra Khanna, Special Programme of Research, Development & Research in Training in Human Reproduction (HRP), World Health Organization (WHO);

Dr. O.A. Ladipo, Executive Secretary/Program Director, South to South Cooperation in Reproductive Health (Salvador, Bahia, Brazil);

Dr. Carolyn Makinson, Mellon Foundation;

Drs. James Shelton, Judith Manning, and Erin McNeill, Research Division, Office of Population, Agency for International Development.

Sincere appreciation was expressed to Dr. Jorge Martinez Manautou who will rotate off the committee on September 30, 1993 following two three-year terms.

Dr. Deborah Anderson was reappointed to the Committee for a three-year term.

b. Minutes/summaries of 1992/93 meetings

1) Minutes of 1992 TAC meeting

Minutes of the annual meeting, held July 2, 1992, were accepted as circulated with the agenda.

2) Report of interagency meeting, Long Acting Progestins: Management of Bleeding Disturbances, June 10/11, 1993 (Anita Flick)

While the availability and use of long-acting progestin contraceptives, such as NORPLANT[®] and Depo Provera, have increased, the intermenstrual bleeding episodes frequently associated with progestin-only contraceptives, have contributed to user dissatisfaction and sometimes discontinuation, particularly among cultures with "menstruation taboos". FHI hosted an interagency meeting, June 10/11, 1993, in search of solutions related to progestin-related menstrual disturbances.

The following consensus was achieved at the interagency meeting:

- Effective counseling, which focuses on a user's understanding of the progestin-only method and its known side effects should

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be included in any protocol/algorithm developed to address progestin-related irregular or prolonged bleeding.

- Further study of progestin-related intermenstrual bleeding disturbances and the evaluation of treatment regimens for various user classifications (ie, adolescents, breastfeeding women, diabetics, obese women, anemic women, and HIV-positive women or those with HIV-positive partners).
- Further evaluation of potential pharmacologic treatments of progestin-related intermenstrual bleeding.

Following its review of the meeting summary, the Committee recommended steps that would be directed toward management of the progestin-related bleeding disturbances and increasing user knowledge and product satisfaction:

- the identification of essential endpoints and the development of counseling programs as a family planning service delivery tool;
- studies that would assess the effectiveness of any treatment regimen as well as any secondary or long-term effects.

c. Status report of transcervical sterilization using iodine (Anita Flick)

Since 1974, FHI has pursued the development of a safe and an effective sclerosing agent to transcervically occlude the Fallopian tubes as a simple and inexpensive nonsurgical approach that could be delivered in Third World clinical settings by paramedical personnel.

Early preclinical data supported the concept of an iodine formulation as a single dose procedure, however, instability of the original sclerosing formula led to reformulation of a higher iodine concentration. In June 1992, the US/Food & Drug Administration (FDA) placed the reformulated iodine on hold subject to the outcome of preclinical animal studies.

Pursuant to the Committee's recommendations and in consultation with reproductive physiology experts, the pig and the rabbit were selected as suitable models to evaluate the human Fallopian tube anatomy. Using the pig model, the Committee received a briefing of FHI's animal studies now in progress. Reproductive structures were reached through a mid-line abdominal incision and an injection of between 0.75 and 2.0 ml of the test compound was injected directly into the lumen of the left tube of four eight-month old pigs (each of an approximate weight of 300 pounds) at the junction of the uterus and the Fallopian tube and directed toward the fimbriated end. Each animal served as its own control, thus the right Fallopian tube was injected with the same volume of the control solution which contained the same components as the sclerosing compound (without the iodine). Fifty days following treatment, the Fallopian tubes and sections of the uterus and ovaries of each animal model were surgically removed and evaluated macroscopically and microscopically. No significant abnormalities were observed in the tissues from the side labelled as placebo. Varying degrees of the same pathologic event were observed on the treatment side - obliteration of the oviduct and replacement of the oviduct by a fibrotic nodule that contained a central slit-like lumen. The composition of this nodule was confirmed by collagen staining and electron microscopy. The remnant lumen was never lined by epithelium. With the presence of an occasional macrophage in the lumen, the probability of a true lumen exists. Even with the high degree of fibrosis that occluded the lumen of the

oviducts, very mild if any inflammation was present, which consisted of lymphocytes. Minimal inflammation outside the lesion was noted with no evidence of any inflammatory response on the mucosal surface of the Fallopian tubes or evidence of gross toxicity to adjacent smooth muscle, blood vessels, or other tissues.

The Committee generally agreed that the preliminary study results justified proceeding with the planned efficacy and toxicity testing, but that these tests should be incorporated into a more extensive evaluation of the tubal structure and functionality, especially with regard to ectopic pregnancy plus a more long-term evaluation with respect to the issue of recanalization.

2. Technical Issue

Pursuant to direction from the Committee, the technical issues [Agenda Items 2 (a) and 4 (a)] were set out in a moderator format and the discussant and moderator (committee members) for each technical issue received questions and background materials in advance of the meeting from the respective staff presenters.

a. Barriers and spermicides (Michael Harper, Moderator)

1) Efficacy and safety for pregnancy and STDs (David Sokal and Ronald Roddy, Presenters; Willard Cates, Jr., Discussant)

The Committee reviewed five study concepts for the efficacy and safety of contraception under consideration by FHI and was asked to prioritize them and comment on foreseeable strengths and/or weaknesses:

- a) Among low-risk populations using condoms for family planning, would FHI's thermoplastic condom be as effective as the latex condom?
- b) Among high-risk populations using condoms primarily for STD (sexually transmitted disease) prevention, would thermoplastic condoms cause more or less irritation than latex condoms?
- c) Would it be useful to conduct a clinical study to verify the mathematical estimates of the superior contraceptive effectiveness of condoms plus spermicides compared to condoms alone in low-risk populations?
- d) Given that several FHI studies have found C-film to be more acceptable than vaginal foaming tablets, should a comparative study of the contraceptive efficacy of these two spermicidal products be conducted?
- e) Should FHI pursue studies of the "Gynaeseal diaphragm tampon", an Australian barrier device originally designed as an aid to menstrual hygiene?

Following the Committee's discussion, the studies were ranked in the following order:

- 1st priority - There was strong consensus in favor of a study to compare the effectiveness of thermoplastic and latex condoms for the prevention of pregnancy.

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There was general support for adding another arm to this study to compare the effectiveness of spermicides.

- 2nd priority - Comparison of the effectiveness of spermicidal film versus spermicidal foaming tablets.
- 3rd priority - A study of whether or not plastic condoms produce more or less irritation than do latex condoms.
- 4th priority - A study of the Gynaeseal diaphragm tampon.

Despite generally disparaging comments with regard to the Gynaeseal diaphragm tampon, two discussants encouraged FHI to evaluate the efficacy and safety of the device at some point, noting that the Reality™ Vaginal Pouch was initially viewed with similar skepticism. FHI should not rule out preliminary studies of this device, such as acceptability of the device for feminine hygiene.

Several discussants suggested that a large sample size would be essential to measure the difference between the efficacy of condoms used alone versus condoms used with a separate spermicidal preparation. The feasibility of such a study would be difficult.

Currently FHI's strategy for assessing the efficacy of barrier products against gonorrhea and chlamydia infection is to also test for efficacy against HIV if the product appears appropriate. Pursuant to this strategy, the following questions were presented to the Committee:

- a) Should FHI test first against HIV and collect gonorrhea and chlamydia data secondarily?
- b) Considering the technical aspects, the Committee was asked to rank the barrier methods that should be tested for STD protection.
- c) In the context of sexually transmitted infections, is FHI's definition of "safety" (the method does not increase the rate of infection) acceptable?

While the Committee considered FHI's strategy appropriate for assessing barrier products for efficacy first against gonorrhea and chlamydia infection and secondarily against HIV, there may be situations when the strategy should be reversed.

In the opinion of the Committee, the barrier methods to receive priority testing for STD protection should be 1) male latex condoms versus male plastic condoms and 2) female plastic condoms versus male condoms. While other barrier methods were considered important, no particular order of priority was designated.

With regard to FHI's definition of "safety", several members of the Committee suggested substituting the word "risk" for "rate". Therefore, the safety definition should be "the method does not increase the risk of infection".

With the disparity of efficacy data on condom usage (plastic versus latex), with and without spermicides, to prevent pregnancy as well as the transmission of STDs, the Committee emphasized the necessity of obtaining

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this critical data and urged FHI to take the lead. Behavioral dynamics are critical to acceptability and contraceptive use, therefore, the Committee recommended that the condom efficacy studies include an acceptability component.

In the absence of a standardized in-vitro method for comparing the speed of dissolution of various spermicidal preparations, the Committee was advised that FHI had initiated pilot work to develop an in-vitro test for spermicidal preparations and that the CONRAD Program had begun work on an in-vivo test.

Dr. Cates commended FHI for its vision and initiative in recent years in assuming the lead in the prevention of STDs and HIV.

- 2) Behavioral research and program issues
(Charles Morrison and Nancy Williamson, Presenters; Rochelle Shain, Discussant)

Behavioral dynamics contribute significantly to client satisfaction and continued use of contraceptive methods. The Contraceptive Use and Epidemiology Division is conducting research designed to better describe and understand barrier contraceptive use by family planning clients, particularly the use of condoms and spermicides used in conjunction with other contraceptives (dual-method approach). A review of the literature on contraceptives and STDs has suggested the dual contraceptive approach for those couples who want to protect themselves from both pregnancy and disease.

While the condom is generally viewed as less effective in preventing pregnancy than some other contraceptive methods, such as steroidal, there are others who would debate that condom use in conjunction with spermicide use would offer a high degree of both pregnancy and STD protection. These suppositions are based upon the consistent use of condoms and spermicides. Thus, a critical question for family planning policymakers and providers is: Will family planning clients and their partners use barrier methods consistently to protect themselves from unwanted pregnancy, from disease or from both pregnancy and disease? There is little data to support the consistent use of condoms and/or spermicides or in conjunction with other family planning methods.

Salient research questions in this area were presented to the Committee:

- a) Among current female contraceptive users, what impact does a decision to add condoms and/or spermicides as a second method to an initial highly effective contraceptive (such as steroidal and IUDs) have:
- on condom/spermicide use as a dual method?
 - on use of the initial contraceptive (especially oral contraceptives)?
- b) Among new female contraceptive users who want both pregnancy and STD protection:
- what methods do they choose to use (dual or condoms/spermicides alone)?
 - do they use their chosen method(s) consistently?

- c) Among men who receive contraceptive counseling and condoms or spermicides through family planning clinics:
- do they use condoms and/or spermicides consistently?
 - what impact does the use of other contraceptives by their partner(s) have on condom and spermicide use?
- d) Among family planning clients who use condoms/spermicides as a dual or sole method, what factors influence consistent and long-term condom and spermicide use? Factors to be examined include:
- sociodemographic variables including age, ethnic group, educational levels, etc.
 - concurrent use of other contraceptives
 - reasons for using condoms/spermicides
 - sex with regular versus irregular or anonymous partners
 - sex while using drugs or alcohol
 - discussing the use of condoms/spermicides with a sexual partner
 - the acceptability (or perceived acceptability) of condoms/spermicides to a sexual partner
 - psychosocial factors such as self-efficacy to use condoms, social norms, perceived benefits versus barriers to condom use
 - having a sexual partner with a known STD/HIV.

There are a number of possible research approaches to address these questions. One approach would be to conduct longitudinal, observational studies among family planning clients where:

- condom/spermicide use is measured prospectively and accurately over the long-term (a year or less);
- situational/contextual and psychosocial variables are accurately measured.

Other approaches would include cross-sectional studies with retrospectively collected data or the conduct of randomized trials of counseling or educational interventions.

In seeking the advice of the Committee, two pertinent questions were presented:

- a) How do you prioritize the four stated research questions and are there any other research questions related to condom and spermicide use among family planning clients that the Committee feels are particularly important for FHI to address?
- b) Which research methodologies are best suited to consider the research questions?

The Committee suggested that barrier method use among current users of other methods and the impact of partner's contraceptive behavior on the use of barrier methods by men were the most important questions and could be designed as one study. The Committee felt that factors influencing condom and spermicide use could be incorporated into any of the other research questions.

In relation to research strategies, the Committee felt that longitudinal studies would be useful and fairly simple to test the impact of different counseling interventions on long-term condom and spermicide use. At the same time, the Committee recognized that the dual method approach could have some negative impact on initial contraceptive use and on the continued use of the barrier contraceptive.

STDs, including HIV, continue unabated, posing a major threat to the reproductive health of men and women worldwide. Developing countries not only lack the treatment therapies for STDs, but a public health mechanism for diagnostic testing and counseling. One approach to addressing this menacing reproductive health dilemma would be to add STD services to the services of family planning clinics in developing countries. With that in mind, three questions were presented to the Committee:

- a) Would the addition of STD treatment contribute to increasing family planning access or improving quality of family planning services or pose a threat to these goals?
- b) Should donors redefine family planning as a reproductive health issue rather than strictly a population issue, to what extent should reproductive health problems be addressed?
- c) Should FHI consider an intervention study that would empirically investigate the pros and cons of adding STD services to family planning facilities?

While the Committee viewed the STD and HIV epidemic as a serious threat to reproductive health and was sympathetic to an integrated approach to family planning and STD services, the Committee raised the following concerns:

- Would it be better to start with a naturalistic observation of family planning facilities where STD services had been added rather than an intervention study?
- Would the contribution of family planning be greater if the focus was on educational intervention rather than STD treatment?
- Where would the resources come from?

It was noted that FHI's AIDSCAP program and other Cooperating Agencies of USAID/W would be providing some resources to add STD diagnostic, treatment, and counseling services to the services provided by family planning clinics in some developing countries. The impact of adding STD services to these family planning facilities should be assessed and should influence any decision of an integrated approach.

3. Progress Reports

- a. Status report of FHI Materials Technology advances, including quality assurance testing and thermoplastic condom development (Howard Price)

The work activities of the Materials Technology Division encompass two major functions:

- Process and product development of new contraceptives;

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- Product quality assurance and compliance of contraceptives and developing test methodology.

The Process and Product Development Group is in the final stage of developing two different designs of thermoplastic male condoms (slip-on and roll-on) the objective of which is to produce a product at least comparable to traditional latex condoms in performance and cost, but with increased environmental stability and compatibility with lubricants. Polymers and condom fabrication technology have been selected to offer the prospect of condoms with better material uniformity and improved tactile properties. Patents have been filed to cover the novel designs and methodology associated with the product development. Based upon the US/FDA response to FHI's IDE (Investigational Device Exemption) submission on the roll-on model, a 510(k) determination of equivalency will be sought for the two condom designs.

The slip-on condom, a twin-aperture design, may be donned from either side of the aperture. Several thermoplastic films are being evaluated. Comparative acceptability studies will be conducted to confirm material selection for this design. The size of the flange generated a suggestion that a larger flange may offer increased protection.

The roll-on condom is comparable to the traditional latex condom, however, with little elastic constraint except at the basal retention ring. The retention ring has been redesigned, consisting now of a knitted spandex ring. Biocompatibility testing on the final product is underway. A Phase I clinical trial is in progress with a second clinical trial planned later this year to compare the roll-on condom with the traditional latex condom.

The specific program areas of the Product Quality Assurance and Compliance Group include:

- Condom production surveillance;
- Evaluation of condom field stocks and field complaints;
- Condom prospective aging study;
- Quality assurance of contraceptive products.

A major initiative of this group has been the establishment of a quality assurance program for latex condoms for FHI's primary donor. This program area involves test method development for other contraceptives (for example, oral contraceptive packaging and the Copper T 380A IUD), standards development, quality assurance audits, and product surveillance. Contraceptives recently included in the AID commodities procurement program, such as Depo Provera and VCF (vaginal contraceptive film), will be phased into the program of development and quality surveillance.

FHI has received accreditation of its product testing laboratory by The American Association of Laboratory Accreditation. FHI participates in interlaboratory latex condom testing and data evaluation and was instrumental in the formation of an interagency technical advisory group. A five-year prospective aging study of latex condoms is being conducted by FHI at three climatically different Third World sites to evaluate the environmental effect upon long-term storage conditions of latex condoms. The study, approximately midpoint, involves environmental monitoring, periodic sampling, laboratory testing, and human-use performance.

This division is also involved in the development of standards used to measure the quality of condoms for the ISO (International Organization for Standardization) and ASTM (American Society for Testing & Materials).

b. Status report of medical barriers to contraceptive access (Susan Palmore)

Medical barriers, as defined by Shelton and Jacobstein, are "dysfunctional practices based at least partly on a medical rationale, but which are in fact unjustifiable from a scientific public health risk/benefit perspective".

Largely through the support of the US government, a variety of safe and effective contraceptive methods have been introduced to developing countries during the past two decades; however, many local medical practitioners have imposed barriers that prohibit access to contraceptive methods to vast numbers of women, particularly the disenfranchised. Medical barriers impede family planning service delivery and the individual's ability to take advantage of available benefits, which frequently result in poor quality of care.

Typical medical barriers to contraceptive access in developing countries are:

- legal and regulatory restrictions;
- restrictions on types of providers;
- process hurdles;
- outdated contraindications;
- age and parity criteria;
- provider bias.

A coalition of the Cooperating Agencies, including FHI, and USAID/W has been formed to remove medical barrier constraints, to increase access to contraception and to improve quality of care by improving family planning services through:

- synthesis and harmony of existing Family Planning Service Guidelines;
- expansion of contraceptive choices;
- enhanced competence;
- strengthened provider-client relations;
- assurance of continuity of care;
- provision of appropriate family planning services.

To reduce medical barriers, FHI is engaged in the following initiatives:

- publications that focus on improving access to contraceptives;
- Contraceptive Technology Update Seminars (12 in 1993);
- educational modules on contraceptive methods;
- scientific and policy meetings;
- service delivery research to identify inefficient and costly medical practices;
- regional experts' meetings.

Dr. Senanayake commended FHI, USAID/W, and the Cooperating Agencies for its initiative to remove medical barrier constraints in developing countries and recommended an assessment of the impact in due course. Other educational tools that would reinforce the initiative would be the FIGO (International Federation of Gynaecology & Obstetrics) gynecology/obstetrics educational modules.

The patent for Depo Provera, previously held by Upjohn, has expired, therefore, Depo Provera, recently approved for contraceptive use by the US/FDA, is being introduced into developing countries where contraceptive injectables are not

in use and being manufactured locally in a number of Third World settings. To avoid any undue problems with the Depo Provera introduction strategy, a quality assurance system for the local manufacturer of Depo Provera was urged by the Committee.

4. Technical Issue

- a. Methodologies for contraceptive introduction
(Karen Hardee and Carol Connell, Presenters; Judith Rooks, Discussant;
William Droegemueller, Moderator)

Traditionally, new contraceptive methods have been evaluated for safety, efficacy, and acceptability through clinical trials. Clinical trials often take several years to complete and have not always yielded information useful to policymakers and program managers in introducing the method once it has received regulatory approval. Recent evidence has suggested that practices instituted during clinical trials to assure protocol compliance, including conservative eligibility criteria and frequent follow-up schedules, are often carried forward in service delivery, thus, contributing to barriers faced by clients in need of family planning services. The IUD in the 1960s, misunderstood use of the oral contraceptive, and dissatisfied NORPLANT^R users in developing countries are illustrative of the gap between clinical research and family planning service delivery.

Depo Provera, recently approved by the US/FDA and approved in 80 other countries, and several other contraceptive methods will soon be available for introduction in developing countries. To facilitate the introduction of these methods, FHI is considering a new approach to answer critical questions for policymakers and service providers during the introduction process - a Rapid Feedback Research approach to improve contraceptive service delivery, client acceptability, and overall method mix in the family planning program. The research components would be complemented with a well-planned information and training strategy. The studies would be population-based rather than institution-based commencing with a country assessment of interest, regulatory status, experience with and consumer demand for the method, the service delivery system, and other organizations involved with the product.

The following questions were presented to the Committee:

- 1) Would the Rapid Feedback Research approach be an appropriate methodology for introducing contraceptive methods to developing countries?
- 2) How should the safety issues be elicited?
- 3) How should study populations be selected?

While supportive of the concept to bridge the gap between clinical research and service delivery, Rapid Feedback Research, the keystone of the new approach, should not be applied as a substitute for clinical research of experimental contraceptive methods, according to the Committee. The new methodology would be appropriate, however, in the introduction of US/FDA-approved contraceptive methods and in assessing efficacy rates based on programmatic use. Long-term safety should be assessed during contraceptive introduction. Community leaders and women's advocacy groups should be consulted in the introductory phase. The Committee further stated that the introduction of new and approved contraceptive methods should be free of clinical research encumbrances. During a country assessment, FHI should also assess the current

methods mix and encourage the cafeteria approach to increase the access of all appropriate contraceptive methods rather than focus on a single method.

5. Progress Reports

a. Status of research and program initiatives

1) Product submissions to the US/FDA (Filshie Clip and Reality™ vaginal pouch) (Carol Connell)

FHI submitted a Premarketing Approval (PMA) application for the Filshie Clip, a tubal occlusive device for female sterilization, to the US/FDA (Food & Drug Administration) in September 1992. Attributing the delay to a backlog of product applications, including the Reality™ Vaginal Pouch, the FDA has not rendered a filing decision to FHI. If regulatory review of the Filshie Clip PMA fails to commence soon, FHI will request an update of the application status.

A PMA application for the Reality™ Vaginal Pouch was submitted to the US/FDA by the manufacturer, Wisconsin Pharmacal, based upon data from several sources, including Phase II/III studies conducted by FHI and the CONRAD Program. On May 7, 1993, the FDA approved the Reality™ Vaginal Pouch for its intended use based upon the supporting data and other information.

2) NET (injectable and pellets) (Carol Connell)

For a number of years, FHI has pursued the development of a 90-day steroidal contraceptive injectable, NET (Norethindrone) microspheres, containing less than half the equivalent steroid of currently available injectable contraceptive products. Since 1991, Medisorb, a company established by Stolle and DuPont, has been performing the product development work and the pre-clinical testing. Medisorb's initial formulation contained an unacceptable chloroform residual, which was resolved this year with another reformulated compound. Inasmuch as the microsphere production technology is not a precise science, the manufacturing scale-up has been beset with insurmountable problems since its inception.

FHI is preparing a submission to the US/FDA to target the safety aspects of the first clinically tested microspheres formulation, which was abandoned by FHI in 1989 due to the low NET release rates.

FHI's pursuit of the NET (Norethindrone) pellet implants has been directed toward the development of an inexpensive and removable biodegradable contraceptive implant with 12 to 18 months protection against pregnancy.

In progress is the preliminary analysis of the Phase II-A study of five NET pellets to assess the pharmacokinetic profile (safety and efficacy).

Within the past year, FHI has transferred the IND (Investigational New Drug) for Annuelle to the manufacturer who will use FHI's research data to continue the research and development initiative. FHI's studies have evaluated two systemic regimens (four pellets, 2.75 mm diameter, and five pellets, 3.0 mm diameter), each demonstrating a contraceptive effect beyond one year expectation. FHI will continue to follow the study subjects to monitor the contraceptive residual of the Annuelle product until the return to fertility.

3) Quinacrine long-term safety study in Chile (David Sokal)

The retrospective cohort study in Valdivia and Santiago, Chile of cancers in women transcervically sterilized with quinacrine hydrochloride has been completed and a report drafted. In brief, the fears of excess cancer occurrence at numerous sites were not confirmed. In the retrospective study, 17 cancers were identified which occurred during the follow up of 1,491 women who had received quinacrine, and who contributed a total of 7,941 person-years of observation. Unfortunately, there is little population-based data on the incidence of cancer in Chile. Based on cancer registry data from Cali, Colombia, the expected number of cancers in a cohort of women of this age is 18.5, thus, an excess of cancers was not observed. There was one provocative observation, however, a single case of uterine sarcoma (leiomyosarcoma). While FHI's study was negative, the power to detect an increase in a rare cancer such as leiomyosarcoma was low. Since quinacrine has mutagenic properties in some test systems, FHI plans to continue to follow these women and will consider the performance of additional mutagenicity testing of quinacrine.

FHI is contemplating two and possibly three additional studies as a follow-up to the retrospective cohort study in Chile, and based upon the advice of two advisors from the University of North Carolina/Department of Epidemiology, FHI plans to:

- perform additional analyses of the retrospective cohort dataset to look at the long-term risk of pregnancy, especially ectopic;
- continue to follow-up the women in this cohort on an annual basis for an additional five years; and
- perform a battery of short-term mutagenicity tests on quinacrine using modern toxicologic methods.

b. Mellon-sponsored projects (Arlene McKay)

Since 1983, FHI has received support from the Mellon Foundation for contraceptive development and related activities. In FY 1994, the Mellon grant will support the Postdoctoral Fellowship Program in Contraceptive Technology, research on transcervical female sterilization, collaboration between scientists working in reproductive biology research and contraceptive development, and development of a research program to study the impact of contraceptive use on the quality of women's lives.

The goal of the Postdoctoral Fellowship Program, initiated in 1991, is to ensure a new generation of scientifically capable researchers in Third World countries who will be able to conduct contraceptive development and evaluation research. The 1991 Fellow, Dr. Xu Jin-Xun, Deputy Director of the Science and Technology Division of the Shanghai Municipal Family Planning Commission, was awarded a re-entry grant to implement an IUD (TCu-380A) clinical research study of his design in China comparing two immediate postplacental vaginal insertion techniques. FHI will monitor and provide technical assistance for the study.

Chosen from among applicants from research centers associated with Family Health International, the World Health Organization (Human Reproduction Programme), and South to South Cooperation in Reproductive Health, the 1993-94 Fellow will be Dr. Carlos Petta who is affiliated with CEMICAMP and the University of Campinas in Campinas, Brazil where he serves as both a staff physician and a researcher

in human reproduction. The research centers have indicated that the fellowship program addresses a critical need in the design and management of contraceptive research and of their commitment in supporting the re-entry study and allowing the fellows to return to positions that will permit implementation of the knowledge and experience gained at FHI.

Mellon support has enabled FHI to continue its research on transcervical female sterilization with the development of a research program in Vietnam to evaluate the risks/benefits of quinacrine hydrochloride pellets administered to 32,000 women of reproductive age since 1989 and to continue the follow-up of women in the retrospective cohort study in Chile. Through the support of another foundation, FHI will conduct a prospective quinacrine transcervical sterilization study in Vietnam (with and without oral ibuprofen).

As an extension of the Postdoctoral Fellowship Program, FHI will convene annual meetings of representation from Mellon-funded reproductive biology centers and contraceptive development programs, agencies supporting contraceptive development research, the pharmaceutical industry, and the US/FDA. The goals are to ensure communication between reproductive biologists and contraceptive development researchers, enhance understanding of the processes involved in basic biological research as well as in the contraceptive development process, and to identify promising leads. The first meeting will be held in the Research Triangle Park area on November 7-9, 1993.

To assess the needs and expectations of potential contraceptive users at all phases of the development process, FHI is adapting Quality of Life (QOL) research strategies from the medical field and drug industry to the contraceptive development field. FHI has established a multi-disciplinary QOL Team whose responsibility is to develop and validate an instrument to evaluate the QOL of women of reproductive age which can be used in contraceptive research. Qualitative and quantitative research, including focus groups to develop the instrument and surveys to test the instrument, will be conducted over the next twelve months.

6. General Review of Program

In advance of the meeting, the Committee was provided copies of FHI's organizational charts and the FY 1993 Workplan (Sections I-V; Appendix I) of FHI's AID Cooperative Agreement, Contraceptive Technology and Family Planning Research. Between meetings, the Committee receives copies of the semi-annual reports of the AID-funded contraceptive technology and family planning research. The program goals are to increase contraceptive choices and access to contraception by enhancing the capacity of family planning researchers and programs in developing countries to evaluate and provide these methods.

Utilizing its skills, institutional capabilities, and experience over the years, FHI will focus its attention on the following program areas to achieve the intended objectives:

- Contraceptive technology development and clinical trials
- Contraceptive materials evaluation
- Contraceptive acceptance and use
- Contraceptive introduction
- Reproductive epidemiology
- Institutional development
- Training
- Information dissemination

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- USAID Mission program support
- Interagency collaboration.

The workplan priorities for the current fiscal year include:

- continued emphasis on the development and regulatory approval of new contraceptive technologies;
- testing to assure the quality of contraceptive products;
- studies to improve acceptability of and compliance with contraceptive use;
- an expanded initiative to improve access to contraception by addressing medical barriers to contraception;
- the development and implementation of strategies for introducing Depo-Provera;
- continued studies to evaluate both long- and short-term risks and benefits of contraceptive use;
- research to support family planning service delivery programs, including studies to improve cost effectiveness and quality of care; and
- assuring that research findings and any new documented information are widely disseminated in written formats that will be beneficial to service providers, policymakers, and family planning clients.

FHI's contraceptive technology work program is implemented through the following divisions:

- Clinical Trials (Ms. Carol Connell, Director)
- Contraceptive Use and Epidemiology (Dr. Douglas Nichols, Acting Director)
- Field Operations (Ms. Lynda Cole, Director)
- Materials Technology (Dr. Howard Price, Director)
- Policy and Research Utilization (Ms. Susan Palmore, Director)
- Service Delivery Research (Dr. Barbara Janowitz, Director).

(Secretary's note: The AIDSCAP Division is funded by an AID Cooperative Agreement from the Office of Health and the work program is overseen by an independent Technical Advisory Group.)

FHI established a field office in Nairobi, Kenya in January 1992, under the direction of Ms. Kathy Jesencky, to reinforce its family planning initiatives in developing countries, particularly in Africa. In January 1993, FHI placed a resident advisor, Dr. Shyam Thapa, in Kathmandu, Nepal to work with the Ministry of Public Health.

7. Proposed Expert Meetings, 1993/94

Not any expert meetings were proposed for 1993/94.

8. Date/Site of 1994 Meeting

The 1994 annual meeting of the Technical Advisory Committee will be held at FHI on Wednesday/Thursday, June 29/30, 1994.

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9. Adjournment

The meeting adjourned at 2:40 pm.

Agenda Item 1 (b-3)

Minutes
of
Quinacrine Toxicology Experts Meeting
April 5, 1994

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Quinacrine Toxicology Experts Meeting, April 5, 1994, AIDSCAP Office, Arlington, Virginia:

"Toxicological Issues of Developing Transcervical Tubal Occlusion with Quinacrine"

Executive Summary

The goal of this meeting was to evaluate the previous nonclinical and clinical experience with quinacrine and to develop a strategy for approval of an IND with an indication for Transcervical Tubal Occlusion (TCTO). Two toxicology consultants, and a number of U.S. and foreign research scientists and government officials were invited to review the existing data and give recommendations for FHI's next steps. (For a complete list of participants, see Appendix A.)

Dr. King welcomed the participants and gave a brief overview of FHI's interest in further investigation and development of quinacrine as an agent for TCTO. In the first session, Dr. David Sokal gave a historical perspective of quinacrine's use as an antimalarial in World War II, as a treatment in giardiasis and systemic lupus erythematosus, and as a sclerosing agent in the management of recurring pleural and peritoneal effusions and recurring pneumothoraces. In addition, he reviewed human toxicity data and quinacrine's formulation.

In the second session, Dr. Diane Campen discussed prior studies on quinacrine's pharmacology, pharmacokinetics, and toxicology. In addition, Dr. Jaime Zipper of Chile presented new studies he has undertaken regarding quinacrine's anti-cancer activity in mouse tumors. Dr. Ray Tice discussed the mutagenicity and genetic toxicology of quinacrine, and Dr. Campen outlined what is known about quinacrine's reproductive toxicity.

In the third session, Dr. Zipper presented his earlier clinical studies in the use of quinacrine as an agent for TCTO. Carol Connell, RN, reviewed the TCTO studies completed under prior INDs and Dr. Sokal gave an overview of the retrospective study being undertaken in Chile with previous acceptors of quinacrine TCTO.

During the fourth session, the necessary steps before applying for an IND were discussed with the toxicology experts, researcher scientists, and government officials. As there have been positive prior assays for mutagenicity, it was recommended that FHI undertake the following mutagenicity tests from the International Committee on Harmonization (ICH)'s toxicology core battery assays:

1. Bacterial Gene Mutation in *Salmonella typhimurium*
2. Mammalian Cell Gene Mutation in Mouse lymphoma
3. *In vitro* Cytogenetics in CHO cells or human lymphocytes
4. *In vivo* Cytogenetics in mouse micronuclei

In addition to the ICH core battery assays, the toxicologists recommended an Unscheduled DNA synthesis assay in rat liver. After these genetic toxicology assays are complete, FHI may start a Phase II study at the same time that it collects data on a two-year carcinogenicity study in rats.

Recommendations

Carol Connell asked for comments on FHI's proposal to submit an IND for a Phase III clinical study of quinacrine. FHI foresaw that the only additional data needed to support this IND would be the genetic toxicology panel as recommended by the International Conference on Harmonization (ICH). Dr. Jordan (FDA) said that data were presented at the meeting that supported the mutagenicity of quinacrine in procaryotic systems. He said that tests would have to be repeated in mammalian cells for an IND. If quinacrine was still positive in the mammalian mutagenicity studies, then FHI would need two-year carcinogenicity data before starting the Phase III study. He said that FHI should discuss the approach that would be used for the carcinogenicity studies with the FDA.

In reply to a question from Dr. Campen, Dr. Jordan then stated that there were insufficient clinical safety data for a Phase III study. Dr. Reno (Toxicology Consultant) asked the question, "What if the tests show that quinacrine is a positive mutagen?" Jordan replied that FDA would require a two-year carcinogenicity study. Dr. Tice (Toxicology Consultant) asked if the FDA would accept studies done in transgenic animal models. Dr. Jordan replied that the FDA would not accept those data because those models had not been fully validated. Dr. Jordan also said that no more acute animal toxicity studies were necessary prior to submitting an IND, due to the preponderance of clinical data on acute toxicity. However, he did say that reproductive toxicity, including teratogenicity in two species (rat and rabbit), would be required and that probably Segment I studies would be required. These reproductive toxicity studies would be needed before going into a trial of non-hysterectomized women. If FHI does a pre-hysterectomy study, then the reproductive toxicity data would not be needed.

Dr. Heywood of the World Health Organization questioned repeated intravaginal dosing in rodents. He stated that in mice, there is always a decidual reaction by this route which leads to carcinomas. Therefore, he questioned whether FHI would be able to use both rats and mice for a two-year carcinogenicity study. Dr. Jordan said that interval dosing might be acceptable in a two-year study. Dr. Corfman (FDA) then responded that FHI was not ready for a Phase III study, that additional toxicology studies including the genetic toxicology panel as proposed by the ICH would be required, but that details of protocols should be discussed with Dr. Jordan.

Dr. Corfman questioned whether quinacrine was a reasonable tubal occlusion method. He based his question on the fact that the data had been presented to support a failure rate of 5% after three injections of quinacrine. He indicated that there were still formulation questions, questions regarding peritoneal spillage, and questions regarding the tissue retention of the material and that these all had to be addressed pre-IND. In summary, he said that FHI was looking at a pre-hysterectomy Phase I study. He also suggested that the IND request be discussed in front of an advisory committee because there were so many issues.

Dr. Heywood then responded to the question of non-IND directed studies outside of the US. He said that there were three primary issues that needed to be resolved. The first was the genetic toxicology, the second was the persistence of quinacrine in the tissue, and the last was the teratogenic potential. As far as the genetic toxicology issue, he said that there would be more

FAMILY HEALTH INTERNATIONAL
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extensive genetic toxicology studies required for the European Community. He said that genetic mutation in bacteria (the Ames test) would need to be repeated. Genetic mutation in mammalian cells (the mouse lymphoma test would be recommended) and cytogenetics both *in vitro* and *in vivo* need to be done. The micronucleus test in mice with ip injections and the human lymphocyte or chinese hamster ovary tests should be done to fulfill these requirements. If there were a positive result in the cytogenetics *in vivo*, then an *in vitro/in vivo* unscheduled DNA synthesis study should be done in the rat. If the mammalian *in vivo* studies were positive, then a two-year carcinogenicity study would be required. Dr. Heywood said that due to the problems with intrauterine installation, that oral administration may be acceptable in those studies. Dr. Heywood was concerned that with an efficacy of only 90 to 95 percent, there was a definite concern for the teratogenic potential of the chemical. The dose used for any of the teratogenicity/reproductive studies should be determined based on the kinetics of the chemical rather than dosing level and he recommended that the dose selected be one which produces slight maternal toxicity.

After the general meeting, FHI representatives and the two toxicology consultants met to discuss possible next steps. These people were: Ms. Carol Connell, Dr. Diane Campen, Dr. Ray Tice, Dr. David Sokal, Dr. Howard Miller, Dr. Fred Reno and Dr. Jaime Zipper. Dr. Tice said that as far as the genetic toxicology panel goes, the Ames test would probably not have to be repeated and that the mammalian mutagenicity tests will probably be positive. He said that the human lymphocyte cytogenetics test will probably give a positive result. The results from the micronucleus test are predicted to be equivocal and that if the unscheduled DNA synthesis test is done, it will probably be negative. These predictions were based on his knowledge of the current data and on the mechanism of action of quinacrine as a binder to double-stranded DNA.

To summarize the specific genetic toxicology tests, a bacterial gene mutation assay needs to be done in both *Salmonella typhimurium* and *Escherichia coli*, mammalian cell gene mutation such as the mouse lymphoma or the chinese hamster ovary HGPRT test, *in vitro* cytogenetics using either chinese hamster ovary cells or human lymphocytes, the *in vivo* cytogenetics tests would be either bone marrow chromosomal aberration assay in rats or a micronucleus assay in rat or mouse. The FDA right now is requesting the mouse lymphoma assay. This may not be the assay that is recommended by the working group of the ICH, but for right now, FHI needs to meet FDA requirements.

The approximate prices of these tests are \$2,500 for the bacterial gene mutation, about \$10,000 for the mouse lymphoma, about \$10,000 for the chinese hamster ovary gene mutation, about \$10,000 for chromosomal aberrations in chinese hamster ovary cells, about \$13,000 for chromosomal aberrations in human lymphocytes. The *in vivo* cytogenetics test would cost about \$30,000 for a bone marrow chromosomal aberration test and the micronucleus assay in the rat would be about \$15,000. The *in vivo/in vitro* UDS assay in Rat Primary Hepatocytes is about \$25,000.

APPENDIX A - List of Participants

Dr. Michael Harper	Baylor College of Medicine
Dr. Jaime Zipper	University of Chile
Dr. Judy Manning	USAID
Ms. Joanne Spicandler	USAID
Mr. Jeffrey Spieler	USAID
Dr. Anne C. Wentz	NICHD
Dr. Phillip Corfman	USFDA
Dr. Alexander W. Jordan	USFDA
Dr. Tran Thi Trung Chien	Vice Minister of Health, Vietnam
Dr. Do Trong Hieu	MCH/FP Dept. MOH, Vietnam
Dr. Vu Quy Nhan	Center for Pop. Studies and Information, Vietnam
Dr. Ralph Heywood	WHO
Dr. Patrick J. Rowe	WHO
Dr. Fredrick E. Reno	Toxicology Consultant
Dr. Raymond Tice	Toxicology Consultant
Dr. Amy Pollack	AVSC

FHI Participants:

Dr. Theodore King	Dr. Howard Miller
Carol Connell	Dr. Diane Campen
Dr. David Sokal	Vivian McLaurin
Carolyn Reusché	

Agenda Item 2 (a)

Nonsurgical Female Sterilization

- 2) Progress report on the iodine studies
- 3) Quinacrine (previous FHI work and current activities)

Progress Report on the Iodine Studies

FAMILY HEALTH INTERNATIONAL
TECHNICAL ADVISORY COMMITTEE
JUNE 29, 1994

IODINE NON-SURGICAL FEMALE STERILIZATION
Progress Report

FHI remains committed to developing a safe and effective method for non-surgical female sterilization. We continue to believe that an iodine-based formulation that can be delivered transcervically and that can be effective with a single application is a very promising approach for an inexpensive, less invasive alternative to surgical sterilization for women in the developing and developed world.

As we reported last year, following recommendations from the 1992 Technical Advisory Committee (TAC) meeting, FHI conducted a pilot study using a pig model to evaluate potential efficacy and safety of our current iodine-based formulation. Results of this pilot study were encouraging. In all four (4) pigs, lesions were seen in the treated oviducts that blocked portions of the oviducts to varying degrees. The lesions consisted of fibrotic nodules that contained a central slit-like lumen which was not lined by epithelium. Despite the fibrosis, there was little associated inflammation.

Based on the results of this pilot study, a follow-up study was designed and initiated in the summer of 1993. In response to recommendations made by TAC and experts in the field of reproductive physiology, two animal models were selected: the pig and rabbit. It was felt that the validity of our results would be strengthened if confirmed in two species.

The objectives of this expanded study were two-fold: (1) To evaluate the dose-dependency of the fibrotic effects seen in the pilot pig study (using the original 5.5% iodine concentration as well as 4.0% and 2.5% concentrations) and (2) To further evaluate the safety of the formulation. As with the pilot study, each animal served as its own control: the iodine-based formulation was directly injected into the left oviduct and a placebo formulation injected into the right oviduct.

There were several differences between the pilot study and the expanded pig and rabbit studies in terms of the study design:

(1) Prior to initiation of this expanded study, the Materials Technology Development (MTD) Division performed an in depth investigation of the current iodine formulation. They determined that there were gradual pH drifts in the formulation over time toward a higher acidity (lower pH), especially at room temperature and above. Laboratory studies indicated that two components were principally responsible for the pH drift. In an attempt to control for this pH drift in the

expanded study, freshly prepared material was made and stored at four (4) degrees celsius until immediately prior to injection.

(2) Assuming that the material would most likely be administered to women immediately following menses during the follicular phase of their cycle, an attempt was made to mimic this stage in the pig study. Pre-pubertal rather than mature pigs were used. These animals were hormonally induced to ovulate after iodine administration. In retrospect, this hormonal treatment probably led to marked induction of tubal secretions and increases in tubal size which could have affected study results.

(3) To more thoroughly evaluate the potential effects of peritoneal spillage, no attempt was made in the expanded study to capture material that overflowed into the peritoneum. In the pilot study, overflow was captured using a glass tube. However, because these younger pigs had a tubal size that was approximately one-third the size of the older pigs used in the first study, an extensive spillage of material into the abdominal cavity and the wound site occurred in many of the animals. The volume of formulation used in the rabbits also resulted in some peritoneal spillage.

(4) Finally, the time between treatment and sacrifice was extended from 50 days in the pilot study to 65 days in the expanded study.

The results from this study were significantly different from the pilot study. Only a few animals in both the pig and rabbit studies were found to have the fibrotic nodules that were seen in the first study suggesting occlusion. Definite lesions were identified in 7 of the 24 pigs and 2 of the 18 rabbits; however, it should be noted that only four sections of each oviduct were taken such that actual lesions could have been missed in the sectioning. This suggestion is supported by the fact that attempts to flush the oviducts prior to histologic sectioning were almost never successful on the treated sides (2 of 23 attempts in the pigs; 0 of 17 attempts in the rabbits). In contrast, almost all attempts on the placebo side were successful (19 or 24 attempts in the pigs; 13 of 16 attempts in the rabbits).

There were three findings in this expanded study that were not seen in the pilot study. (1) A large number of ovarian and oviductal adhesions were noted in almost all pigs and rabbits. Additional less severe adhesions of the abdominal wall, bladder, or surrounding tissues were also found. Despite these adhesions, none of the tissue samples from these areas showed any significant foci of inflammatory cells or sclerosis. (2) There were extensive epithelial-lined cysts with periluminal fibrosis that were located primarily in the mesovarium. Although these structures were noted on both the treatment and control sides in both species, they were more extensive on the treatment side. (3) Finally, there were granulomas primarily located in the mesovarian and ovarian portions of the reproductive tract on the treated side. These granulomas were poorly organized and composed of multinucleated giant cells, foamy macrophages, and a mucoid-type material. There did not appear to be a concentration dependency to the adhesions, cysts or granulomas.

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The reasons for these new observations are unclear, but probably relate to extensive peritoneal spillage of the material in the expanded study. Adhesions would be expected from a large volume of an irritating agent in the peritoneal cavity. Other possible causes include: differences in the animal models, differences in the pH of the formulations, differences in exposure time to the material, or unidentified differences in the formulations used.

In an effort to address concerns over stability of the current iodine-based formulation as well as potential concerns raised in the expanded animal study, the Divisions of Regulatory Affairs and Quality Assurance (RA/QA), Materials Technology Development (MTD) and Clinical Trials have drafted a product development plan to define the steps necessary to develop a new formulation and proceed to clinical testing. MTD currently has identified several possible ways to modify the iodine formulation and change the original components that were determined to be responsible for pH drift. In addition, materials felt to be unsuitable for parenteral usage (two of the viscosity modifiers) will be changed. Several of these formulations will be screened in small efficacy tests in rabbits. Results of these screening studies will be used to determine one or more paths for pursuit in formulation activities. The selected prototype material(s) will be formulated and subjected to sterility and stability testing and eventual GMP production for appropriate toxicity and efficacy testing. The results of these tests will be the basis upon which the FDA determines whether to approve a Phase I clinical trial. The first Phase I clinical trial will be a 24-hour pre hysterectomy study, as has been previously discussed with TAC.

Quinacrine (previous FHI work and current activities)

FHI's Role in Search for Nonsurgical Sterilization

For two decades, scientists at Family Health International (FHI) and elsewhere have conducted research directed toward finding a safe, effective method of nonsurgical female sterilization. One of the most promising methods extensively studied by FHI is a drug called quinacrine.

The availability of a nonsurgical sterilization method would help meet a growing need for an alternative permanent family planning method. Surgical sterilization, the only permanent method currently available, is the most popular modern contraceptive method in both industrialized and developing nations. Worldwide, approximately 20 percent of the men and women of reproductive age have undergone a sterilization procedure. An estimated 170 million men and women rely on sterilization for family planning, and the number is expected to reach 270 million by the year 2000.¹

The demand for sterilization, however, far outpaces health workers' ability to provide surgical services. Nonsurgical sterilization could increase access to family planning,

especially in rural areas where physicians, medical facilities and equipment often are in short supply.

"A nonsurgical sterilization method that is safe, highly effective, inexpensive and easy to administer would make voluntary sterilization accessible to millions of women who desire permanent contraception but currently lack access to surgical methods," says Dr. Theodore M. King, FHI president and chief operating officer.

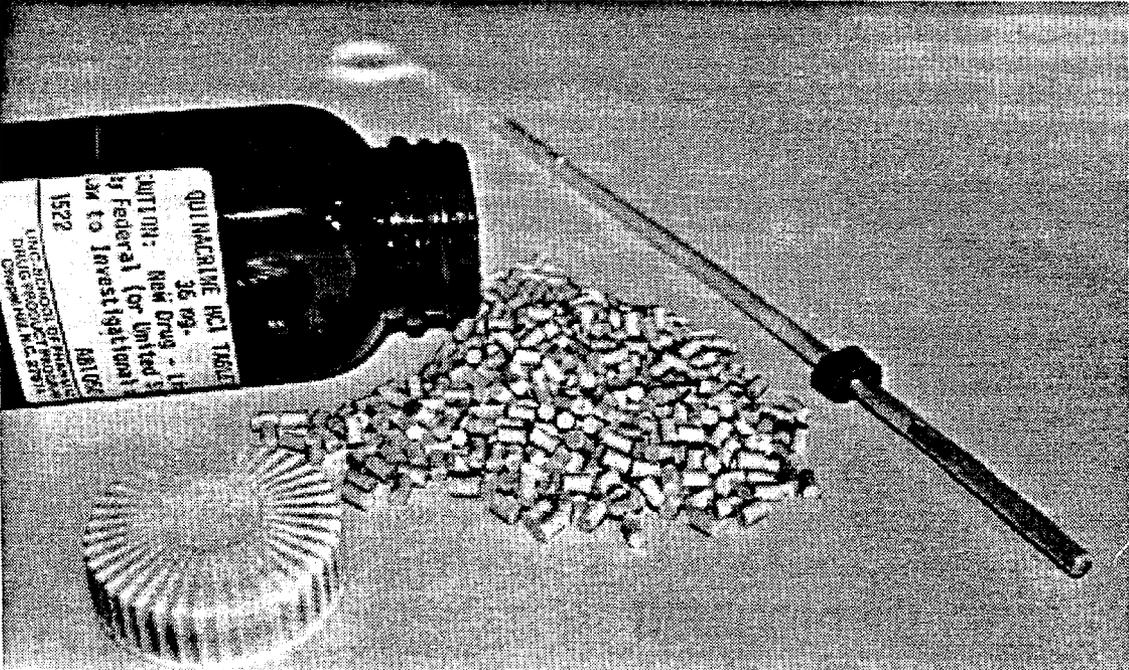
"Extensive data exist showing that quinacrine has great promise as a nonsurgical method; however, questions about the drug's toxicity, potential carcinogenicity and teratogenicity remain unanswered," Dr. King says. "Also, concerns have been raised that this method, like other contraceptives that are not completely controlled by the user, could be administered without the clients' full knowledge or consent.

"As with any contraceptive method, rigorous studies are needed to ensure safety and efficacy of quinacrine," Dr. King says. "FHI supports a stringent review process by appropriate regulatory bodies, such as the

U.S. Food and Drug Administration (FDA), to address these concerns. Follow-up studies can help confirm the results of FHI's initial retrospective study in Chile, concerning quinacrine's possible association with increased risks of cancer."

Dr. King notes that improved training and supervision for providers, education about quality of care issues, and appropriate informed

QUINACRINE PELLETS ARE INSERTED INTO THE UTERUS, SEVEN PELLETS AT A TIME, USING A MODIFIED IUD INSERTER.



NASH HERNDON/FHI

choice procedures can help ensure that women who choose to undergo nonsurgical sterilization fully understand the risks and benefits, as well as the irreversibility of the method. Furthermore, research is needed to address the potential for contraceptive abuse by identifying circumstances that promote abusive practices within service systems and understanding their impact on the user.

FHI'S EXPERIENCE

In the 1960s, several groups of researchers began to investigate nonsurgical sterilization techniques, including the use of chemical agents to block the fallopian tubes. In Chile, Dr. Jaime Zipper and his colleagues explored the use of quinacrine hydrochloride, a drug long used to prevent and treat malaria and other parasitic diseases. Dr. Zipper conducted studies on quinacrine's contraceptive effects in rats and rabbits.

In the early 1970s, Dr. Zipper began administering quinacrine in a slurry solution to women in Chile. The technique was abandoned due to a tendency toward spillage of the slurry into the peritoneal cavity, which resulted in concerns about toxicity. Pregnancy rates also were unacceptable.

FHI became involved in quinacrine research in 1976, when its researchers transcribed and analyzed clinical trial data from Chile. At that time, FHI scientists began working with Dr. Zipper to develop a new method of administration. Quinacrine delivered in the form of pellets, which do not spill or leak into the peritoneal cavity, was the result of these collaborative efforts.

In 1977, in conformity with U.S. FDA guidelines at that time, scientists at FHI (then called the International Fertility Research Program) worked with local investigators to conduct clinical trials on quinacrine pellet insertions in Chile. Investigators found that pellet insertions eliminated the risk of transient psychoses previously reported in 2 percent of the women who received the slurry solution. Other side effects observed in the earlier work with slurry, including abdominal pain and amenorrhea, were less frequent with pellets at least in part because spillage was eliminated.²

Initially, three insertions were required of quinacrine pellets that would dissolve in about 10 minutes. In the 1980s, researchers from FHI and the University of North Carolina refined the process so that two insertions of 100-minute pellets were sufficient to close the proximal portion of the fallopian

1976

At the request of Chilean scientist Dr. Jaime Zipper, FHI begins transcribing and analyzing data from a clinical trial of quinacrine administered in a slurry solution to 200 Chilean women. High pregnancy rates (9.9 per 100 women after 12 months) and toxicity prompt FHI research on a new method of administration.

1977

FHI researchers develop 10-minute releasing quinacrine pellets.

1977

FHI works with Dr. Zipper to initiate clinical trials of 10-minute releasing pellets administered with thiopental sodium to 165 Chilean women. The 12-month pregnancy rate after three insertions is 4.3 per 100 women.

1979

FHI initiates clinical trials of 10-minute releasing quinacrine pellets without thiopental sodium among 81 women in Baroda, India; 151 women in Valdivia, Chile; and 143 women in Santiago, Chile. Twelve-month pregnancy rates after three insertions are 0.0 per 100 women in Baroda; 0.7 in Valdivia; and 3.3 in Santiago.

1981

Following FHI-sponsored animal studies in the United States on mutagenicity and teratogenicity, FHI receives an exemption for an Investigational New Drug (IND) application from the U.S. Food and Drug Administration.

1981

FHI develops 100-minute releasing pellets.

1984

FHI initiates clinical trial of 100-minute releasing pellets on 112 women in Santiago, Chile. Twelve and 24-month pregnancy rates are 2.0 per 100 women.

1984

FHI begins a Phase I clinical trial of quinacrine in the United States, investigating the effects of 10-minute releasing quinacrine pellets on 10 women 24 hours prior to hysterectomy.

1985

FHI conducts a Phase I clinical trial in the United States, investigating the effects of 10- and 100-minute releasing quinacrine on 11 women 30 days prior to hysterectomy.

1989

FHI identifies eight cancer cases during long-term follow-up of women who received quinacrine pellet sterilizations in FHI-sponsored clinical trials in Chile.

1990

FHI chooses to withdraw the IND. FHI discontinues funding for prospective studies in Chile and initiates a retrospective cohort study on Chilean women who received quinacrine pellets.

1992

FHI receives a request for data from the Vietnamese government, which began an introductory program of quinacrine sterilization in 1989.

1993

Through the retrospective study in Chile, FHI documents 17 cancer cases among 1,492 quinacrine sterilizations performed from 1977 through 1989. FHI finds no evidence that quinacrine increases the risk of cancer above the normal risks for women in age-specific groups. FHI recommends continued surveillance of this cohort.

1994

At the request of the Vietnamese government, FHI begins a retrospective study of 31,781 quinacrine procedures carried out by the Ministry of Health in Vietnam. FHI begins analysis of sociodemographic data from all procedures, plus a survey of a sample of 1,800 quinacrine users in three provinces.

1994

FHI convenes a toxicology expert meeting on quinacrine. Experts conclude further research is needed on toxicity, teratogenicity, and potential carcinogenicity. FHI makes plans to apply for a new IND in order to conduct further testing on quinacrine safety.

tubes. The 10-minute and 100-minute release rates refer to the approximate time it takes pellets to dissolve in the uterus. The longer release rate resulted in higher rates of tubal occlusion. Pregnancy rates for women who received 10-minute releasing pellets were 3.3 per 100 women after a year, while rates for women who received 100-minute pellets were 2 per 100.³ The 10-year efficacy rate for older quinacrine regimens is about 93 percent. More recent regimens, using only two insertions, appear to have a similar failure rate, according to FHI data.

In the late 1970s, FHI sponsored preclinical studies on the mutagenicity and teratogenicity of quinacrine, which confirmed mutagenicity in a bacterial system. The studies did show that quinacrine, when given to rats and monkeys early in pregnancy, usually resulted in fetal deaths and resorption, but found no evidence of chromosomal damage or birth defects. Following completion of these studies, the U.S. FDA gave FHI permission to conduct Phase I clinical trials in the United States of quinacrine pellet insertion in women scheduled for hysterectomies. Two Phase I studies were conducted in the United States in the mid-1980s. These studies confirmed the findings of Dr. Zipper and others that immediate side effects were minor and self-limiting.

Meanwhile, FHI-supported research continued in Chile. In 1989, long-term follow-up studies detected eight cancer cases in six different anatomical sites among 572 Chilean women who received quinacrine pellets years earlier during clinical trials.⁴ Among the eight was one case of uterine leiomyosarcoma. Because of this, FHI discontinued prospective quinacrine research and initiated a retrospective study on the health of quinacrine recipients in Chile.

The retrospective study, which included 1,492 Chilean women who were voluntarily sterilized with quinacrine from 1977 through 1989, identified a total of 17 cancer cases. The pattern of cancer occurrence was evaluated using conventional cohort analysis, as well as sensitive space-time cluster methods. Because no cancer incidence data

were available in Chile, data from a similar population in Colombia were used for comparison. Although the occurrence of an unusual cluster of cancers was confirmed, no evidence was found of excess cancer risk due to quinacrine.⁵ Because the study was too small to rule out the increased risk of an uncommon cancer, such as leiomyosarcoma, FHI will continue to monitor this group for another five years.

ADVANTAGES, DISADVANTAGES

Assuming that quinacrine pellets are shown to be non-carcinogenic, quinacrine's advantages as a contraceptive are its short-term safety, its potential to increase access to family planning, and its low cost. These factors may appeal to women who do not live near surgical facilities, who cannot afford the expense of surgery, or who do not want to spend time away from family.

More than 80,000 quinacrine pellet sterilizations have been performed worldwide, and no deaths have been attributed to quinacrine pellets. The comparable death rate for female surgical sterilization is from 2 to 20 per 100,000 procedures.⁶

Although no deaths have been documented in the scientific literature, three deaths have been reported among women who received quinacrine in a slurry solution. In one case that FHI is aware of, researchers have not determined if quinacrine was responsible or if xylocaine, contained in the slurry, was the cause.⁷ The slurry method is no longer used.

BECAUSE SURGICAL STERILIZATION REQUIRES EXPENSIVE EQUIPMENT AND HIGHLY-SKILLED STAFF, IT IS OFTEN UNAVAILABLE TO MANY WOMEN, ESPECIALLY THOSE IN RURAL AREAS. NURSES PREPARE FOR STERILIZATION SURGERY AT THE EVANGELINA RODRIGUEZ FAMILY PLANNING CLINIC IN SANTO DOMINGO, THE DOMINICAN REPUBLIC.

Quinacrine pellets are placed in the uterus, through the cervix, with a modified IUD inserter. The procedure does not require an abdominal incision or a lengthy recuperation. Insertion can be performed by trained non-physicians, and it can be performed in an outpatient setting. Because no anesthesia is required, some women whose health problems might make them unfavorable candidates for surgical sterilization could receive quinacrine.

Also, quinacrine is not expensive. Pellets and inserters typically cost less than U.S. \$1 for two insertions.

BEST AVAILABLE DOCUMENT

In addition to the remaining questions on long-term safety and the potential for abuse, a potential disadvantage of quinacrine use is the greater chance of contraceptive failure when compared to surgical sterilization. The efficacy rate for two insertions of quinacrine is approximately 95 to 98 percent after 12 months, according to various studies, while the rate for surgical methods is 99 percent or greater after 12 months.

Because quinacrine, like surgical sterilization, is considered a permanent, irreversible method, there is the potential for client regret.

COMPARISON OF COMPLICATIONS

Side effects of quinacrine pellet insertion appear to be temporary and minor. An FHI study, involving 112 women in Chile, found approximately 15 percent experienced amenorrhea lasting one to three months following quinacrine insertions.⁸ Other side effects, reported in FHI studies and studies by other groups, include lower back pain, heavier menstrual bleeding, headaches, and vaginal itching. Symptoms lasted from a few hours to a few days.

Because quinacrine produces inflammatory changes, there is the potential for cervical stenosis, or narrowing, as a complication. Also, quinacrine can cause uterine adhesions, which can result in abdominal pain and bleeding. In rare cases, these problems can become severe and warrant a hysterectomy.

Stenosis and adhesions typically are not reported after surgical sterilization; however, problems may occur that are not present with quinacrine insertion. Surgical sterilization carries some risk of major complications, including infection, hemorrhage or anesthesia-related injuries. Also, there is a risk of bowel or bladder injuries and uterine perforation. While rates vary, major complications occur in less than 1 percent of the surgical cases. Minor complications after female surgical sterilization, such as wound infection or slight bleeding, occur in less than 5 percent of cases.⁹

Questions have also been raised about the risks of ectopic pregnancy in women with failed quinacrine sterilization. Ectopic pregnancy rates vary widely from one country to another, and recent research indicates that this is also true for ectopic pregnancy following surgical sterilization. Because the prevalence of surgical sterilization in Vietnam is too low to provide data for comparison, a recent study in that country compared the ectopic pregnancy rate following quinacrine sterilization with ectopic pregnancy among IUD users. The rates were similar.¹⁰

CURRENT, FUTURE WORK

At the request of the government of Vietnam, FHI this year began a retrospective study of quinacrine recipients in that country. From 1989 through 1992, the Ministry of Health in Vietnam performed 31,781 quinacrine pellet sterilizations in 24 provinces. With financial assistance from the U.S.-based Buffett Foundation, FHI is collecting data from a randomly selected sample of 1,800 quinacrine sterilization cases in three Vietnam provinces. Researchers are comparing the perceptions and experiences of quinacrine recipients with those of women who use IUDs, the only contraceptive that has been widely used in Vietnam.

In addition to obtaining data on health-related outcomes, such as complications, side effects and menstrual pattern changes, FHI researchers are asking women about factors that influenced their decisions to use either method and the impact of quinacrine sterilization on aspects of their lives other than health. Investigators plan to explore the relationships among client satisfaction, provider counseling and service delivery. Through this study, researchers also will measure the level of regret among quinacrine users. Information gained could be used to improve client services, to improve provider training and to develop educational materials. The retrospective study is expected to be completed this year.

Also, FHI is analyzing data from records of all quinacrine sterilizations performed in the Vietnam Ministry of Health field trial. Researchers hope to learn about the sociodemographic characteristics of women who underwent quinacrine sterilizations and to determine the impact of health care provider experience and timing of insertion on quinacrine efficacy.

Because of concerns raised by international donor agencies, quinacrine sterilizations have been suspended by the Vietnam Ministry of Health until the retrospective study and other evaluations can be completed.

In April 1994, FHI organized an expert panel, which met in Washington, to evaluate quinacrine research. Toxicology and drug development experts attended, as well as representatives from the World Health Organization, the FDA and several service delivery programs.

Because toxicity studies on quinacrine were conducted more than 10 years ago and FDA requirements for evaluating toxicity have been modified significantly, the panel recommended additional animal studies for quinacrine. These will include bacterial gene mutation, mammalian cell gene mutation, in vitro cytogenetics in CHO cells or human lymphocytes, and in vivo cytogenetics in mouse cells. In addition, the panel recommended a two-year carcinogenicity study on rats. FHI plans to repeat these pre-clinical studies, as well as to reapply for an exemption for an Investigational New Drug (IND) application from the FDA, which would allow FHI to repeat clinical trials in the United States following favorable results from completion of toxicology studies.

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Quinacrine Status Update

Family Health International has been involved in the study of quinacrine hydrochloride pellets as a method of transcervical tubal occlusion since the early 1980s when FHI held an IND to study quinacrine in the U.S. In 1987, reports from a study conducted in Chile seemed to indicate a larger than expected number of cancer cases occurring in the study population. FHI stopped its prospective studies and initiated a retrospective study to evaluate the incidence of cancer in the Chile cohort. FHI canceled its IND in 1990, and at that time had no plans to continue work on quinacrine. We have recently completed the analysis of data from FHI's retrospective study in Chile (submitted for publication) and concluded that there was indeed an unusual cluster of cancers, but that the cluster was unrelated to the use of quinacrine. However, there was one provocative finding, a single uterine leiomyosarcoma. We plan to continue to follow this cohort of women for an additional five years.

Meanwhile, several clinicians around the world continued to explore the use of the quinacrine method of transcervical tubal occlusion. A recent study of about 31,000 women in Vietnam has focused renewed attention on quinacrine. Due to the renewed interest in the method, FHI believes that the safety and efficacy of this method should be re-evaluated within the context of a planned research strategy, including the preclinical and clinical studies required to evaluate its use. If quinacrine is proven to be safe, this method could be an important alternative to surgical sterilization, especially in the developing world.

Last year, FHI received a grant from the Buffett Foundation to evaluate the use of quinacrine for transcervical tubal occlusion in Vietnam. Several studies were proposed: a retrospective study of women who received quinacrine between 1989 and 1993; a prospective, short-term, double-blind evaluation of the safety and efficacy of ibuprofen (a non-steroidal anti-inflammatory drug) given at the time of quinacrine insertion; and, a prospective, open evaluation of the long-term (i.e., at least 5 years) safety of quinacrine insertion.

In January 1994, the government of Vietnam suspended the use of quinacrine in its sterilization program. The Minister of Health approved the conduct of our retrospective study, and pending the results of this study and other evaluations of quinacrine, the Minister of Health will consider the conduct of the short-term prospective clinical trials.

The retrospective study was initiated in March 1994 and will enroll a sample of 1800 quinacrine acceptors and a comparison sample of 1800 IUD users. This study was designed to elicit an understanding of the factors related to the method choice decision; a description of the service delivery aspects; women's perceptions of the physical effects of the methods; women's perceptions of the effects of the method on their lives. A 5-year safety surveillance study of subjects enrolled in the retrospective trial will be initiated in the Fall 1994. This study will evaluate women at least annually for side effects that may emerge and that can be related to quinacrine. Long-term efficacy will also be evaluated with documentation of pregnancies and pregnancy testing conducted prior to menstrual regulation.

Other activities in which FHI has participated during the past year include the AVSC (Association for Voluntary Surgical Contraception) meeting on quinacrine held in December 1993 and an FHI-sponsored meeting of specialists in toxicology and experts from WHO, NIH, FDA, USAID and other funding foundations. This meeting was held on April 5, 1994 (a summary of this meeting is enclosed). Participants were asked to review previous preclinical toxicology studies done with quinacrine. These studies were done prior to many, recent refinements in toxicologic standards and practice. Clinical safety data that has been accumulated, not only from quinacrine's use as a non-surgical female sterilization method, but from other treatment indications, including oral administration for malaria prophylaxis will also be reviewed.

Based upon the recommendations of FHI consultants and the FDA, FHI has submitted protocols to the FDA for the conduct of specific genetic toxicology studies. Upon FDA review and approval of these protocols, FHI will subcontract this work to an appropriate laboratory. The final reports from these studies along with other appropriate documentation and a Phase I clinical trial protocol will be submitted to the FDA in an IND application for the use of quinacrine HCl pellets as a method of transcervical tubal occlusion.

Agenda Item 2 (b)

Improving Provider Practices

- 1) Progress report
- 2) Risk/benefit model
- 3) Case study in Mexico

Progress Report

Improving Provider Practices

Roberto Rivera

Improving Provider Practices is part of a broader strategy named Maximizing Access and Quality (MAQ). As the name indicates, MAQ's main purpose is to maximize access and quality of family planning services. Currently, it is one of the high priority initiatives of USAID. At FHI, it is a multidivisional activity, also of high priority. It is considered that improving provider practices will have an important impact on maximizing access and quality. It has been recognized that a number of provider practices remain in family planning services that limit the access to contraception. Many of these practices are no longer necessary given current knowledge of contraceptive use. The risks and benefits associated with contraception have been better defined in the last few years. These findings should now be translated into service practices in order to improve the access and quality of contraceptive use. Updating norms and procedures for family planning services and the immediate updating of the health providers training have been identified as two key interventions. Several of FHI's divisions are collaborating with other agencies in this area. FHI has an important role in the review of procedures required for the delivery of contraceptives. There is a recognition that some procedures may not be appropriate for all clients in all settings, or are not related, or may actually be irrelevant to the safe use of the contraceptive method. However, these procedures remain in practice and reduce the access and quality of services.

FHI also participated in a WHO coordinated initiative to review the medical criteria for the use of selected methods of contraception. This review was a reaffirmation of situations that represent an unacceptable risk for the use of the method. Equally important to the WHO review was the identification of unwarranted restrictions that still are actively used in service programs, and unnecessarily limit access to contraceptive use.

FHI is actively participating in the updating of national family planning norms and procedures, in training and educational events designed to discuss current contraceptive knowledge, in identifying local or regional barriers to access or quality, and in the production of educational modules on different contraceptive methods. Identifying service delivery or provider practices that should be changed, and documenting the programmatic and clinical implications of making such changes, pose a number of research questions now under investigation by the organization. The TAC members can provide valuable guidance in the selection of different education and research activities aimed to maximize access and quality of family planning services.

Risk/Benefit Model

FAMILY HEALTH INTERNATIONAL

Technical Advisory Committee
June 29/30, 1994

Technical Session: Improving Provider Practices Risk/Benefits

FHI's effort to improve provider practices encompasses the risk/benefit work performed within the Division of Contraceptive Use and Epidemiology. Dr. Schwingl will briefly review the risk/benefit work; however her comments will focus on two major areas. First, the need to broaden our concept of risk to incorporate women's perceptions of the risks and benefits of contraception. Specifically, questions will concern 1) possible approaches which could be used to measure women's perceptions of the risks and benefits associated with childbirth, contraceptives, and family planning; 2) how to measure the impact these perceptions have on contraceptives choice; and 3) an exploration of alternative approaches which could be used to convey the risks and benefits of oral contraceptives. The second focus area has to do with the utility of using decision algorithms or decision trees to present women with information on the risks and benefits of various contraceptives. Such decision trees would ideally incorporate medical facts as well as consideration of women's values about various aspects of contraception. The discussion should focus on the utility of this approach in particular developing countries, and the type of presentation tools which would be most appropriate.



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Case Study in Mexico

Technical Advisory Committee
June 29/30, 1994

**Technical Session: Improving Provider Practices
Case Study in Mexico**

In this presentation, Mr. David Hubacher will describe how the Service Delivery Research Division has examined whether the clinic practice of recommending frequent IUD follow-up visits is warranted. This study conducted with the Mexican Social Security Institute, recruited two groups of new IUD acceptors into different follow-up regimens. The four-visit regimen consisted of return visits at 1, 3, 6, and 12 months postinsertion, while visits for the other regimen were scheduled at 1 and 12 months postinsertion. After one year of follow-up, the percentages with problems in the two groups were compared. The study found that the four-visit scheme identified many more problems than the two-visit scheme (24% versus 16%, respectively). Most of the difference was attributable to problems that were treated with antibiotics. Presumably, if women in the 2-visit group had been given the other follow-up instructions, they would have received the same quantity of interventions, including antibiotics. Without a definitive diagnosis, however, there are no means of determining whether antibiotics administered in the four-visit scheme were necessary. Perhaps these results are explained by the hypothesis that more frequent provider contact leads to more medical interventions (regardless of whether the interventions are medically indicated).

The discussion for TAC should focus on two major themes. The first is how FHI can continue to conduct research on provider practices given the difficulty of measuring a health impact (the Mexico study is one example of how elusive the true health impact can be). The second theme for discussion has to do with the trade-offs that exist between health risks and program costs, and whether the results from these types of studies can be generalized to other programs in other countries.

Agenda Item 2 (c)

Progress Reports of Research and Program Initiatives

- 1) Filshie Clip
- 2) NET products
- 3) Timing of onset of contraceptive effectiveness in NORPLANT[®] implant users
- 4) Mellon-sponsored projects

Filshie Clip

THE FILSHIE CLIP SYSTEM: Progress Report

Introduction

The Filshie Clip System is a tubal occlusion system consisting of surgically applied clips and their applicator. Surgical approaches used to apply the clips to the Fallopian tubes are laparoscopy and minilaparotomy. The product was initially developed by Dr. Marcus Filshie and then licensed to Femcare, Ltd. It became commercially available outside the United States in November, 1982.

In 1985, FHI initiated a series of large-scale clinical trials of the Filshie Clip System, involving 39 different sites in over 20 countries. After the studies were completed in 1989, FHI analyzed the data and prepared a premarket approval application (PMA) for the product. In September, 1992, FHI submitted the PMA and has since served as Femcare's U.S. representative on the PMA. Femcare, Ltd., is manufacturer of the device and GynoPharma will be the US distributor.

Progress

The PMA was filed in October, 1993. In November, 1993, a deficiency letter was received from the FDA, requiring response within 180 days. The questions fell into the following general categories:

- device materials and manufacturing
- device specifications and physical properties
- quality assurance procedures
- clinical
- statistical

In order to coordinate the efforts of the three parties (Femcare Ltd., GynoPharma, and FHI), a steering committee was formed early in 1994. The committee consists of Andrew Martin from Femcare, Ltd., Kirsten Deutsche from GynoPharma, and Julie Omohundro from FHI. There have been several meetings and teleconferences of the steering committee to discuss the strategy and content of responses. The individual deficiencies were divided by category and assigned to the applicable companies. FHI is responsible for the clinical and statistical questions, with Femcare and GynoPharma responsible for the questions regarding manufacturing and quality assurance. Each of the members of the steering committee has been responsible for the coordination of responses from individuals within their respective organizations.

In addition to the activities in responding to the FDA deficiency letter, FHI is actively involved in preparing for FDA inspections at the clinical trial sites and at FHI. Two of the clinical trial sites in the United Kingdom (London, England, and Edinburgh, Scotland) were inspected in May. Manufacturing sites have not yet been inspected.

NET Products

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FAMILY HEALTH INTERNATIONAL
TECHNICAL ADVISORY COMMITTEE
JUNE 29, 1994

NET Products (Pellets and Injectable)

Progress Report

FHI continues to maintain an interest in conducting research which could lead to the development of new and improved long-acting steroid delivery systems. We currently have two projects in this area: the norethindrone biodegradable implant (called NET pellets or ANNUELLE®) and a 90-day norethindrone injectable microsphere system (called NET-90). Programmatically, products such as these would increase contraceptive options available to women and provide easy-to-use, effective hormonal methods that would not require a high degree of use compliance.

NET Pellets

Subject follow-up is continuing in the Phase IIa Pharmacokinetic Evaluation of NET Pellets which was begun in October 1991 at two US sites (East Virginia Medical School in Norfolk, VA and Cornell Medical Center in New York City). A total of 39 subjects were enrolled and randomly assigned to either a four or five pellet treatment group. During the first 13 months of the study, women were protected against pregnancy only by the NET pellets. After 13 months, women were to be provided with a alternate method of contraception (preferably a barrier method). Serum NET concentrations are being monitored until they reach the limit of detection of the NET assay or until the subjects discontinue from the study. There have been no reported pregnancies to date.

Two issues with this product have been identified through the current study. First, serum NET concentrations have remained higher than originally anticipated in each of the pellet groups. The four pellet system appears to provide NET serum concentrations sufficient to provide contraceptive protection for longer than the one year originally hoped. The five pellet system appears to have potential to provide contraceptive effectiveness for 2 years or longer. The second issue is that the tail of product release has been longer than expected. The tail is defined as the period of time during which serum NET concentrations are less than 0.3 ng/ml (the level thought to provide effective contraceptive protection) but above the limit of detection of the NET assay. Based on these ongoing results, a protocol amendment was implemented to extend follow-up from the 24 months originally planned to 36 months to allow for full evaluation of the NET tail. The 24 month follow-up period ended in May 1994. The approximately 15 subjects remaining in the study will continue to be followed through at least April 1995, as appropriate.

In December, 1993, a Progress Report describing the first 15 months of experience of subjects in the study was submitted to Endocon, Inc., manufacturer of the product and holder the Investigational New Drug Exemption (IND). (*FHI had transferred its IND to Endocon in September 1992 following the completion of a product development agreement between ourselves and Endocon.*) Because norethindrone release from both the systems has been longer than anticipated, Endocon is interested in investigating possible ways to limit the product's effectiveness by breaking up the pellets *in situ*. A protocol amendment has been drafted to test the use of vibration to break up pellets in a subset of the women who have five pellets. In addition, the protocol may be amended to add a third treatment arm of a reformulation which would theoretically have a shorter tail.

Endocon has requested that FHI prepare a progress report of the first 25 months of experience of women in this study. Current plans are that this report will be submitted to the FDA in early 1995 and discussed at an end-of-Phase II meeting with the FDA. It is unclear whether a Phase IIB or Phase III study of either of these dosage forms will be pursued, nor whether FHI will have a role in any future studies. Any FHI role will be decided by Endocon and the large pharmaceutical company that has an agreement with Endocon providing them the rights to this product.

NET 90

During the past 8 to 10 years, FHI has conducted several Phase I, II and III clinical studies of various NET-90 formulations. A final safety report compiling data from these studies has been completed and reviewed by in-house staff. FHI has not been involved in clinical trials of this product since 1991.

Because of problems related to the formulation and scale up of production recognized during FHI's Phase III clinical trials, the product has been undergoing reformulation for the last several years. Product reformulation and preclinical testing has been undertaken by Medisorb, a joint venture between Stolle R&D and Dupont. A verbal report from Medisorb indicates that several formulations have undergone pharmacokinetic testing in baboons. Results have apparently been encouraging, although they have not been shared with FHI. Two of these formulations are felt to be suitable for clinical testing and a Phase I study of one or both of these formulations could begin as early as the fall of 1994.

FHI's role in future studies of NET-90 is unclear at this time pending negotiations that are ongoing between USAID and the pharmaceutical company that has the rights to this product.

Timing of Onset of Contraceptive Effectiveness
in NORPLANT[®] Implant Users

FAMILY HEALTH INTERNATIONAL
TECHNICAL ADVISORY COMMITTEE
JUNE 29, 1994

**THE TIMING OF ONSET OF CONTRACEPTIVE EFFECTIVENESS
IN NORPLANT® IMPLANT USERS
AS DETERMINED BY CHANGES IN CERVICAL MUCUS**

Progestin-only contraceptives may exert their effects at at least four (4) different levels. These include suppression of ovulation, production of a "hostile" cervical mucus, effects on the endometrium which include reduction in the number and size of endometrial glands and inhibition of the synthesis of progesterone receptors, and reduction of tubal motility. All these may occur to varying degrees. Although production of a "hostile" cervical mucus may not be the singular mode of action of these contraceptives, its role is crucial.

In women not using hormonal contraception, cervical mucus quantity and quality varies dramatically throughout the menstrual cycle, depending on the relative levels of estrogen and progesterone. During the pre-ovulatory phase, under estrogen dominance, cervical mucus becomes increasingly watery, alkaline and favorable for sperm penetration. In contrast, during the post-ovulatory phase, with increasing progesterone levels, the cervical mucus becomes scanty, thick, and unfavorable for sperm penetration; it also contains increasing numbers of leukocytes. Administration of progestin-only contraceptives results in a cervical mucus which is similar to that seen in the post-ovulatory phase, and is thus described as "hostile" to sperm penetration.

Progestin-only methods such as NORPLANT® implants and progestin-only pills (POPs) are said to be effective within several hours by causing a thickening of the cervical mucus. However, there has been little biological data collected or presented which actually demonstrates this.

There are numerous investigational possibilities in the areas of timing to, and mechanisms for, effectiveness of progestin-only methods of contraception. However, FHI has the strongest interest in performing those studies which we feel would have the greatest potential programmatic impact. Of particular interest is research on the timing required to reach contraceptive effectiveness for progestin-only methods, and the relationship of menstrual cycle day at the time of product initiation. In addition, the loss of effectiveness when a POP is missed or delayed is important.

Information gathered from these studies will potentially have a great impact on the guidelines set for back-up contraception following initiation of progestin-only methods, especially where lengthy periods are often specified for methods such as NORPLANT® and progestin-only pills. Also of importance will be suggestions for back-up contraceptive use following missed or delayed pills.

Our current study was designed as the first of a possible series of studies to address many of these issues. This study will investigate the changes in cervical mucus within the first hours to days after NORPLANT® implant insertion and will seek to better estimate when the cervical mucus is hostile enough to successfully prevent conception. A total of 60 women who request NORPLANT® as their method of contraception and are between days 8 and 13 of their menstrual cycle are to be recruited for the study. Cervical mucus samples will be taken at 0, 6, 12 and 24 hours, and 3 and 7 days following insertion. In addition, blood samples will be taken at the same times to evaluate progesterone and levonorgestrel serum concentrations. *In vitro* sperm penetration and mucus scoring will be evaluated for determination of mucus "hostility" and serve as a surrogate for attainment of contraceptive efficacy.

It is our desire to follow this study with similar studies to evaluate the timing of the onset of effectiveness in DMPA and progestin-only pill users. We also have a strong interest in the potential loss of effectiveness of progestin-only pills where a delay in ingestion of the pill by as little as three hours may result in the need for back-up contraception for a yet undetermined period of time. And finally, we would like to investigate the effect of estrogen treatment on cervical mucus, and subsequent loss of effectiveness, in progestin-only method users who are being treated for method-specific bleeding problems.

Mellon-sponsored Projects

ANDREW W. MELLON FOUNDATION SPONSORED PROJECTS

Since 1983 The Mellon Foundation has provided support to FHI for contraceptive development and related activities. Primary activities supported by the Mellon Foundation include the Postdoctoral Fellowship Program in Contraceptive Technology, research on nonsurgical female sterilization, collaboration between scientists working in reproductive biology research and contraceptive development, and development of a research program to study the impact of contraceptive use on women's quality of life.

Postdoctoral Fellowship In Contraceptive Technology Research

The goal of the fellowship program is to increase the number of scientifically capable researchers in Third World countries who will be able to conduct contraceptive development and evaluation research in their respective countries. Through the program, we seek to provide fellowships to promising key researchers working in centers currently associated with FHI, or to candidates well qualified to become part of our network.

FHI is now in the third year of the Postdoctoral Fellowship in Contraceptive Technology Research. Our 1993-1994 Mellon Fellow, Dr. Carlos Petta, is affiliated with CEMICAP and the University of Campinas in Brazil where he serves as both a staff physician and a researcher in human reproduction. Upon his return, he will conduct a study with a re-entry grant which is part of the Mellon Fellowship. Dr. Petta's study will be on the timing of onset of contraceptive effectiveness in Depo-provera users as determined by changes in cervical mucus.

For the 1994-1995 postdoctoral fellowship program, applications were received from 19 highly qualified applicants in 12 different countries. Dr. Joseph Ruminjo from the Department of Obstetrics and Gynecology, the University of Nairobi, will be the 1994-1995 fellow and will join FHI in September.

Our first fellow, Dr. Xu Jin-Xun from The People's Republic of China, is using his re-entry grant to conduct a comparative study of two immediate postplacental vaginal insertion techniques used to apply the Tcu-380A IUD. FHI is providing technical assistance and study monitoring and anticipates that Dr. Xu will return to FHI to finish the data analysis and study write up in 1995.

Nonsurgical Female Sterilization

Mellon support has permitted FHI to conduct the retrospective study on the safety and efficacy of quinacrine hydrochloride pellets as a transcervical method of nonsurgical female sterilization in Chile. It has enabled us to analyze and prepare reports and articles for publication, and to develop and initiate a follow-up to the retrospective study. This follow-up will allow us to examine the health experiences of participants in the retrospective study and will cover the five year period, 1991-1996.

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Coordination of Mellon Funded Reproductive Biology Research Centers and Contraceptive Development Programs

This program reflects the need to bridge the fields of reproductive biology and contraceptive development. FHI is responsible for coordinating periodic meetings that bring together researchers from the Mellon Reproductive Biology Centers and contraceptive development programs, agencies supporting contraceptive development research, the pharmaceutical industry and the FDA. The first meeting was held in November, 1993. (A full report of the meeting accompanies this document.)

FHI is also responsible for facilitating communication and interaction on pertinent topics in between the meetings. We are working with the centers to define the mechanisms that will best foster interaction. These include an informal newsletter, conference calls, and small working groups.

The next meeting will be held early in 1995. At the recommendation of the directors of the Mellon Reproductive Biology Centers, we plan to expand the meeting format and increase the number of participants. In particular, the directors want more of their junior staff to attend.

The Impact of Contraceptive Use on the Quality of Life

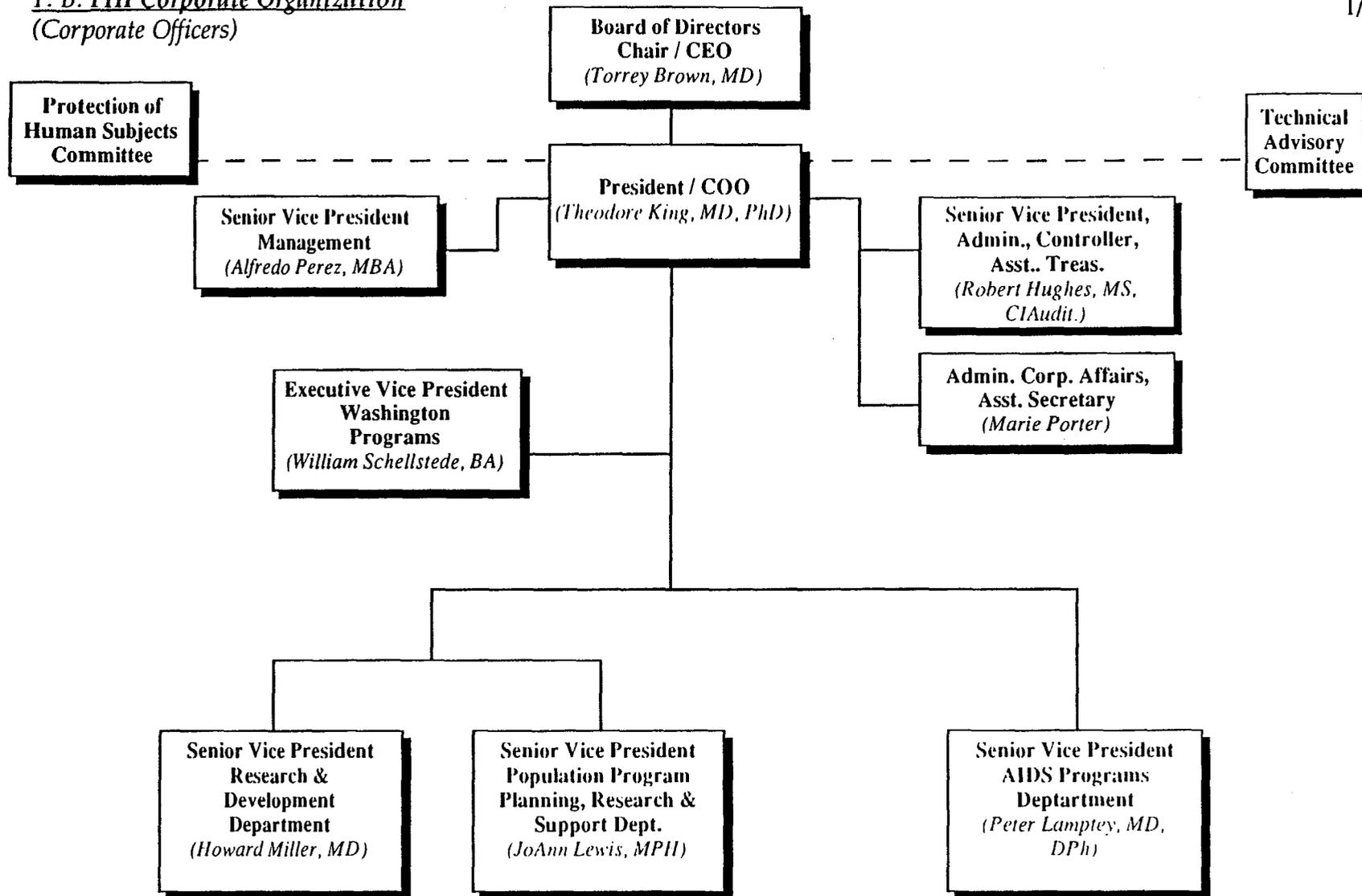
FHI has a long-standing concern about the acceptability of new methods of contraception. We believe that to successfully develop and introduce acceptable new contraceptive methods, we should consider the needs and perspectives of the potential users throughout the development process. Since 1993, we have been working to adapt Quality of Life (QOL) research strategies from the medical and drug development field to our contraceptive development and reproductive health programs.

The primary goal is to design an assessment method for the purpose of evaluating users' perceptions and the conditions which are thought to influence contraceptive use and reproductive health care utilization. Major accomplishments to date have been the development of a QOL research database and a draft QOL assessment instrument which addresses physical, psychological/spiritual, social and environmental domains. Integration of QOL assessment concepts and modification of the draft instrument for use in different reproductive health study areas is anticipated during the next twelve months. A theoretical framework is being developed that addresses family planning and the quality of women's lives. It will be presented at the American Public Health Association meeting this year.

Agenda Item 3

General Review of Program

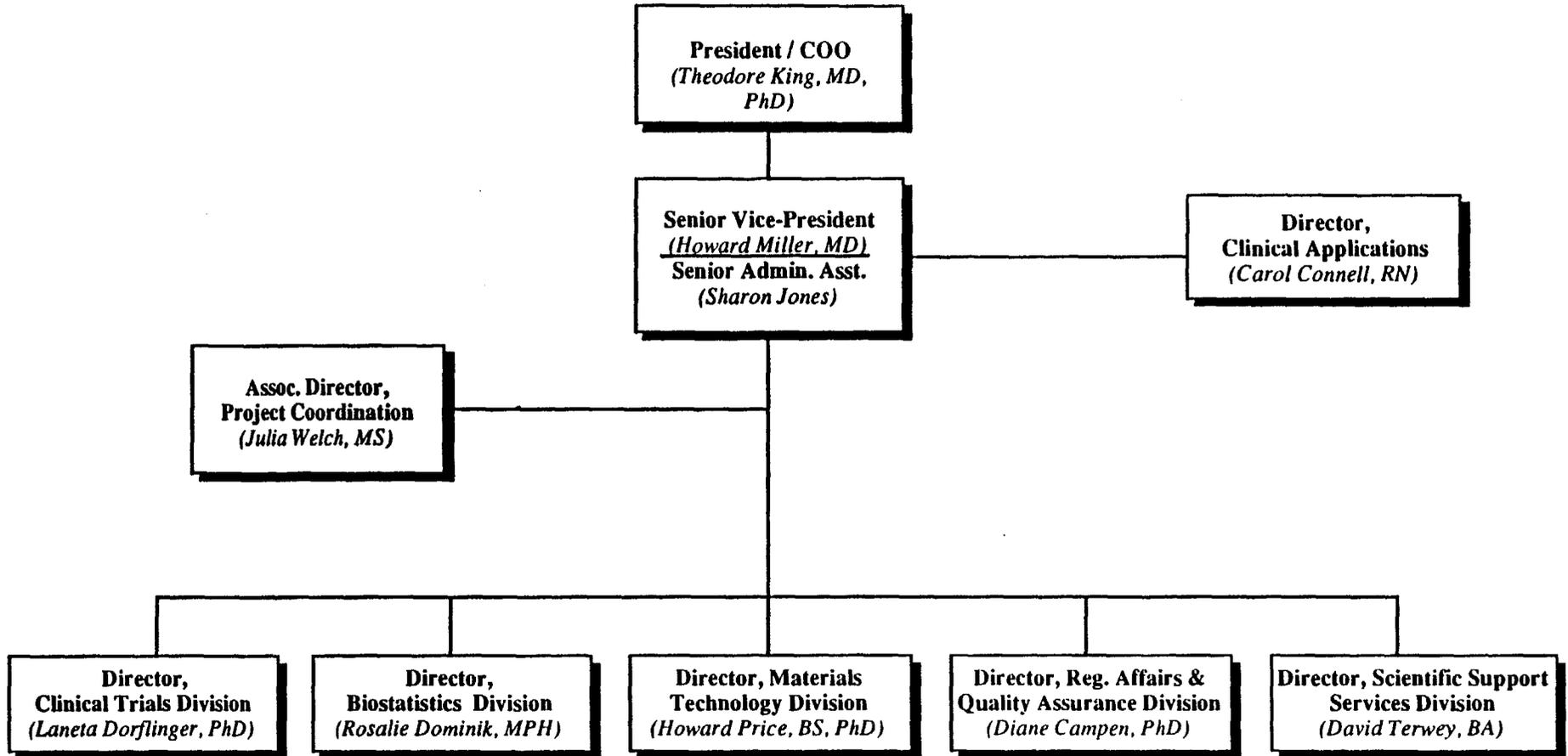
1. B. FHI Corporate Organization
(Corporate Officers)



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3. A. Research and Development
Department

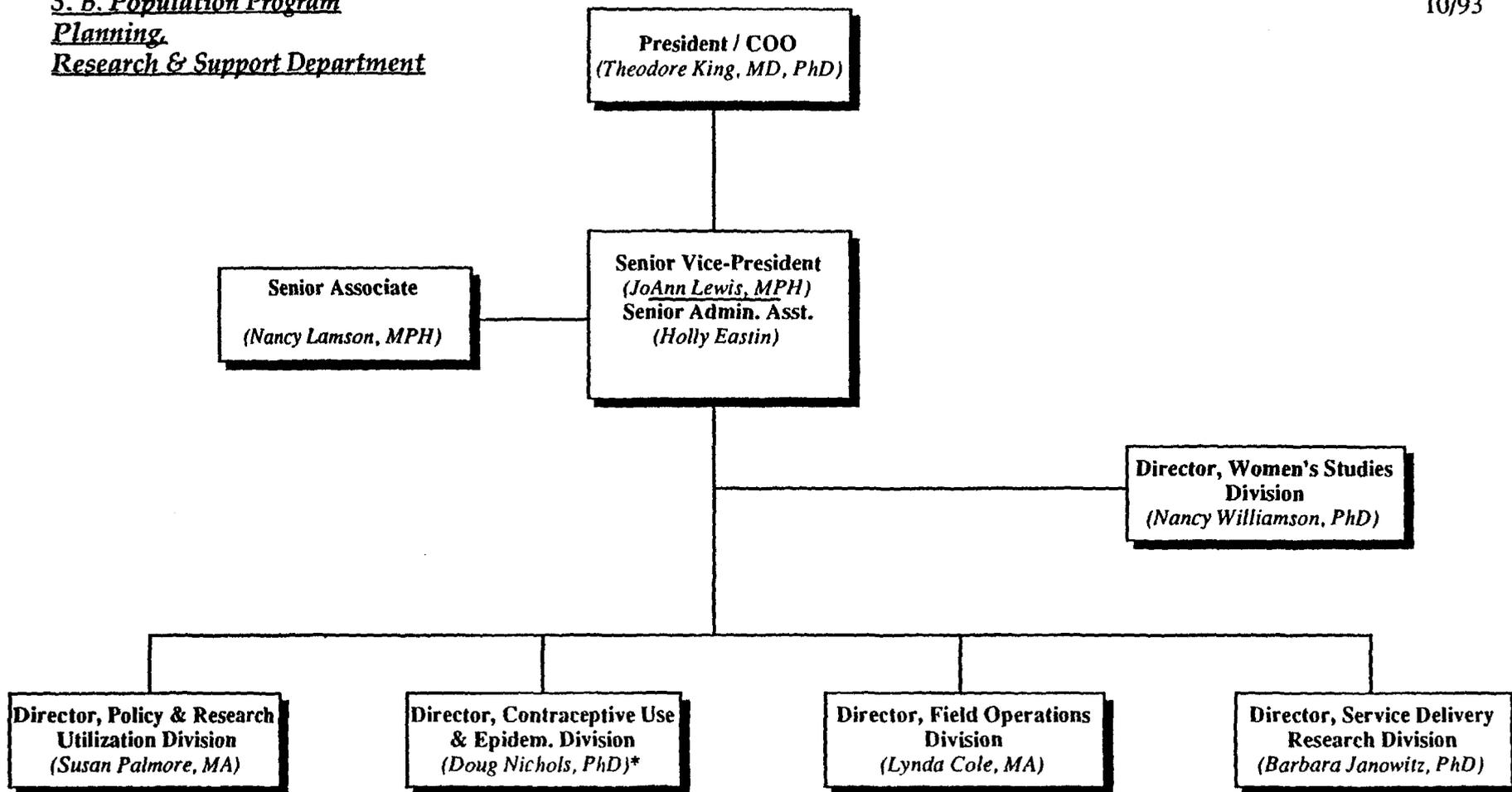
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3. B. Population Program
Planning.
Research & Support Department

10/93



* Acting

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FHI

**CONTRACEPTIVE TECHNOLOGY
AND FAMILY PLANNING RESEARCH**

**COOPERATIVE AGREEMENT
DPE-3041-A-00-0043-00**

WORKPLAN 1994

*SUBMITTED TO
OFFICE OF POPULATION, RESEARCH DIVISION
UNITED STATES AGENCY FOR
INTERNATIONAL DEVELOPMENT*

JANUARY 1994



FAMILY HEALTH INTERNATIONAL • Durham, NC 27709 USA

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OMITTED

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I. OVERVIEW

This document constitutes the fourth annual workplan for Cooperative Agreement No. DPE-3041-A-00-0043-00, entitled "Contraceptive Technology and Family Planning Research" implemented by Family Health International (FHI). FHI is a private, not-for-profit organization dedicated to improving the health of individuals worldwide, with an emphasis on developing countries. During the past two decades, FHI has worked in more than 100 countries, carrying out joint research programs and providing technical assistance to help solve problems identified by governments, clinical researchers, and health care providers in family planning, reproductive health and, for the past seven years, in AIDS prevention. FHI works closely with international health and development organizations, including the U.S. Agency for International Development (USAID), its overseas Missions and cooperating agencies (CAs); the World Health Organization (WHO); the Pan American Health Organization (PAHO); the National Institutes of Health (NIH); the Centers for Disease Control and Prevention (CDC); the United Nations Population Fund (UNFPA) and a host of other agencies working in related areas.

FHI was founded in 1971 with the specific mandate of providing the USAID's Office of Population with the data needed to make decisions concerning the purchase and provision of contraceptives for USAID programs in developing countries. This entailed designing and implementing clinical trials to evaluate, in developing country settings, the safety and efficacy of different contraceptive types and brands.

FHI has also conducted clinical trials whose primary purpose is to introduce new contraceptive methods or new technologies to developing countries. Examples of contraceptive methods introduced by FHI to less developed country (LDC) programs include laparoscopic sterilization, minilaparotomy sterilization, progestin-only oral contraceptives, postplacental intrauterine device (IUD) insertion, and Norplant (levonorgestrel implant, Leiras Pharmaceuticals, Turku, Finland).

The need to base contraceptive program decisions on sound research was recognized by USAID soon after the Office of Population was founded. While the questions continue to change and evolve, program decisions still need to be based on well-conducted research. USAID has continued to rely on FHI and other cooperating agencies to meet that need.

Because many questions in contraceptive service provision cannot be addressed adequately through clinical research, FHI's role was expanded by USAID to include a "social science" or programmatic research component. Programmatic research at FHI is responsive to the needs of service programs at the country level, and now includes, for example, ways to improve compliance and enhance the acceptability of new methods. The past three years

have been characterized by closer linkages with other divisions in the Office of Population, including the Family Planning Services Division, the Commodities and Program Support Division (CPSD), and the Information and Training Division.

During the past two years we have worked closely with the Office of Population and its other CAs, taking a leadership role to develop and implement a strategy aimed at improving service practices to increase access to contraception.

Our role continues to evolve to meet USAID's research needs. As the U.S. pharmaceutical industry has reduced its efforts in the development of new contraceptives, the U.S. Government (the National Institutes of Health [NIH] well as USAID) has played an increasingly important role in sponsoring private companies to work in contraceptive development and evaluation. FHI, the Population Council and Contraceptive Research and Development Program (CONRAD) collaborate closely in this important endeavor, which has consumed a growing proportion of the funds provided under FHI's Cooperative Agreement with the Office of Population. FHI's work in this area includes providing data for the approval of new methods by the U.S. Food and Drug Administration (FDA), a prerequisite for USAID purchases of commodities for LDC service programs. During the past year, the U.S. FDA granted marketing approval for the REALITY® vaginal pouch (Wisconsin Pharmacal, Jackson, WI); FHI provided support to the manufacturer and CONRAD in the preparation of the FDA application. Data from FHI studies are also used on a regular basis for product approval by regulatory agencies in developing countries.

Responding to concerns of women's advocacy groups, as well as to the worldwide epidemic of HIV infection and other sexually transmitted diseases (STDs), FHI continues to focus increasing attention on barrier methods and spermicides. For many years, condoms were not a major method provided by many family planning programs, because their clients are usually women, many men dislike using condoms, and storage can be difficult in some climates. In response to USAID's request, FHI is carrying out a program of quality surveillance and is evaluating the integrity of latex condoms stored under specified conditions, both in the laboratory and in actual use. Improved quality surveillance has the potential for significantly reducing wastage associated with poor storage conditions. In the coming year, we will expand our quality surveillance work to other contraceptive products. A product development priority is the continued work on design improvements in the thermoplastic male condom.

The safety of contraception includes long-term unanticipated consequences, as well as short term effects. A relatively small, but important, part of our resources is dedicated to research concerned with the long-term safety of the contraceptive methods provided by USAID in developing countries. A priority for this area is contraceptive interaction with STDs, including HIV. Resources are also being invested to improve a lifetable computer model to evaluate the risks and benefits of various contraceptives.

FHI strives to balance a centrally-funded research and research support agenda of broad relevance to programs worldwide with meeting particular program needs in specific countries. We also recognize the importance of country-level input into the broader issues for setting global research and development priorities. To this end, we have taken steps to strengthen our field presence, with the establishment of a field office in Nairobi, Kenya in January 1992, and with the placement of a resident advisor to the Ministry of Public

Health in Nepal in January 1993. We remain responsive, as resources permit, to requests from USAID Missions around the world, but with emphasis given to those countries designated as priority by the Office of Population.

The following sections of this report describe FHI's program and FY'94 planned activities under the Contraceptive Technology and Research Cooperative Agreement. Section II lays out the broad goal, program priorities and key interdivisional initiatives. The FHI divisions tasked with implementing the program are also briefly described.

Section III presents the detailed annual workplan for FY'94, by division. Each of the divisions, with the exception of the support divisions, presents an overview of planned activities for the upcoming year. Following this introduction, a detailed individual workplan for each subproject within a division is presented.

The budget for FY'94 is presented in Section IV, in summary by division, as well as regionally by program area, and by country. Appendices follow the body of the main report.

II. COOPERATIVE AGREEMENT

A. COOPERATIVE AGREEMENT GOAL

The broad goal of the Contraceptive Technology and Family Planning Research Cooperative Agreement No. DPE-3041-A-00-0043-00 is to enhance the freedom and abilities of individuals in the developing world to choose voluntarily the number and spacing of their children. The specific purpose of the work to be carried out is to increase the means available to developing country couples to achieve their desired family size by developing and introducing a range of safe, effective, and acceptable methods of family planning and by enhancing the capacity of family planning researchers and programs in developing countries to evaluate and provide these methods.

B. FHI DIVISIONS IMPLEMENTING THE COOPERATIVE AGREEMENT

Under FHI's organizational structure, the Contraceptive Technology and Family Planning Research Cooperative Agreement is implemented by two departments, the Research and Development Department and the Population Program Planning, Research and Support Department.

The divisions comprising the Research and Development Department are: Clinical Trials, Materials Technology Development, Biostatistics, Regulatory Affairs and Quality Assurance, and Scientific Support Services. The Population Programs Department consists of four divisions: Contraceptive Use and Evaluation, Field Operations, Policy Research and Utilization, and Service Delivery Research.

A brief description of each division is given below. Although Biostatistics, Regulatory Affairs, and Scientific Support Services are part of the Research and Development Department, they are listed separately. As support divisions, they provide assistance and back-up to the entire organization.

1. Research and Development Divisions

The Clinical Trials Division (CT) conducts Phase I through large-scale Phase IV clinical trials to evaluate new contraceptive technologies and to provide the data necessary to obtain U.S. and developing country regulatory agency approvals for worldwide product introduction and use. CT also conducts studies on approved contraceptives to obtain and

disseminate information about the efficacy, safety, and acceptability of these methods in different cultural settings.

The Materials Technology Division (MTD) coordinates and manages FHI's contraceptive development and quality testing programs. MTD also supports research conducted by other divisions on consumer condom preference and condom functionality. Particular emphasis is placed on the development and testing of promising new thermoplastic condoms and quality surveillance of latex condoms.

2. Population Program Planning, Research and Support Divisions

The Contraceptive Use and Epidemiology Division (CUE) supports research to assist programs to improve the use of contraceptive methods. The research which the division conducts is broad-based and involves the study of a variety of methods within diverse populations. CUE's research, at present, focuses on acceptability and barrier methods, contraceptive compliance, contraceptive benefits and risks, contraception and STDs/HIV, and breastfeeding and postpartum contraception.

The Service Delivery Research Division (SDR) carries out studies which aim to improve the delivery of family planning services, with the overall goal of increasing access to contraception. The emphasis of the division's work is to inform management and policy decisions which can lead to increased access to contraception. Divisional priorities are: improving resource allocation and financial sustainability, improving quality of care, reducing barriers that limit access to contraception, and the evaluation of new combinations of methods and delivery systems.

The Policy Research and Utilization Division (PRU) staff works to improve the dissemination and use of research findings to appropriate family planning providers and planners. The division's work falls under four categories: reproductive health information dissemination, health communication and training, activities to improve access to contraception, and technical assistance and training for family planning related policy development. Oversight of FHI's specialized reproductive health library, which serves the needs of the entire organization, is also the responsibility of this division.

The Field Operations Division (FO) serves as the principal coordinating point for FHI's country specific programs and activities, and provides support for FHI regional and country offices.

3. Support Divisions

The Biostatistics Division is involved in all stages of clinical and programmatic research. Biostatisticians collaborate with clinicians and researchers to define research objectives and to determine appropriate study designs and sample sizes. Biostatisticians develop and carry out the data analysis plans for all clinical studies and some programmatic studies. For many programmatic studies, biostatisticians serve as consultants to staff outside the Biostatistics Division who plan and carry out their own analyses. In addition, the division

has recently begun to support the product stability and quality control activities of the Materials Technology Division.

Major analysis efforts in FY'94 will include the analysis of the Lea's Shield™ Phase II clinical trial, the Roll-on Thermoplastic Condom Phase I study and the biodegradable norethindrone (NET) Pellets Phase II trial.

Biostatistics staff also plan statistical seminars and classes for FHI research staff and facilitate workshops for collaborating researchers. This fiscal year, Biostatistics staff will offer a 16 week course in basic statistical methodology to FHI research staff.

The Regulatory Affairs and Quality Assurance Division (RA/QA) provides regulatory technical support necessary for research and program divisions. The RA/QA staff maintain a current working knowledge of FDA regulations and guidelines applicable to contraceptive drugs and medical devices. The RA/QA staff develop and implement procedures within FHI in order to comply with the applicable FDA regulations. Examples of ongoing regulatory activity are coordination and submission of responses to FDA questions resulting from a Premarket Approval Application (PMA) for a sterilization device (Filshie Clip), interaction with the FDA on issues related to development of the plastic condom, follow-up of Investigational Device Exemption (IDE) and Investigational New Drug Exemption (IND) submissions and review of all clinical trial protocols. In addition, staff participate as regulatory advisors on interdivisional project working groups.

The Regulatory Affairs and Quality Assurance staff are also responsible for the development, implementation, and compliance auditing of standard operating procedures for interdivisional activities and compliance auditing of Good Laboratory Practices (GLP), Good Manufacturing Practices (GMP), and Good Clinical Practices (GCP) studies for the company.

The Scientific Support Services Division (SSS) provides computer, network and graphics services for all the other divisions of FHI. Virtually every employee of the company uses these services in some way. The most basic of SSS services is the electronic mail (Email) system. The Email system is used extensively in FHI's headquarters in Research Triangle Park (RTP), but also supports the staff at the FHI Arlington, VA. office and connects them to RTP based staff. In the past year we have also added Email connections to the FHI regional office in Bangkok, Thailand and most recently, Nairobi, Kenya. Additionally, we have linked FHI's Email system with services provided by MCI. This not only gives FHI direct Email access to USAID, but also limited connection to other Email systems like the Internet, MCIMAIL, ATTMAIL, and many others.

The foundation for FHI's Email system is a series of Digital Equipment Corporation (DEC) VAX computers. SSS supports and manages VAXs located in RTP, Arlington, Bangkok and Nairobi. A separate VAX, located in RTP, provides significant computer power to support our scientific and statistical users. The bulk of this effort is spent in support of the Contraceptive Technology and Family Planning Research Cooperative Agreement. All of these VAXs are connected using sophisticated networking technology to provide all users access to any VAX server connected to the network, subject to appropriate security guidelines.

In addition to managing the hardware and software, SSS personnel provide systems analysis and customized software development services for FHI. During the past year we completed the first phase of development of a major new system called CRIS (Clinical Research Information System). The second phase of CRIS development should be completed in mid-FY'94. CRIS was designed to reduce the amount of custom programming necessary to implement new clinical studies in support of the Contraceptive Technology and Family Planning Research Cooperative Agreement. Several other major programming projects are underway for this Cooperative Agreement and other FHI projects.

The third major mission of SSS is to provide graphic development and other technical services to FHI staff. An increasingly important dimension to these technical services is the support of over 100 desktop computers around the network. These are primarily IBM-compatible personal computers (PCs), but also include a number of Macintosh computers. Virtually all of these desktop computers are connected to our network and utilize network services such as shared printers, hard disks, CDROMs, and backup services. SSS also offers training and a centralized "hotline" support for all services.

C. FY'94 PROGRAM PRIORITIES AND INTERDIVISIONAL INITIATIVES

1. Program Priorities

During the 5-year period covered by the Cooperative Agreement, FHI is continuing to build upon the work it has carried out for the past two decades with funding from the Office of Population. Workplan priorities for the current fiscal year include:

- continued emphasis on the development and regulatory approval of new, safe, and effective contraceptive technologies;
- testing to assure the quality of contraceptive products;
- studies to improve acceptability of and compliance with contraceptive use;
- research and interventions to improve access to contraception by improving family planning service delivery practices;
- the development and implementation of strategies for introducing depot medroxyprogesterone acetate (DMPA);
- continued studies (unique among Office of Population CAs) to evaluate both long- and short-term benefits and risks of contraceptive use;
- research to support family planning service delivery programs, including studies to improve cost effectiveness and quality of care; and

- assuring that research findings and information are widely disseminated in formats that are useful to service providers, policymakers, and family planning clients.

2. Major Interdivisional Initiatives

FHI is organized by departments and divisions, as described in a previous section, with each division having primary responsibility for key components of FHI's contraceptive technology and research program. However, collaborative work among divisions is mandated by the complexity of the issues that FHI addresses in this program. Interdivisional working groups were established in FY'93 to provide a mechanism for collaboration across departments and among divisions in key program areas: contraceptive introduction, improving service practices to improve access to contraception, postpartum contraception, adolescent reproductive health, and family planning and STDs/HIV.

In FY'94, FHI will continue to use a broad range of skills and institutional capabilities to focus its efforts to meet the goal and purposes of this program. Five areas will continue to be the focus of major interdivisional initiatives in the upcoming year. Ongoing and planned work in these areas are described in the following section.

■ Barriers and Spermicides

FHI's research agenda includes a growing emphasis on contraceptive methods which may also provide protection against STDs. In accordance with this priority, clinical and programmatic research on a range of barrier methods, including male and female condoms and vaginal contraceptive film (VCF® is ongoing or planned for FY'94.

FHI's work in the development of a non-latex male condom illustrates the interdivisional nature of these activities. The development efforts of MTD are supported by CT research to evaluate the safety and efficacy of FHI's thermoplastic condom designs, and by CUE studies of the acceptability and feasibility of prototype condoms during intercourse. All of these efforts are supported by the Biostatistics, Scientific Support Services and Regulatory Affairs/Quality Assurance Divisions.

FHI staff from several divisions will also be involved, as part of an interagency group headed by the World Health Organization (WHO), in a multicountry prospective study of diaphragm use in selected developing countries. This study grew out of a recent meeting organized by WHO during which strong support was expressed by women's health advocates for the promotion of fertility regulation methods which: 1) are user-controlled; 2) provide protection against STDs; 3) have minimal or no side effects; and 4) foster knowledge of one's own body. FHI will be responsible for the implementation of studies of the acceptability, service delivery requirements, and use effectiveness of the diaphragm in one or more countries. These and other research activities on barrier and spermicide methods are an important component of FHI's FY'94 plan.

■ **Improving Service Practices to Increase Access to Contraception**

At USAID's request, FHI is leading an international initiative to reduce unnecessary barriers to contraception, with a goal of increasing access to quality contraceptive services. For the past two years, FHI has been an active partner with USAID and other CAs in efforts at an international level, as well as in various developing countries. An interdivisional working group, established in FY'93, coordinates and tracks FHI activities in this area.

This will continue to be a major focus in FY'94, and many of the subprojects that constitute FHI's FY'94 workplan are important components of FHI's interdivisional focus on reducing barriers to contraception, particularly through improving service practices. As part of its efforts to increase access to contraceptive use, FHI conducts research to identify restrictive barriers to family planning service delivery which can be removed without negative consequences for the health of clients. FHI also works with local organizations and other CAs to influence policy and practice revision.

Education and training activities are an important component of FHI's emphasis on addressing barriers to contraceptive use. FHI conducts contraceptive technology update (CTU) seminars and is developing a series of standard modules for use in these workshops. During the past year significant progress was made in the development of modules on injectable contraceptives, the lactational amenorrhea method (LAM), and postpartum contraception; these should be completed and produced in this fiscal year.

FHI will continue a broad range of research, policy and practice revision, and education and training activities in FY'94 to improve service practices and increase access to contraception. Projects are ongoing or planned in Cameroon, Jamaica, Mexico, Honduras, Ghana, and Haiti.

■ **Contraception, Family Planning and STDs/HIV**

FHI's interdivisional efforts in this program area have increased steadily over the past four years, and will have an even greater scope in FY'94 with additional attention given to the examination of issues related to the integration of STD services in family planning programs.

FHI is a leader in research on the risk of sexually transmitted disease outcomes, including HIV, among users of specific family planning methods. In FY'94, studies will include: a randomized trial of spermicide use and HIV incidence (funded by NIH), a comparison of the incidence of cervical infections among women using non-spermicidal latex condoms and those using spermicidally lubricated condoms, female condom use and STD infections, and female condom use by HIV-discordant couples. Two additional studies in this area are planned, pending availability of funding. These are a study of short-term complications of IUD use among HIV-positive and HIV-negative women in Kenya, and research on whether combined OC use increases susceptibility to HIV infection.

Programmatic research will also be a priority in FY'94. Service providers recognize the value and importance of integrating STD and family planning services in order to enhance reproductive health and optimize use of resources. However, there are many issues involved in integration of services. Staff from several of FHI's program divisions will collaborate to prepare a strategy delineating needs assessment and research activities which FHI can undertake, both epidemiologic and programmatic, to address these issues.

Two programmatic research activities are planned for FY'94. The following have been identified as appropriate research priorities: determining the appropriate level of integration of family planning and STD/HIV services at service delivery points, development of an STD risk assessment methodology for individual clients and clinic populations, evaluation of the usefulness of the syndromic approach for STD diagnosis in family planning settings, and assessment of the costs of adding STD services to family planning programs.

In addition to these activities, an acceptability study of dual method use (latex condoms vs. choice of latex condoms and nonoxynol-9 (N-9) film among OC users), begun in FY'93, will continue.

■ **Contraceptive Introduction**

An interdivisional working group was established to develop a strategy for contraceptive introduction and to coordinate and track organizational activities in this program area. FHI's work in contraceptive introduction is intended to assist developing countries to integrate new methods into their programs by providing a bridge from research to service delivery. FHI works closely with service delivery agencies in carrying out work to meet this objective.

FHI's efforts in the first three years of this Cooperative Agreement were focused on the development of country strategies for the introduction of Norplant, and on improving the availability and use of methods during the postpartum period. During the last year, considerable attention has been devoted to the development of an introduction strategy incorporating new methodologies for contraceptive introduction that will meet the need for lower cost, rapid implementation strategies to introduce methods such as DMPA into countries where injectables are not now used. FHI is working closely with the Population Council, the Association for Voluntary Surgical Contraception (AVSC), and other CAs to develop and implement a cooperative plan and standard resources for introduction of DMPA in selected countries.

In FY'93, a part of the DMPA introduction initiative, and at the request of USAID/Manila, an interdivisional FHI team, in collaboration with Pathfinder, assisted the Mission and the Department of Health to develop a country strategy for the introduction of DMPA. FHI staff also traveled to Amman, Jordan to work with USAID/Amman and Jordanian counterparts to explore possibilities for collaboration in the introduction of safe and effective birthspacing technologies such as DMPA, Norplant and postpartum IUD insertion, which have not been part

of Jordan's family planning program. Further work on both of these initiatives is planned for the upcoming year.

Studies continue in support of introduction of contraceptive methods. These include research to assess the acceptability of contraceptive methods which are not widely used; cost effective resupply strategies for DMPA in Ecuador; and reasons for switching to and from DMPA in the Wake County medical system in North Carolina.

In addition to research and technical assistance, FHI's education and training activities can be (and are) used to initiate and support contraceptive introduction. For example, the contraceptive technology modules and contraceptive technology update seminars (described in a previous section as part of the interdivisional effort to improve service practices) are available for use as part of an integrated approach to introducing specific methods, such as injectables.

Contraceptive introduction efforts focusing on DMPA, Norplant, and postpartum contraceptive methods will continue in selected countries during FY'94. In addition, FHI and the Population Council will hold a meeting during the USAID Cooperating Agencies Meeting in February, to discuss programmatic research priorities to support DMPA introduction. CAs with interest in DMPA introduction in selected Latin American countries will participate.

■ **Postpartum Contraception**

In addition to FHI's efforts to introduce new methods into family planning service delivery systems, we are committed to the expansion of method acceptance and use for existing methods. As mentioned above, a main focus in this area is postpartum contraception.

FHI is conducting research in the acceptability and cost of immediate post-placental insertion (IPPI), the timing of initiation of progestin-only contraceptives in lactating women, and clinical trials of the lactational amenorrhea method. In addition, two in a series of modules on contraceptive methods being developed by FHI are dedicated to this area: a module on LAM and a module on postpartum contraceptive technology, which will provide a general overview of recommended contraceptive methods for use during the postpartum period. These modules are designed for use by presenters and trainers in seminars, courses, and workshops targeting family planning providers and planners. Work in these areas will continue in FY'94.

In the next section (Section III), individual workplans are presented for each ongoing or new subproject for FY'94. The subprojects are presented as part of each division's FY'94 workplan. Individual workplans include project objectives, a brief description, activities and outputs for FY'94, and possible barriers to completion of planned work. In addition, the implementing agency (if other than FHI) and collaborating agencies are presented, if applicable. Budget figures are given, both for the current fiscal year and for the life of the project under the Cooperative Agreement. Both figures include FHI in-house and field costs.

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III. ANNUAL WORKPLAN - FISCAL YEAR 1994

A. RESEARCH & DEVELOPMENT DIVISIONS

1. Clinical Trials

During much of its history, FHI has conducted clinical trials to provide data on the safety and efficacy of existing contraceptive methods in countries or for programs where these methods had not been previously used, or to answer questions about the appropriateness of a specific method in a particular setting. During the past few years, FHI has increasingly focused on activities, including well-controlled clinical trials, necessary to secure approval of new contraceptives by the FDA. The long-term goal of these activities is to increase the contraceptive choices for couples in developing countries. In this effort, FHI works closely with CONRAD and, as appropriate, with other CAs. In our collaborations with CONRAD, they have generally focused on preclinical and Phase I work, whereas FHI has carried out Phase II and Phase III studies. In a few instances, FHI has been, and continues to be, involved in earlier stages of contraceptive development and evaluation including preclinical and Phase I studies. At present, in our collaborative projects with CONRAD, FHI is responsible for regulatory affairs, data management, and data analysis activities.

Since the mid-1980s, FHI has developed a strong in-house capacity to manage the research and development activities required to secure FDA approval for new contraceptives. For example, results of our clinical trial (conducted in collaboration with CONRAD) led to FDA approval of the REALITY® Female Condom and we have submitted a Premarket Approval Application (PMA) to the FDA for the Filshie Clip System for female sterilization. Staff have considerable skills and experience in clinical trials, clinical data management, biostatistics, and regulatory affairs and quality assurance. FHI also has sophisticated computer facilities which are essential to providing the documentation necessary to secure approval for new products. Finally, FHI's international investigator network, numbering more than 260 clinical research centers in 55 countries, provides a unique resource for carrying out clinical trials.

Currently, FHI's activities can be categorized into two main areas:

- **Development and Evaluation of New Contraceptives**

Work in this area is aimed at providing sufficient data to the FDA and other regulatory agencies to secure marketing approval of new products. Activities have included Phase I, II, and III clinical trials, preclinical toxicity testing, the filing and upkeep of INDs and IDEs necessary for clinical investigations, and the filing of a

PMA for regulatory approval of one product. Research is currently being supported or planned by FHI on the following products: non-latex male condoms, an iodine sclerosing formulation for non-surgical female sterilization, the Filshie Clip for female sterilization, NET pellets, NET injectable microspheres, Lea's Shield™, FEMCAP™, and VCF®.

■ **Clinical Trials to Provide Information to Programs on Available Contraceptives**

The main purpose of these trials is to produce data for local family planning programs on the safety and efficacy of contraceptives already approved for use; to enable health providers to become familiar with these products; and to provide data for policy decisions on the methods to be offered in a country program. Studies to date have included clinical trials of progestin-only and combined oral contraceptives, intrauterine devices, male and female sterilization techniques, and various barrier methods. Special trials are also conducted to address particular questions related to the use of a method such as the comparison of no-scalpel to standard-incision vasectomy, the comparison of various IUDs, the timing of initiation of progestin-only pills in breastfeeding women and the timing of the contraceptive effectiveness of progestin-only contraceptives (using changes in cervical mucus as a surrogate for effectiveness).

FY'94 Program, Objectives, and Expected Outputs

During FY'94, FHI's contraceptive development program will continue to emphasize the development of barrier methods of contraception (particularly the plastic condom and Lea's Shield™, as well as research on the efficacy of vaginal contraceptive film) and non-surgical female sterilization (iodine formulation). Data analysis of the Phase II study of the Lea's Shield™ will be completed and a Phase III clinical trial initiated. A clinical trial to compare the contraceptive efficacy of a plastic condom with a marketed latex condom will be designed in consultation with staff of the Food and Drug Administration. Preclinical toxicology studies of the current iodine formulation will be completed and a Phase I clinical trial designed. In addition, the clinical trial of the long-acting biodegradable NET pellet system will be continued, the clinical trial of the timing of initiation of the progestin-only pill will be completed, follow-up in the remaining clinical trials of Norplant implants (Senegal and El Salvador) will continue, work will be initiated to help better understand the timing of the contraceptive effect of progestin-only contraceptives and activities will be initiated to identify other long-acting steroidal contraceptive products on which FHI might collaborate to develop. Our pilot project to better understand the timing of effectiveness of male sterilization will continue in close cooperation with Association for Voluntary Surgical Contraception (AVSC). Data analysis of a study on the use of condoms and vaginal spermicides in women at risk of contracting sexually transmitted diseases will be completed. Finally during this year, we will work closely with the FDA during their review of our PMA for the Filshie Clip System which was submitted during FY'92.

Details of CT subprojects are contained in individual workplans, presented by type of method, as listed below.

■ **Barrier Contraceptives and Spermicides**

Continuing Projects:

- Use of Condoms and Vaginal Spermicides by Women at High Risk of Contracting Sexually Transmitted Diseases
- Phase II Efficacy and Safety of Lea's Shield™ Used with and Without Spermicide

New Projects:

- Safety Assessment of the Slip-On Thermoplastic Male Condom
- Contraceptive Efficacy of Plastic vs. Latex Condoms
- Clinical Evaluation of Vaginal Contraceptive Film
- Phase III Comparative Lea's Shield™
- Pilot Study of the Physical Characteristics of Spermicidal Preparations

■ **Female Sterilization**

Continuing Projects:

- Preclinical Iodine
- Filshie Clip Premarket Approval Application

New Projects:

- Phase I Iodine Trial

■ **Long-Acting Steroid Delivery Systems**

Continuing Projects:

- Phase IIA Pharmacokinetic Evaluation of Biodegradable Norethindrone Pellet Implants
- Pre-Introductory Clinical Trial of Norplant Contraceptive Subdermal Implants (Senegal)
- Pre-Introductory Trial of Norplant Subdermal Implants (Ghana)
- Clinical Trial of Norplant Contraceptive Implant System (El Salvador)
- Phase I, II and III Evaluation of the Safety and Pharmacokinetics of Norethindrone 90-day Injectable Microspheres

New Projects:

- Timing of Onset of Contraceptive Effectiveness in Norplant Implant Users

■ **Intrauterine Devices**

Continuing Projects:

- TCu 380A Intrauterine Device (IUD) Clinical Research

■ **Oral Contraceptives**

Continuing Projects:

- Time of Progestin-Only Oral Contraceptive Initiation Among Lactating Women

■ **Male Sterilization**

Continuing Projects:

- Pilot Study of the Time to Infertility After Vasectomy
- No-Scalpel Versus Standard Incision Vasectomy

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Project Title: Use of Condoms and Vaginal Spermicides by Women at High Risk of Contracting Sexually Transmitted Diseases

Country(s): Colombia
Division: Clinical Trials **FCO: 2202**
Technical Monitor: John Lewis

Project Objectives: To determine whether providing spermicides in addition to condoms increases the percentage of protected sexual acts or whether increased spermicide use is associated with decreased condom use without an overall increase in contraceptive use. A secondary objective is to determine whether providing spermicides with condoms affects the rate of STD transmission among a population of Colombian women at high risk for STDs.

Project Description: This study was initiated in 1990 and conducted at the Laboratorio de Investigaciones de Enfermedades Venéreas in Bogota, Colombia. Enrolled women were randomly assigned to one of three study groups. One group was to use condoms only. The second group was given condoms and spermicide to use concurrently. The third group was given condoms and spermicides, but instructed to use the latter only if the male partner refused to use a condom. A total of 200 women were recruited to participate for a period of 12 weeks.

Implementing Agencies: Laboratorio de Investigaciones de Enfermedades Venéreas, Bogota, Colombia

FY'94 Planned Activities: The data will be cleaned and analyzed and a final report will be written.

Expected Outputs, FY '94: A final report and a manuscript for publication will be prepared.

Possible Problems, Barriers to Completion: None

Initiation Date: August 1990
Projected End Date: September 1994

Funding Source: USAID/W
FY '94 Budget: \$83,574
Total Budget: \$252,600

**Project Title: Phase II Contraceptive Efficacy and Safety of
Lea's Shield™ Used With and Without Spermicide**

Country(s): United States
Division: Clinical Trials **FCO: 2658**
Technical Monitor: John Lewis

Project Objective: To test the contraceptive efficacy of a new barrier method, Lea's Shield™, which has the potential to be used continuously for 48 hours, preferably without a spermicide. FHI is collaborating with CONRAD to complete this project.

Project Description: Lea's Shield™, a vaginal barrier device, is designed as an alternative to currently available vaginal barrier contraceptives and can be used for up to 48 hours after insertion. This contraceptive efficacy study is a six-month, Phase II, clinical trial conducted by CONRAD in collaboration with FHI. FHI has served as the project's data and regulatory affairs manager. The study was initiated in 1991 and approximately 300 volunteers were recruited and randomly assigned to use Lea's Shield with or without spermicide. Research results will be used as part of the pre-marketing application to the FDA.

Implementing Agency: None (CONRAD project)
Collaborating Agency: CONRAD

FY'94 Planned Activities: The final case report forms (CRFs) will be received at FHI. Data cleaning and analysis will take place and a final report will be written.

Expected Outputs, FY '94: The final statistical report will be provided to CONRAD for inclusion in the final study report.

Possible Problems, Barriers to Completion: None

Initiation Date: October 1991
Projected End Date: September 1994

Funding Source: USAID/W
FY '94 Budget: \$102,051
Total Budget: \$404,760

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Project Title: Vaginal Methods - General Development

Country(s): United States

Division: Clinical Trials

FCO: 2070

Technical Monitor: Gaston Farr

Project Objective: To support in-house activities related to barrier contraceptive research development, manuscript writing, data file management, and staff support.

Project Description: General development activities for barrier contraceptives clinical research, including data file management and manuscript preparation, are supported under this project.

FY'94 Planned Activities: The development of a clinical trials methodology monograph detailing FHI's past work in research of barrier contraceptives is in progress.

Expected Outputs, FY '94: A monograph detailing FHI's past work in development and research of barrier contraceptives will be completed.

Possible Problems, Barriers to Completion: None expected.

Initiation Date: August 1990

Projected End Date: October 1994

Funding Source: USAID/W

FY '94 Budget: \$31,604

Total Budget: \$200,000

83

Project Title: Safety Assessment of the Slip-On Thermoplastic Male Condom (Clinical Trial)

Country(s): United States

Division: Clinical Trials

FCO: 2212

Technical Monitor: Randy Dunson

Project Objective: To evaluate the acceptability and safety of FHI's slip-on male condom made of an alternative polyurethane to that used in the roll-on design.

Project Description: This project evaluates the feasibility, acceptability and safety of FHI's slip-on thermoplastic condom when used during vaginal intercourse. About 50 monogamous couples will be recruited at a single site. Safety will be evaluated through vaginal and colposcopic examination.

Implementing Agency: To be determined

FY'94 Planned Activities: A study outline will be developed and preliminary site selection will take place.

Expected Outputs, FY '94: The study outline will be approved.

Possible Problems, Barriers to Completion: The FDA is becoming more demanding in their expectations for medical device submissions. Additional regulatory action or directions could result in a revised workplan.

Initiation Date: January 1994

Projected End Date: To be determined

Funding Source: USAID/W

FY '94 Budget: \$54,137

Total Budget: Life Of Project (LOP) budget not yet determined.

84

Project Title: Contraceptive Efficacy of Plastic vs. Latex Condoms

Country(s): To be determined
Division: Clinical Trials **FCO:** 2207
Technical Monitor: Randy Dunson

Project Objective: To assess the contraceptive efficacy of FHI's thermoplastic condom when compared with a conventional latex condom (both used with or without spermicide).

Project Description: This project will support the management and field costs of a randomized, multicenter comparative trial designed to assess the contraceptive efficacy of FHI's thermoplastic condom when compared with a conventional latex condom (both used with or without spermicide). In addition, the study will establish the contraceptive efficacy of conventional latex condoms in a prospective, well-controlled clinical trial, an important contribution to family planning research. It is estimated that approximately 600 subjects will be recruited and followed for a period not to exceed 6 months of product use. The study is expected to have a 2-3 year duration.

Implementing Agency: To be determined

FY'94 Planned Activities: A study protocol will be developed and study sites selected.

Expected Outputs, FY '94: An approved study protocol will be the output of FY 94.

Possible Problems, Barriers to Completion: Decisions from the FDA regarding proposed study design could cause delays.

Initiation Date: October 1994
Projected End Date: To be determined

Funding Source: USAID/W
FY '94 Budget: \$75,337
Total Budget: LOP budget not yet determined.

85

Project Title: Clinical Evaluation of Vaginal Contraceptive Film

Country(s): To be determined

Division: Clinical Trials

FCO: 2211

Technical Monitor: John Lewis

Project Objective: To assess the efficacy of Vaginal Contraceptive Film VCF® (Apothecus, Inc.) in preventing unintended pregnancy. Also, to assess use compliance and acceptability when used by women choosing VCF® as their sole means of contraception as a possible substitution for vaginal tablets used in USAID programs. VCF® will be compared to another commercially available vaginal spermicide formulation.

Project Description: This international, multicenter, comparative efficacy study will be conducted at 4 sites that have not yet been identified. A total of 500 women will be recruited to use Vaginal Contraceptive Film or a vaginal foaming tablet as their sole means of contraception. VCF® is a barrier method commercially available in the United States which contains the spermicide nonoxynol-9. The study is expected to begin in mid-1994 and subjects will be followed for a period of six months.

Implementing Agency: None yet selected

FY'94 Planned Activities: Multiple sites will be selected. The study will be initiated and 500 subjects will be recruited.

Expected Outputs, FY '94: A protocol and case report forms will be approved.

Possible Problems, Barriers to Completion: Identification of suitable sites.

Initiation Date: October 1993

Projected End Date: Not yet projected

Funding Source: USAID/W

FY '94 Budget: \$103,358

Total Budget: LOP budget not yet determined.

86

Project Title: Phase III Comparative Lea's Shield™

Country(s): To be determined

Division: Clinical Trials

FCO: 2659

Technical Monitor: John Lewis

Project Objective: To test the contraceptive efficacy of a new barrier method, Lea's Shield™, which has the potential of being used continuously for 48 hours, preferably without a spermicide.

Project Description: Lea's Shield™, a vaginal barrier device, is designed as an alternative to currently available vaginal barrier contraceptives and can be used for up to 48 hours after insertion. This project will support the management and field costs of a randomized, multicenter, comparative Phase III clinical trial of the contraceptive efficacy of the Lea's Shield™ when compared to another barrier method. Data from this clinical trial are intended to be used to seek product approval from the FDA.

Implementing Agency: Not yet determined

FY'94 Planned Activities: Protocol development, site selection and study initiation are planned for 1994.

Expected Outputs, FY '94: An approved protocol will be generated.

Possible Problems, Barriers to Completion: Issues concerning Silastic[®] supply for manufacture of the Lea's Shield™ could cause delays. Unforeseen delays completing Phase II study are also possible.

Initiation Date: August 1993

Projected End Date: August 1995

Funding Source: USAID/W

FY '94 Budget: \$205,651

Total Budget: LOP budget not yet determined.

87

Project Title: Pilot Study of the Physical Characteristics of Spermicidal Preparations

Country(s): United States
Divisions: Clinical Trials & Materials Technology FCO: 2208
Technical Monitor: David Sokal

Project Objectives: To develop a method that can be used to compare the speed of dissolution of various spermicidal preparations under different conditions. A second objective is to assess the feasibility of developing an in vitro system for spermicide evaluation which would mimic vaginal conditions.

Project Description: While there are standard methods for the evaluation of many contraceptive methods (e.g., condom testing, hormonal assays, etc.) there is at least one major deficiency in current methodologies: there is no standardized method to measure the speed of dissolution of vaginal preparations (e.g. vaginal tablets or vaginal film) under wet and moist conditions. Such a method would be useful in the evaluation and comparison of new and existing spermicidal products and formulations.

Collaborating Agencies: While FHI will be implementing this project, we have discussed it with colleagues at CONRAD and the Population Council, and will keep them informed of our progress. We will also solicit their advice about what other formulations to test, and once the method is developed we will test formulations on request from CONRAD or the Population Council.

FY'94 Planned Activities: A methodology that can be used to compare the dissolution speed of vaginal contraceptive film and vaginal foaming tablets under wet and moist conditions will be developed and tested.

Expected Outputs, FY '94: Comparative data on at least two vaginal formulations will be collected.

Possible Problems, Barriers to Completion: Difficulties in developing a new laboratory methodology are likely to occur. They may necessitate trying several additional methods in addition to the planned approach.

Initiation Date: March 1993
Projected End Date: March 1995
Funding Source: USAID/W
FY '94 Budget: \$20,093
Total Budget: LOP budget not yet determined.

88

Project Title: Preclinical Iodine and Phase I Iodine Trial

Country(s): United States

Division: Clinical Trials

FCO: 2087

Technical Monitor: Randy Dunson

Project Objective: To evaluate the safety and efficacy of the transcervical/intratubal delivery of an iodine compound as a nonsurgical method of tubal sterilization.

Project Description: FHI is working to complete the necessary preclinical efficacy and toxicity testing of the iodine formulations so that the FDA will lift its clinical hold, allowing us to proceed with Phase I clinical studies. The aim of the Phase I study will be to evaluate the safety of several doses of an iodine compound when delivered transcervically as a nonsurgical method of tubal sterilization.

Implementing Agency: North Carolina State University

FY'94 Planned Activities: The study product will be re-formulated and a Phase I protocol developed. Preclinical efficacy and toxicology studies will continue.

Expected Outputs, FY '94: An acceptable formulation will be determined and a protocol approved. Additional preclinical efficacy and toxicology testing will be initiated.

Possible Problems, Barriers to Completion: Developing a formulation with pH stability is a potential challenge.

Initiation Date: August 1990

Projected End Date: Not yet projected

Funding Source: USAID/W

FY '94 Budget: \$203,449

Total Budget: \$364,300

Project Title: Filshie Clip Premarket Approval Application

Country(s): Worldwide

Division: Clinical Trials

FCO: 2091

Technical Monitor: Becky Pinaro

Project Objective: To obtain FDA approval of an effective and easy-to-use tubal occlusion device that limits tubal damage, thus facilitating potential sterilization reversal.

Project Description: The Filshie Clip is a small device that was developed by Dr. Marcus Filshie and is manufactured by Femcare, Ltd. It is similar in concept to the Falope-Ring Band and Hulka Clip and is widely used in a number of countries outside the United States. It can be applied to the Fallopian tube by laparoscopic surgery or minilaparotomy, and has the advantage of potentially being more easily reversible than other tubal occlusion methods. In FY '94 staff will respond to queries from the FDA on a Premarket Approval Application submitted in September 1992.

Collaborating Agencies: Femcare Ltd., Gynopharma

FY'94 Planned Activities: FHI's Regulatory Affairs, Biostatistics and Clinical Trials Divisions will interact with the FDA throughout the PMA review process. They will respond effectively and as quickly as possible to the FDA's queries. Because many of the 48 trials were closed in the early 1980s, and few sites have been visited since 1989, FHI and Femcare will try to incorporate site visits into already planned travel. It is possible that key staff will make one or more trips to Washington, D.C. to confer with FDA representatives about the PMA. The FDA may want to conduct on-site inspections of clinical study centers. To this end, file maintenance and organization will be on-going.

Expected Outputs, FY '94: Responses to FDA questions will be provided throughout FY '94. A safety update will be submitted to the FDA the first week of January, 1994.

Possible Problems, Barriers to Completion: If the FDA indicates that site inspections are going to be conducted, problems may arise with a few centers, given that the Filshie Clip studies were completed several years ago. Patient source documentation may be stored and/or hard to retrieve. NOTE: FHI has had routine communication with Filshie sites to remind them that they must continue to store these records on-site.

If the FDA requests further/different types of statistical analysis of the Filshie data, staff time may need to be reallocated from other projects.

Initiation Date: August 1990

Projected End Date: April 1995

Funding Source: USAID/W

FY '94 Budget: \$154,071

Total Budget: \$1,126,700

90

Project Title: Phase IIA Pharmacokinetic Evaluation of Biodegradable Norethindrone Pellet Implants

Country(s): United States
Division: Clinical Trials **FCO:** 2041
Technical Monitor: Becky Pinario

Project Objective: To develop a safe inexpensive, biodegradable contraceptive implant that will be effective for 12 to 18 months, but that can be removed at any time.

Project Description: This Phase IIA study is designed to assess the serum levels of norethindrone, progesterone and estradiol, the serum chemistry effects and any adverse experiences following insertion of one of two dosage forms of norethindrone pellet implants. In addition, contraceptive efficacy during the first 13 months of the trial will be evaluated.

Implementing Agencies: CONRAD; Eastern Virginia Medical Center, Norfolk, VA; Cornell Medical Center, New York, NY

FY'94 Planned Activities: Subject follow-up for safety parameters will continue under an amendment which extended follow-up past the original 24 months to 36 months. This will allow full evaluation of the tail of norethindrone levels in subjects. An analysis of the one year data will be completed in December 1993.

Expected Outputs, FY '94: Follow-up of subjects will continue and a final report will be written.

Possible Problems, Barriers to Completion: None

Initiation Date: August 1991
Projected End Date: August 1995

Funding Source: USAID/W
FY '94 Budget: \$230,867
Total Budget: \$790,500

**Project Title: Pre-Introductory Clinical Trial of Norplant
Contraceptive Subdermal Implants**

Country(s): Senegal
Division: Clinical Trials **FCO: 2880**
Technical Monitor: Pilar Sketo

Project Objectives: To: (1) conduct Phase III pre-introductory trials of Norplant subdermal implants, introducing the method into countries without previous implantable contraceptive experience; (2) provide training to physicians in proper insertion and removal of Norplant implants and in patient counseling; and (3) determine the method's overall acceptability in different populations.

Project Description: FHI has been conducting studies of Norplant implants since 1984. During this time approximately 8650 subjects have been admitted to studies at 43 centers in 11 countries (El Salvador, Senegal, Nigeria, Ghana, Philippines, Pakistan, Sri Lanka, Bangladesh, Nepal, Singapore, Haiti). Most of the sites have already been closed. Ongoing clinical work currently involves approximately 734 subjects at five centers in El Salvador and at one center in Senegal, where a pre-introductory clinical trial began in 1986 with 50 women. Based on positive responses, the study in Senegal was expanded to include 333 women by 1991. Follow-up will continue for all enrolled subjects until the implants have been used five years or until they are removed.

FHI has used this study to introduce the Norplant system into countries without previous implant experience and to provide physician training with the method. These studies have provided additional insight into the product's overall acceptability among various cultures while assisting these countries in efforts to gain regulatory approval of this method. Much of the acceptability data, especially that relating to menstrual disturbances, are being used to develop additional studies to improve user satisfaction and increase continuation rates.

Implementing Agency: Department of Obstetrics and Gynecology, University of Dakar

FY'94 Planned Activities: An annual monitoring visit is planned and data collection will continue.

Expected Outputs, FY '94: None

Possible Problems, Barriers to Completion: None

Initiation Date: August 1990
Projected End Date: August 1995

Funding Source: USAID/Senegal and USAID/W
FY '94 Budget: \$21,493
Total Budget: \$76,600

012

**Project Title: Pre-Introductory Clinical Trial of Norplant
Contraceptive Subdermal Implants**

Country(s): Ghana
Division: Clinical Trials **FCO:** 2032
Technical Monitor: Pilar Sketo

Project Objectives: To: (1) conduct Phase III pre-introductory clinical trials of Norplant subdermal implants, introducing the method into countries without previous implantable contraceptive experience; (2) provide training to physicians in inserting and removing Norplant implants properly and in patient counseling; and (3) determine the method's overall acceptability in different populations.

Project Description: FHI has been conducting studies of Norplant implants since 1984. During this time approximately 8650 subjects have been admitted to studies at 43 centers in 11 countries (El Salvador, Senegal, Nigeria, Ghana, The Philippines, Pakistan, Sri Lanka, Bangladesh, Nepal, Singapore, Haiti). Most of these sites have been closed and final reports written. The site in Ghana has been closed; however, a final report has not yet been completed.

FHI has used these studies to introduce the Norplant system into countries without previous implant experience and to provide physician training with the method. These studies have provided additional insight into the product's overall acceptability among various cultures while assisting these countries in their efforts to gain regulatory approval of this method. Much of the acceptability data, especially that relating to menstrual disturbances is being used to develop additional studies to improve user satisfaction and increase continuation rates.

Implementing Agency: School of Medical Sciences, University of Science and Technology, Kumasi, Ghana

FY'94 Planned Activities: Data analysis and preparation of a final report are planned.

Expected Outputs, FY '94: The final report will be completed.

Possible Problems, Barriers to Completion: None.

Initiation Date: August 1990
Projected End Date: February 1994

Funding Source: USAID/W
FY '94 Budget: \$47,776
Total Budget: \$76,700

Project Title: Clinical Trial of Norplant Contraceptive Implant System

Country(s): El Salvador
Division: Clinical Trials **FCO: 2887**
Technical Monitor: Pilar Sketo

Project Objectives: To: (1) conduct pre-introductory clinical trials of Norplant subdermal implants in Phase III pre-introductory clinical trials, introducing the method into countries without previous implantable contraceptive experience; (2) provide training to physicians in proper insertion and removal of Norplant implants and also in patient counseling; and (3) determine the method's overall acceptability in different populations.

Project Description: There are currently four study sites in San Salvador including the ADS (San Salvador Clinic), the Ministry of Health (Maternidad Hospital), the Salvadoran Social Security Institute (ISSS), and the ANTEL Hospital. Enrollment began in February 1988 and was completed in August 1989. A total of 401 subjects were enrolled, with 12 having reached their fifth year of follow-up as of July 1993. There have been 66 early removals since the last report in June 1992.

Implementing Agency: Asociacion Demografica Salvadoreña

FY'94 Planned Activities: Monitoring of the sites will continue and the trial will be completed. Semiannual reports will be written for ADS and the USAID San Salvador Mission.

Expected Outputs, FY '94: Further information on continuation and acceptance of this product will be collected.

Possible Problems, Barriers to Completion: None expected.

Initiation Date: July 1991
Projected End Date: August 1995
Funding Source: USAID/El Salvador and USAID/W
FY '94 Budget: \$36,696
Total Budget: \$179,000

94

Project Title: Phase I, II and III Evaluation of the Safety and Pharmacokinetics of Norethindrone 90-day Injectable Microspheres

Country(s): Worldwide
Division: Clinical Trials FCO: 2031
Technical Monitor: Becky Pinario

Project Objective: To develop a safe, FDA-approved, injectable contraceptive that will provide continuous efficacy over 90 days while utilizing less total dose than that of other available injectable contraceptives.

Project Description: These studies were conducted at 23 sites in six countries: Phase II Clinical (1986-1987) - six sites in the U.S., Italy and Chile; Phase II Endocrine (1986-1987) - two sites in the U.S.; Phase III (1987-1989) - 15 sites in the U.S., Chile, Mexico, and Singapore; and Phase I (1990-1991) - one site in the U.S. A final report for each of these studies has been initiated.

This research has been used to direct further development of norethindrone 90-day injectable microspheres, but problems related to formulation and scale-up of production of the microspheres have arisen. All future work regarding this product is pending negotiations between USAID, FHI and Ortho, to whom activities regarding this project will be transferred.

FY'94 Planned Activities: FHI expects completion of the final safety reports on the Phase I, II and III studies. The IND for this product will be transferred to Ortho, pending negotiations between USAID, FHI and Ortho.

Expected Outputs, FY '94: The final reports will be written.

Possible Problems, Barriers to Completion: Revisions to the final report due to possible requests by USAID and/or Ortho could cause delays. There may also be additional information requested by USAID for the transfer of the IND.

Initiation Date: August 1990
Projected End Date: April 1994
Funding Source: USAID/W
FY '94 Budget: \$32,042
Total Budget: \$308,019

Project Title: Timing of Onset of Contraceptive Effectiveness in Norplant Implant Users

Country(s): United States
Division: Clinical Trials
Technical Monitor: Pilar Sketo

FCO: 2213

Project Objective: To determine the time interval in postinsertion Norplant implant users over which the cervical mucus of the women in the sample population becomes sufficiently impenetrable to sperm to be consistent with an adequate contraceptive effect.

Project Description: This single center, single-blinded clinical trial will investigate the changes in cervical mucus within the first hours to days after Norplant implant insertion and better estimate the interval postinsertion by which the cervical mucus is thick enough to successfully prevent conception.

Implementing Agency: Frances Scott Key Hospital, Johns Hopkins Medical School

FY'94 Planned Activities: The protocol and the case report forms will be completed. The trial will be initiated.

Expected Outputs, FY '94: None

Possible Problems, Barriers to Completion: Slow recruitment is a potential problem.

Initiation Date: November 1993
Projected End Date: October 1994

Funding Source: USAID/W
FY '94 Budget: \$167,923
Total Budget: \$167,923

96

Project Title: TCu 380A Intrauterine Device (IUD) Clinical Research

Country(s): Worldwide
Division: Clinical Trials FCO: 2051
Technical Monitor: Gaston Farr

Project Objective: To establish the efficacy of the copper-bearing TCu 380A IUD when compared to the IUD most commonly used within a given country participating in the study.

Project Description: Studies conducted in 23 countries provided data on safety, efficacy and acceptability of the TCu 380A intrauterine device when compared with standard devices currently provided in family planning programs in a number of developing countries. Country reports are being written for each site participating in this multicenter trial. Most reports should be completed by March 1994.

FY'94 Planned Activities: Three papers will be written comparing the TCu 380A with other IUDs. The IUD data base will be maintained.

Expected Outputs, FY '94: Manuscripts for publication, as well as six remaining consultant reports will be completed.

Possible Problems, Barriers to Completion: None

Initiation Date: August 1990
Projected End Date: August 1995

Funding Source: USAID/W
FY '94 Budget: \$29,406
Total Budget: \$238,000

Project Title: Time of Progestin-Only Oral Contraceptive Initiation Among Lactating Women

Country(s): Kenya, Mexico, Philippines, Zimbabwe
Division: Clinical Trials
Technical Monitor: Tita Oronoz

FCO: 2096

Project Objectives: 1) To compare the 12- and 18-month postpartum pregnancy rates, and the 12- and 18-month continuation rates from time of admission to study among breastfeeding women assigned to begin taking the progestin-only oral contraceptive (POC), OVRETTE^R (norgestrel, 75 mcg) (a) at 6 weeks postpartum, or (b) at 6 months postpartum or return of first menses, whichever comes first. 2) To evaluate acceptability by determining the reasons for pill discontinuation and any relationship to POC initiation time. 3) To evaluate safety by determining frequency and types of adverse experiences.

Project Description: This study's goal is to assess whether acceptability and efficacy can be affected by the time after delivery at which breastfeeding women begin taking the progestin-only contraceptive. This study is being conducted at seven sites in the following countries: Kenya, Mexico, Philippines, and Zimbabwe. A total of approximately 1380 subjects were enrolled prior to the halt of enrollment on July, 1993 due to slow recruitment. At that time, five of the sites (three in Mexico and two in Kenya) had met recruitment goals.

After enrollment into the study, the subjects were assigned to one of two groups to begin using the progestin-only contraceptive at either six weeks or six months postpartum. Subjects are being followed up at 6 weeks and 6, 12 and 18 months. At these follow-up visits subjects are being evaluated for compliance with both this method and methods which they switch to while participating in the study. Pregnancy and acceptability parameters are also being evaluated.

Results of this study should provide insight into more effective distribution of the progestin-only contraceptive and its general acceptability in relation to methods switched-to among the breastfeeding population.

Implementing Agencies: Centro de Investigacion Biomedica Torreon, Mexico; Instituto de Investigacion Cientifica, Durango, Mexico; Jose Fabella Memorial Hospital, Manila, Philippines; Moi University, Eldoret, Kenya; Kenyatta National Hospital, Nairobi, Kenya; National Family Planning Council, Harare, Zimbabwe.

FY'94 Planned Activities: Monitoring of sites will continue through the summer of 1994, at which time sites will be closed. A final analysis and final reports will be initiated.

Expected Outputs, FY '94: Field work will be completed.

Possible Problems, Barriers to Completion: None

Initiation Date: September 1990
Projected End Date: August 1995

Funding Source: USAID/W
FY '94 Budget: \$256,791
Total Budget: \$1,000,000

Project Title: Pilot Study of the Time to Infertility After Vasectomy

Country(s): Mexico
Division: Clinical Trials
Technical Monitor: John Lewis

FCO: 2206

Project Objective: To determine the time and/or number of ejaculations following vasectomy that are associated with (a) the achievement of infertility, (b) the loss of sperm motility, and (c) the loss of sperm eosin staining.

Project Description: This study is being conducted at one site in Mexico in collaboration with AVSC and the Instituto Mexicano de Seguro Social (IMSS). Up to 40 volunteers will be enrolled. Men will undergo a vasectomy and be evaluated by weekly semen analysis to determine the time and number of ejaculations needed to achieve infertility (two consecutive azoospermic samples). In addition, the time to the loss of sperm motility and loss of eosin staining ability will be assessed. It is anticipated that subject recruitment will take approximately 8 weeks and subjects will be followed for a maximum of 24 weeks (the first 16 weeks by weekly examinations and then bi-weekly up to 24 weeks or azoospermia).

Results from this study will be used to design a larger study to better assess standard parameters for the timing to azoospermia and/or the number of ejaculations. It is hoped that information from these studies will be used to better define standard information guidelines for physicians.

Implementing Agency: IMSS
Collaborating Agency: AVSC

FY'94 Planned Activities: Study initiation is planned for the third week in January 1994. Co-monitoring with AVSC will take place at one month and four months.

Expected Outputs, FY '94: None

Possible Problems, Barriers to Completion: Given the stringency of the follow-up schedule, a high number of drop-outs is expected. We plan to recruit 40 subjects in an effort to obtain 20 subjects completing the study.

Initiation Date: March 1992
Projected End Date: April 1995

Funding Source: USAID/W
FY '94 Budget: \$139,971
Total Budget: \$204,400

Project Title: No-Scalpel Versus Standard Incision Vasectomy

Country(s): Indonesia, Brazil, Guatemala, Thailand, Sri Lanka
Division: Clinical Trials **FCO:** 2006
Technical Monitor: John Lewis

Project Objectives: To 1) compare the safety and efficacy of two different techniques for performing percutaneous vasectomy (the no-scalpel puncture technique and the standard incision technique), and 2) introduce the no-scalpel technique into programs in participating countries.

Project Description: From 1986 to 1992 FHI conducted a comparative trial of the no-scalpel vasectomy versus the standard incision vasectomy in Indonesia, Brazil, Guatemala, Thailand, and Sri Lanka. The basis for the study was a method of vasectomy developed by the Chinese that avoids the use of a scalpel by substituting the use of a special vas fixing clamp and a curved hemostat with sharpened points. The stated advantages of this method are that (a) it produces less bleeding and fewer hematomas, and (b) men may be less fearful of the procedure since it does not involve a scalpel.

Implementing Agencies: Perkumpulan Kontrasepsi Mantap (PKMI Indonesia), Promotion of Responsible Paternity (PROPATER, Brazil), Asociacion Pro-Bienestar de la Familia (APROFAM, Guatemala), Population Development Association (PDA, Thailand), Sri Lanka Association for voluntary Surgical Contraception (SLAVSC)

FY'94 Planned Activities: A multi-center report will be written.

Expected Outputs, FY '94: A final report will be completed.

Possible Problems, Barriers to Completion: None

Initiation Date: August 1990
Projected End Date: September 1994

Funding Source: USAID/W
FY '94 Budget: \$29,764
Total Budget: \$338,600

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Project Title: Scientific Paper Writing

Country(s): United States

Division: Clinical Trials

FCO: 2092

Technical Monitor: Dr. I-cheng Chi

Project Objective: To evaluate the risks/benefits equations of commonly-used modern contraceptive modalities. To keep service providers up-to-date about recent contraceptive technology improvements and developments. To inform the scientific community of FHI's work and achievements in contraceptive research.

Project Description: This FCO is used for reporting 1) primary and secondary multi-center analyses on data collected in various contraceptive areas, including tubal sterilization, IUDs, and oral contraceptives during the past five or more years, and 2) preparation of review papers on various contraceptive areas based on findings reported in previous published FHI papers.

FY'94 Planned Activities: Five scientific papers on contraceptive technology will be written. Assistance in paper writing will be given to other FHI staff. The tasks involved include: study topic selection, direction of data analysis, and review of drafts. In addition, consultation is provided to FHI staff in scientific paper submission and publication.

Expected Outputs, FY '94: Publication in refereed scientific journals of three papers on intrauterine devices, one on tubal sterilization, and one of progestin-only oral contraceptives is expected. Also, work will be done to help improve both quality and quantity of publications from FHI.

Possible Problems, Barriers to Completion: None.

Initiation Date: August 1990

Projected End Date: August 1995

Funding Source: USAID/W

FY '94 Budget: \$174,821

2. Materials Technology

The mission of the Materials Technology Division, formed in late 1989, is to provide coordination and management of FHI's contraceptive development and quality testing programs in response to the high priority given to this work by USAID and FHI. Division activities are conducted by two groups, Product Quality and Compliance (PQC) and Product and Process Development (PPD). The PQC Group is responsible for production surveillance and quality assurance testing of contraceptive devices, and the PPD Group is responsible for the development of new contraceptive devices and manufacturing processes.

■ Contraceptive Quality Assurance Testing (PQC)

Until this year, the PQC Group's activities have primarily consisted of a range of projects that evaluate the quality of latex condoms distributed by USAID. These evaluations include assessing the effects of various manufacturing procedures, storage conditions, aging, and usage practices on latex condom integrity. In addition, major efforts have been made to identify and validate testing procedures which most accurately measure condom integrity.

This year, at the request of USAID, the expertise developed in evaluating latex condom quality is being broadened to include quality assurance testing of other contraceptive devices, including OCs, injectables, suppositories and IUDs. Product stability studies will be a major component of this new research area.

■ New Contraceptive Development (PPD)

The primary effort of the PPD Group has been the research and development of two marketable, cost-competitive plastic condoms. These condoms will offer longer storage potential and be more compatible with oil-based lubricants. They may also provide greater sensitivity than latex condoms but will have comparable efficacy in preventing pregnancy or STDs.

FY'94 Program Objectives and Expected Outputs

The quality assurance program for latex condoms will be continued and expanded. Greater emphasis will be placed on comprehensive statistical analysis of test data, and dissemination of the results of these analyses to appropriate organizations and the public.

In order to develop an effective quality assurance and compliance testing program for other contraceptive methods, additional laboratory space, staff, and state of the art testing equipment are being acquired.

The New Contraceptive Research and Development Program will have two primary efforts. The plastic condom program will continue to concentrate on refining and optimizing fabrication equipment, identifying the film material to be used in the final product, acquiring patent rights, and collaborating in the design and implementation of clinical trails for FDA approval.

In addition, the new Iodine Formulation Project will be implemented. This effort will attempt to improve upon an iodine sclerosing product and its delivery system for use as a non-surgical sterilization method. The objective of the project is to develop a product that is safe, effective, and stable.

In addition to these two major endeavors, the New Product Research Project will support investigations of new product ideas and formulation of strategies for further development of those which are most promising.

The subprojects which comprise MTD's FY'94 workplan are listed below. Detailed workplans for each of these subprojects, delineating objectives, activities, and outputs for FY'94, follow.

■ **Contraceptive Quality Assurance Testing Program**

Continuing Projects:

- Condom Field Evaluations
- Contraceptive Research and Test Development
- Condom Functionality Trials
- Condom Prospective Aging Studies
- Condom Production Surveillance
- Program for Appropriate Technology for Health (PATH) Condom Research Activities
- Contraceptive Evaluations
- PATH Uniject Project
- Condom Package Integrity Study
- Condom Laboratory Monitoring

■ **New Contraceptive Research and Development Program**

Continuing Projects:

- Roll-on Thermoplastic Condom Research and Development
- Slip-on Thermoplastic Condom Research and Development

New Projects:

- Iodine Formulation
- New Product Research

Project Title: Condom Field Evaluations

Country(s): Multiple-International
Division: Materials Technology **FCO:** 8011
Technical Monitor: Eli Carter

Project Objective: To assess the quality of contraceptive stocks in storage in selected developing countries and to evaluate, upon request, contraceptive inventories of questionable quality and recommend to USAID their proper disposition.

Project Description: Condom users and potential users must perceive that the condoms they receive are of good quality. Frequent breakage of condoms may discourage their use. This project helps to ensure that the integrity of USAID-provided condoms is adequately maintained during in-country storage.

FY'94 Planned Activities: A minimum of three country contraceptive distribution programs will be evaluated for quality integrity. Representative samples will be evaluated by the MTD laboratories. PQC will continue its proactive role in contraceptive quality assurance by providing technical assistance upon request and disseminating information to the field relating to quality testing, proper storage, and use. Visits to in-country testing laboratories and meetings with governmental, technical, and health care providers will be encouraged during field visits.

Expected Outputs, FY'94: Analysis and reports on all field stock samples will be expanded and presented to USAID.

Possible Problems, Barriers to Completion: Testing lead-times may be affected by workload from other projects and by budgetary constraints which prohibit staff and laboratory expansion.

Initiation Date: May 1989
Projected End Date: August 1995

Funding Source: USAID/W (CPSD)
FY'94 Budget: \$103,097
Total Budget: \$421,578

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Project Title: Contraceptive Research and Test Method Development

Country(s): United States
Division: Materials Technology **FCO: 8012**
Technical Monitor: Eli Carter

Project Objectives To investigate the utility of new and modified physical test methods in the evaluation of latex condoms; and to determine, through prospective and accelerated aging, the potential shelf life of oral contraceptives, IUDs, spermicides, and injectables.

Project Description: This program began in 1990 to address many of the unknowns in condom testing. For many years, condom manufacturers relied on results of tensile and water leakage tests to qualify the product for use. However, little was known or understood of how these tests related to actual use conditions or if these tests allow effectively screened substandard product. Although the air inflation test was gaining acceptance around the world, it was not embraced by U.S. manufacturers because of its perceived complexity and costs. In the last three years, MTD has investigated many potential improvements to tensile and air inflation testing methodology and related equipment. It has collaborated with many research organizations in studying the effects of aging, breakage in use and packaging. Collaborating research organizations have included the American Society for Testing and Materials (ASTM), WHO, Program for Appropriate Technology for Health (PATH), Health Industry Manufacturing Association (HIMA), and the London International Group (LIG). Information gained from comparison of instrumentation will allow for standardization of test equipment and improve inter-laboratory correlations. Planned accelerated stability studies will provide preliminary information for comparison with real time data as it becomes available through testing of naturally aged products from field inventories.

FY'94 Planned Activities: To improve upon the air inflation test method and test equipment, experiments will be conducted to compare and correlate data from two distinctively different state of the art condom air inflation apparatus. Comprehensive stability studies will be initiated for oral contraceptives, IUDs, and spermicides.

Expected Outputs, FY'94: Preliminary data from initial experiments will be evaluated, and lead to the initiation of more detailed controlled studies/experiments. Internal (divisional only) reports will issued.

Possible Problems, Barriers to Completion: The amount of work accomplished will be dependent upon the start-up of the MTD analytical research laboratory and staff availability.

Initiation Date: August 1990
Projected End Date: August 1995

Funding Source: USAID/W
FY'94 Budget: \$45,695
Total Budget: \$457,000

105

Project Title: Condom Functionality Trials

Country(s): United States
Division: Materials Technology **FCO:** 8013
Technical Monitor: Eli Carter

Project Objective: To correlate latex condom breakage during human use with various behavioral and physical factors that affect use.

Project Description: In conjunction with the Contraceptive Use and Epidemiology (CUE) Division, MTD conducts human use studies to evaluate the relationship of the Condom Quality Index (CQI) with breakage in actual use.

FY'94 Planned Activities: Two use iterations will be conducted with samples retrieved from the Prospective Aging Study. Breakage rates will be statistically analyzed for correlation with laboratory test results. Ad hoc studies involving new and/or field aged condoms may be conducted in collaboration with PATH.

Expected Outputs, FY'94: Study results will be included in interim reports on the Prospective Aging Study.

Possible Problems, Barriers to Completion: In many instances pharmaceutical and device manufacturers may not be willing to divulge proprietary information and/or may limit technical scrutiny of production and testing processes. The cost of subcontracted laboratory evaluations may limit the number of production lots that can be evaluated.

Initiation Date: October 1988
Projected End Date: August 1995

Funding Source: USAID/W
FY'94 Budget: \$51,836
Total Budget: \$702,000

106

Project Title: Condom Prospective Aging Study

Country(s): Multiple-International
Division: Materials Technology
Technical Monitor: Eli Carter

FCO: 8014

Project Objective: To determine the effect(s) of adverse storage conditions on the stability of latex condoms over a five year period.

Project Description: Condoms are often stored for long periods under differing climatic conditions, which may affect their quality. This study began in 1990 when five latex condom formulations were placed in storage sites with various climates in Mexico and North Carolina. Later the study was modified to include a study site in Niger. Samples have been retrieved from all study sites on a yearly basis and evaluated for effects of deterioration. Environmental conditions in the storage facilities have been monitored by temperature/humidity recorders. Representative samples from the most extreme sites have been placed in human use studies on an annual basis to study the effect of storage on breakage.

FY'94 Planned Activities: Study sites in Mexico and Niger will be monitored for changes in temperature and humidity, and representative samples will be taken for evaluation at specified intervals. Beginning in October, 1993 and each year following, three newly manufactured condom lots will be added to the study for stability and use behavior monitoring. Selected lots will represent the current USAID procured formulation(s).

Expected Outputs, FY'94: The interim analyses following the evaluation of both the 36 and 48 month sampling will begin to reveal the impact of the storage environments and packaging/lubrication configurations on product performance in laboratory and human use tests.

Possible Problems, Barriers to Completion: Timely placement and retrieval of study samples has proved difficult in the past. Laboratory workload may impact specified testing windows. Subcontracted laboratory services may be affected by cost and scheduling problems.

Initiation Date: August 1990
Projected End Date: August 1995

Funding Source: USAID/W
FY'94 Budget: \$34,529
Total Budget: \$205,000

Project Title: Condom Production Surveillance

Country(s): United States
Division: Materials Technology **FCO: 8015**
Technical Monitor: Eli Carter

Project Objective: To assure pre-distribution quality of condoms procured by USAID for developing country programs.

Project Description: This program began in 1990 to provide closer scrutiny of condom production to ensure that product distributed to developing countries by USAID meets all performance standards. After utilizing the services of two independent testing laboratories, FHI developed internal testing capability and has performed all condom compliance testing for USAID since 1991.

Collaborating Agencies: Aladan Corporation, Safetex Corporation

FY'94 Planned Activities: Monthly visits will be made to production facilities of Aladan Corp. (Eufaula, Alabama; and Richmond, Va.) to sample approximately ten percent of lots produced. Bimonthly audits will be performed to determine the degree of compliance with GMPs and USAID contract requirements. Periodically, shipments to the field will be monitored to determine the impact of transport and handling. The PQC Technical Oversight Committee, established in 1993, will meet every six months to review program status and provide technical expertise to the project. Independent inter-laboratory round robin testing will be conducted semiannually to monitor FHI physical testing capability.

Expected Outputs, FY'94: Product sampling will be conducted monthly (12); audits will be performed bimonthly (6).

Possible Problems, Barriers to Completion: If open communication between USAID, FHI and the contractor is maintained, no problems are anticipated. Inconsistency of test results produced by the manufacturer and FHI will require resolution.

Initiation Date: August 1990
Projected End Date: August 1995
Funding Source: USAID/W (CPSD)
FY'94 Budget: \$347,161
Total Budget: \$1,728,000

1086

Project Title: PATH - Condom Research Activities

Country(s): United States

Division: Materials Technology

FCO: 8016

Technical Monitor: Eli Carter

Project Objective: To provide funding to PATH to conduct specific research projects and to sponsor participation in technical conferences and meetings as deemed appropriate by the USAID/Commodities and Program Support Division and FHI.

Project Description: PATH has significant experience and expertise in condom evaluation and is a valuable resource when condom technical issues arise which require investigation and recommendations to the CPSD and FHI controlled programs (ie: condom production surveillance). This funding is used to cover travel and lodging expenses for meeting attendance, subsequent reporting, and other ad hoc technical assignments. The level of participation and funding is determined by CPSD based on recommendation of FHI.

Implementing Agency: PATH

FY'94 Planned Activities: PATH representatives will attend four American Society for Testing Materials (ASTM) meetings, one International Standards Organization (ISO) meeting, and other meetings at the request of FHI and USAID.

Expected Outputs, FY'94: Technical assistance will be gained in shaping and reevaluating condom manufacture and testing standards.

Possible Problems, Barriers to Completion: Nonattendance due to scheduling/personnel availability.

Initiation Date: October 1991

Projected End Date: August 1995

Funding Source: USAID/W (CPSD)

FY'94 Budget: \$31,593

Total Budget: \$1,090,000

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Project Title: Contraceptive Evaluations

Country(s): United States
Division: Materials Technology **FCO:** 8017
Technical Monitor: Eli Carter

Project Objective: To assure that contraceptive products distributed by USAID comply with product specifications at the time of manufacture. In addition, proper storage and distribution procedures in the field are assessed to ensure each product's acceptability for use throughout its shelf life expectancy.

Project Description: USAID distributes a wide range of contraceptives other than condoms, including IUDs, OCs implants and injectables. In order to verify contractor compliance and to ensure and maintain product acceptance, a production surveillance program for these commodities was established. Since 1992, quarterly audits of manufacturers have been conducted and representative lots selected for evaluation by independent analytical testing laboratories. In-house testing capabilities are being built at FHI in order to expand the program to include additional contractors and to increase the number of lots evaluated.

FY'94 Planned Activities: Periodic audits of contract manufacturers will be conducted to verify compliance with procurement standards for product composition, manufacturing process, etc. Production samples will be taken for independent evaluation by FHI or a qualified referee laboratory. Field stocks will be monitored and periodically evaluated for use acceptability.

Expected Outputs, FY'94: At a minimum, evaluations will be performed on a quarterly basis on three methods (IUDs, four brands of OCs, foaming tablets). Beginning the second quarter of 1994, two more brands of OCs may be added.

Possible Problems, Barriers to Completion: In many instances pharmaceutical and device manufacturers may not be willing to divulge proprietary information and/or may limit technical scrutiny of production and testing processes. The cost of subcontracted laboratory evaluations may limit the number of production lots that can be evaluated.

Initiation Date: October 1992
Projected End Date: August 1995

Funding Source: USAID/W
FY'94 Budget: \$522,626
Total Budget: \$912,000

Project Title: PATH - Uniject Project

Country(s): United States
Division: Materials Technology **FCO:** 8019
Technical Monitor: Eli Carter

Project Objective: To coordinate development of a single dose delivery system for DMPA.

Project Description: Injectable contraceptives such as DMPA are popular among many users. However, in many countries barriers to safe use exist, including a shortage of sterile syringes and the low education level of some providers, making administering proper dosages problematic. In collaboration with PATH, FHI is supporting the development of a sterile, single use, pre-filled mechanism for injecting the contraceptive.

Implementing Agency: PATH

FY'94 Planned Activities: Final modifications of the mechanism will be completed, including a larger needle component, and a company to conduct the aseptic filling of the device will be identified. Human trials of the device using medicinals other than DMPA will be designed and initiated in one or more countries.

Expected Outputs, FY'94: The Uniject mechanism will be completed and a clinical trial will be initiated to test its use.

Possible Problems, Barriers to Completion: Identifying a contractor for the aseptic filling of the device and a U.S. source of acceptably priced DMPA may be more time consuming than originally anticipated.

Initiation Date: June 1993
Projected End Date: May 1994

Funding Source: USAID/W
FY'94 Budget: \$65,728
Total Budget: \$93,000

Project Title: Condom Package Integrity Study

Country(s): United States
Division: Materials Technology Division **FCO: 8028**
Technical Monitor: Eli Carter

Project Objective: To evaluate and compare the protective effect(s) of foil and cellophane packaging used for latex condoms.

Project Description: Two latex condom formulations, both packaged in foil and cellophane materials, are to be oven aged for a period of three years, periodically sampled and evaluated for changes in test performance. These data will help us determine the better packaging material to recommend for future CPSD procurement. This study should resolve the question of which material provides the best protection for latex condoms at elevated temperatures.

Implementing Agency: PATH

FY'94 Planned Activities: Studies will be carried out, and condoms will be evaluated periodically.

Expected Outputs, FY'94: Semiannual interim status reports will be written.

Possible Problems, Barriers to Completion: None expected.

Initiation Date: June 1992
Projected End Date: August 1995
Funding Source: USAID/W (CPSD)
FY'94 Budget: \$33,789
Total Budget: \$70,000

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Project Title: Condom Laboratory Monitoring

Country(s): United States
Division: Materials Technology Division **FCO:** 8029
Technical Monitor: Eli Carter

Project Objective: To evaluate FHI's laboratory testing competence through semiannual inter-laboratory trials.

Project Description: The inter-laboratory trials are designed to evaluate laboratory comparability in the performance of standard latex condom tests (airburst, tensile, water-leakage, etc.). Laboratories participating in these trials are chosen from a list of internationally recognized establishments that routinely perform or have expertise in condom testing. Participating laboratories will be provided test samples taken from a standard condom lot along with specific testing and data reporting instructions. Individual test data will be evaluated and each lab ranked in accordance with a predetermined statistical model. When appropriate, recommendations for performance improvement will be discussed with individual laboratories.

Collaborating Agencies: Aladan Corporation, Akron Corporation, PATH, Smithers Corporation

FY'94 Planned Activities: Trials will be conducted in October 93 and April 94.

Expected Outputs, FY'94: Two interlaboratory trials will be conducted, with reports issued on each trial.

Possible Problems, Barriers to Completion: Possible delays due to scheduling, staff availability, and product supply.

Initiation Date: June 1993
Projected End Date: August 1995
Funding Source: USAID/W (CPSD)
FY'94 Budget: \$67,565
Total Budget: \$141,000

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Project Title: Roll-On Thermoplastic Condom Research and Development

Country(s): United States
Division: Materials Technology **FCO:** 8030, 8031, 8032
Technical Monitor: David Johnson 8034, 8036

Project Objective: To develop a cost-competitive thermoplastic condom that will meet or exceed performance of latex condoms in reliability, comfort, and ease of use while providing an extended shelf-life under adverse environmental conditions.

Project Description: This project employs unique manufacturing techniques and materials in order to develop a condom that uses a knitted or gel elastic ring to hold it in place. Work areas, designated by separate FCOs, include device design, materials research and development, safety and biocompatibility testing, manufacturing process development, and product fabrication.

FY'94 Planned Activities: The last communication from the FDA regarding the gel retaining ring condom requested quantitative data documenting levels of methylene dianiline in the finished product. This testing is currently underway at the National Sanitation Foundation and will be forwarded to FDA when completed. Additional responses and updates will occur as needed. Specifications for raw materials will be modified as necessary to assure reliability, including the negotiation of additional quality testing if appropriate.

A Phase I safety study on the nylon/spandex knitted ring condom is currently underway. A Phase Ib study is under development which will be a comparative study versus latex to assess relative breakage, slippage, and acceptability. An automated stress-softener/ring-welder is near completion which will be used to fabricate product for this Ib study. Shelf-life and associated stability studies will be conducted with this product which will include physical, chemical (gel permeation chromatography [GPC] and methylenedianiline [MDA]), and viral permeability assessments.

Expected Outputs, FY'94: Final action should be received on the knitted ring and stress-softening patent applications. Further action should be received from FDA on the gel ring roll-on 510(k). Preparation of 510(k)'s for the knitted ring should be initiated.

Possible Problems, Barriers to Completion: Shake down and final validation of the semi-automatic stress-softener could require more time than anticipated. This could affect the timing of the Phase Ib study and the ultimate filing of the 510(k). Concurrent production demands for the two products may outstrip equipment and staff capability. The FDA is becoming more demanding in their expectations for medical device submissions. Additional regulatory action or directions could result in a revised workplan.

Initiation Date: August 1990
Projected End Date: August 1995 (510k Submission)

Funding Source: USAID
FY'94 Budget: \$445,958
Total Budget: \$3,137,000

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Project Title: Slip-On Thermoplastic Condom Research and Development

Country(s): United States
Division: Materials Technology **FCO:** 8030, 8031, 8033
Technical Monitor: David Johnson 8035, 8037

Project Objective: To develop a cost-competitive thermoplastic condom that will meet or exceed performance of latex condoms in reliability, comfort, and ease of use while providing an extended shelf-life under adverse environmental conditions.

Project Description: This project employs unique manufacturing techniques and materials in order to develop a condom that uses a double aperture element to hold it in place. Work areas, designated by separate FCOs, include device design, materials research and development, safety and biocompatibility testing, manufacturing process development, and product fabrication.

FY'94 Planned Activities: Candidate films have been selected and several will be chosen for acceptability studies based on biocompatibility results, strength and probable reliability parameters, processability, and cost. Based on the acceptability study results, product design and dimensions will be finalized along with the manufacturing process. Stability studies will be initiated. A comparative clinical trial of this condom versus latex is planned for the latter part of FY '94.

Expected Outputs, FY'94: Final patent actions should be received on the slip-on and stress softening applications.

Possible Problems, Barriers to Completion: Shake down and final validation of the semi-automatic stress-softener could require more time than anticipated. This could affect the timing of the Phase Ib study and the ultimate filing of the 510(k). Concurrent production demands for the two condom product designs may outstrip equipment and staff capability and could result in delays in slip-on development.

The FDA is becoming more demanding in their expectations for medical device submissions. Additional regulatory action or directions could result in revised work plan.

Initiation Date: August 1990
Projected End Date: August 1995 (510k Submission)

Funding Source: USAID/W
FY '94 Budget: \$503,177
Total Budget: \$1,814,000

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Project Title: Iodine Formulation

Country(s): United States

Division: Materials Technology

FCO: 8039

Technical Monitor: David Johnson

Project Objective: To develop an iodine sclerosing solution with acceptable pH stability.

Project Description: Although sterilization is an effective, and in many cases, preferred means of contraception, the need for a surgical operation makes it risky for some women, especially those living in developing countries. Non-surgical sterilization using chemical agents to sclerose the fallopian tubes is another possibility. This new project is working to improve an existing iodine sclerosing compound to provide a safe, effective, stable, one-application means of sterilization.

FY'94 Planned Activities: Several candidate formulations will be prepared and evaluated for their stability. More promising formulations will be evaluated through pre-clinical investigations.

Expected Outputs, FY'94: An assessment of the current composition and its stability characteristics will be completed. New formulations will be made and evaluated for stability, safety and efficacy by pre-clinical investigations. Prospective GMP manufacturers will be identified.

Possible Problems, Barriers to Completion: Minor modifications of the existing formula may not be adequate to obtain a product of the desired stability with retention of safety and efficacy. Delays in obtaining staff, materials, and other resources may cause delays in producing or evaluating reformulations.

Initiation Date: September 1993

Projected End Date: August 1995

Funding Source: USAID/W

FY'94 Budget: \$220,681

Total Budget: \$422,000

Project Title: New Product Research

Country(s): United States

Division: Materials Technology

FCO: 8038

Technical Monitor: David Johnson

Project Objective: To investigate new product ideas and formulate strategies for development of promising ideas.

Project Description: At present, this project concentrates on identifying complementary products to the thermoplastic condoms, including lubricants which may have spermicidal or anti-microbial properties.

FY'94 Planned Activities: Alternate formulations of spermicides and lubricants that are compatible with polyurethane will be investigated.

Expected Outputs, FY'94: A determination of potentially effective spermicide lubricant formulations, which may be compatible with the thermoplastic condoms now in development, will be conducted. Other concepts for new contraceptives will be evaluated as they are presented.

Possible Problems, Barriers to Completion: The workload on priority projects such as thermoplastic condom development and iodine formulation may divert attention from these new undertakings.

Initiation Date: October 1993

Projected End Date: August 1995

Funding Source: USAID/W

FY'94 Budget: \$49,359

Total Budget: \$101,000

B. POPULATION PROGRAM PLANNING, RESEARCH & SUPPORT DIVISIONS

1. Contraceptive Use and Epidemiology

Many factors influence whether and how effectively contraceptive technologies are used by consumers. Aside from the biomedical issues of safety and efficacy, consumer characteristics, differences in needs or preferences for specific methods, and perceived benefits and risks of all methods influence whether individuals adopt and continue to use contraceptives successfully. In addition to pregnancy prevention, family planning methods have a wide range of health consequences for their users, including the possible reduction or increase in risk of contracting sexually transmitted diseases and changes in risk for other diseases and conditions. Research on the non-contraceptive risks and benefits of family planning methods helps programs address concerns about safety, and indicates those family planning methods which may or may not be suitable for users with special needs or contraindications.

The research conducted in the Contraceptive Use and Epidemiology Division is broad-based and involves the study of a variety of methods within diverse populations. Currently, we are focusing on five strategic areas:

■ Acceptability and Barrier Methods

As an integral part of the process of product development and introduction, acceptability research helps to answer questions about consumer preferences for a method, whether users understand how to use it, and perceptions of safety and efficacy as they relate to the adoption and continued use of a method. Research conducted by the Acceptability and Barrier Methods Unit will continue to play an active role in the development of the male thermoplastic condom and to evaluate the acceptability of other barrier methods in light of the impact of product attributes (i.e., size, strength, age, material clarity, delivery mechanism, etc.) on barrier function and acceptability. Additional research will examine behaviors associated with barrier method use and include studies of the acceptability of dual/multiple method use, risk assessment and compliance, and device re-use.

■ Contraceptive Compliance

Recent research has found that users of temporary contraceptive methods often lack knowledge about how to use these methods correctly. Many users do not use methods as instructed, or they receive incorrect or incomplete information. Improving compliance for widely used methods, such as oral contraceptives (OCs), injectables and condoms is likely to have a significant impact on user satisfaction and continuation, and a consequent reduction in unintended pregnancies. Research by the Contraceptive Compliance Unit will lead to improved written instructions for oral contraceptives and further insights into the knowledge of how acceptors use and health care providers prescribe, OCs. Additional studies will examine user satisfaction among DMPA acceptors in U.S. clinics, and will inform the

development of appropriate training materials for service providers of non-permanent methods.

■ **Contraceptive Benefits and Risks**

Using a computer life-table model, the Contraceptive Risks/Benefits Unit is evaluating the effect of combined OCs and progestin-only methods in terms of longevity and deaths caused and averted among users and non-users of these methods. The unit is presently incorporating smoking into the model for U.S. data, analyzing data from three Central American countries with varying local disease patterns, comparing mortality risks for OC users compared with pregnant women, and assessing the interaction of OC use with various risk factors such as diabetes and hypertension.

Associations between contraception and cancer form a second research focus of the Risks/Benefits Unit. Staff have designed and pilot-tested a hospital-based case-control study of the association between vasectomy and prostate cancer in Korea, conducted the pilot phase of a case-control study of U.S. men screened for prostate cancer that will examine the issue of detection bias in previous studies, and completed a case-control study in Jamaica to examine the relationship between DMPA use and cervical cancer.

■ **Contraception and STDs/HIV**

The emphasis of the Contraception and STDs/HIV Unit is to measure the risk of sexually transmitted disease outcomes, including HIV infection, among users of specific family planning methods. To add to the limited quantitative data on spermicide use and HIV, a randomized controlled trial of spermicide use and HIV incidence, funded by the NIH will be conducted. The unit will initiate a study comparing the incidence of cervical infections among women using non-spermicidal latex condoms and users of spermicidally lubricated latex condoms, design a study of female condom use and STDs infections, and continue enrollment and follow-up in a study of female condom use by HIV-discordant couples. Additional plans include the initiation of a study of short-term complications of IUD use among HIV-positive and HIV-negative women in Kenya, and an investigation of whether combined OC use increases susceptibility to HIV infection.

■ **Breastfeeding and Postpartum Contraception**

Many behavioral and programmatic factors affect the use of contraception in the year after the birth of a child. Exploratory research is needed in order to learn what women know and what they want in terms of postpartum contraception. Using detailed data collected in Pakistan and the Philippines, the Unit continues to study the contraceptive effectiveness of lactational amenorrhea method and programmatic issues concerning postpartum contraception. The scope of work in this area also includes research on the safety and efficacy of breastfeeding and of the use of clinical methods during breastfeeding, studies on the relative costs and

benefits of contraception used by breastfeeding women, and work on phenomena that affect breastfeeding prevalence, duration and proper weaning.

CUE continuing and new projects within each of these areas are listed below. Individual workplans follow.

■ **Acceptability and Barrier Methods**

Continuing Projects:

- **Functionality and Acceptability Study of Lubricated Condoms and a Standard Lubricated Latex Condom**
- **Methods of Identifying Condom Users at Risk of Breakage and Slippage**
- **Acceptability of the REALITY® Female Condom Among Commercial Sex Workers, Their Clients, and Couples in the Nkhotakota and Salima Districts**
- **Acceptability of the REALITY® Female Condom Among Selected Females and Males in Mexico City**
- **Dual Method Acceptability: Latex Condoms vs. Choice of Latex Condoms and Nonoxynol-9 Film among OC Users**
- **Prototype Condom Evaluation: Donning**
- **Prototype Condom Evaluation: Acceptability and Feasibility for Use During Intercourse**
- **Acceptability of New Methods Working Group**

New Projects:

- **Assessing the Acceptability, Service Delivery Requirements, and Use Effectiveness of the Diaphragm**
- **Assessing Methods of Identifying Family Planning Clients at Risk of STDs**
- **Feasibility of Female Condom Reuse**

■ **Contraceptive Compliance**

Continuing Projects:

- **Contraceptive Compliance: Development**
- **Further Testing of New OC Use Instructions**
- **Measuring OC Compliance Using the MEMS™ Device**
- **Revision of Package Labeling for Progestin-Only OC Pills**

New Projects:

- **Characteristics of Women Switching to DMPA**

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■ **Contraceptive Benefits and Risks**

Continuing Projects:

- Risk/Benefit Modeling of Oral Contraceptive Use
- Vasectomy and Prostate Cancer in a U.S. Screening Population
- Vasectomy and Prostate Cancer in Korea

New Projects:

- Copper IUD Use and Tubal Infertility
- Norplant Use and Blood Pressure

■ **Contraception and STDs/HIV**

Continuing Projects:

- Nonoxynol-9 Use and HIV
- Condom Use and Cervical Infection
- Barrier Contraceptive Use Among Couples at High Risk of HIV Infection

New Projects:

- Barrier Methods Monograph
- Short-term IUD Risk and HIV

■ **Breastfeeding and Postpartum Contraception**

Continuing Projects:

- Clinical Trial of the Lactational Amenorrhea Method
- Beilagio II: Further Assessment of the Lactational Amenorrhea Method

New Projects:

- Switching from POCs to COCs: Guidelines for Breastfeeding Women

**Project Title: Functionality and Acceptability Study of Lubricated
Tactylon™ Condoms and a Standard, Lubricated
Latex Condom**

Country(s): United States
Division: CUE (Acceptability & Barrier Methods) FCO: 6002
Technical Monitor: Carol Joanis

Project Objectives: The primary objective of this series of studies is to evaluate the functionality (breakage and slippage) of non-latex condoms as compared to the latex condom. The secondary objective is to evaluate the acceptability of each of the non-latex condoms as compared to the standard latex condom and as compared to each other.

Project Description: During the last six years, USAID has supported product development and clinical research in the design of a plastic condom. The goal of this research is to produce a non-latex condom that will be functionally equivalent to latex but will have increased shelf life and improved user acceptance. To this end, several plastic condom designs have been evaluated. The Tactylon™ condom and its various iterations (Tactyl Technologies, Inc.) are represented in this series of studies.

In the first round of testing, the latex condom had the lowest clinical breakage rate (0.89%), while the three Tactylon™ condoms had rates at least twice as high (Tactylon C = 2.18%, Tactylon A = 3.44% and Tactylon B = 3.04%). Tactylon A condoms had the lowest clinical slippage rate (0.72%) while Tactylon C condoms had a slippage rate almost four times as high (2.72%). The latex condom and the Tactylon B condoms had slippage rates in the middles of this range (1.60% and 1.25%, respectively).

Collaborating Agency: CONRAD

FY'94 Planned Activities: A study of best/preferred product from the first trial will be conducted. The study will be a functionality and acceptability study of the Tactylon condom vs. latex and may also evaluate Tactylon™ and spermicide.

Expected Outputs, FY '94: A final report, summarizing breakage and acceptability rates of latex versus the test Tactylon condoms, will be disseminated.

Possible Problems, Barriers to Completion: The FDA is becoming more demanding in expectations for medical device submissions. Additional regulatory action or directions could effect this study.

Initiation Date: January 1993
Projected End Date: September 1994

Funding Source: USAID/W (cost shared with CONRAD)
FY '94 Budget: \$15,152
Total Budget: \$52,490

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Project Title: Methods of Identifying Condom Users at Risk of Breakage and Slippage

Country(s): Dominican Republic, Philippines, Mexico
Division: CUE (Acceptability & Barrier Methods) FCO: 6004
Technical Monitor: Alan Spruyt

Project Objective: To assess different methods of identifying condom users who are at risk of condom failure, and to assess behaviors that lead to condom failure.

Project Description: Within any given condom breakage study, the majority of condom breaks occur among a small group of study participants. If these individuals and the reasons for condom breakage can be identified, better condom use instruction interventions can be developed for those using condoms as contraception or for disease prevention.

In each of three sites, male condom users (130) were given a background interview and five condoms to be used for vaginal intercourse. After a three-week study period, participants were interviewed to determine condom breakage and slippage rates and to assess behaviors that may lead to condom failure (condom breaking or slipping off completely).

Field work is completed and analysis is in progress. Varying by site, 126 to 130 participants completed the study and 2.0% to 5.5% of the condoms failed (sum of breakage and slippage). The data support the hypothesis that past condom failure predicts future condom failure (consistent across all three sites). Preliminary analysis has identified behaviors which appear to be associated with condom failure including: using methods such as teeth, scissors or knives to open condom packages, unrolling condoms before donning, and having particularly intense or long intercourse. Use of additional lubrication and re-use of condoms (behaviors identified in prior FHI research) were reported infrequently.

Implementing Agencies: PROFAMILIA, Dominican Republic; Comprehensive Family Planning Center (JFMH), Philippines; and Instituto de Investigación Científica, Mexico.

FY'94 Planned Activities: FHI plans to complete analysis, present preliminary results at the October 1993 American Public Health Association meeting, write final reports and prepare a journal article for submission.

Expected Outputs, FY '94: An FHI staff member will make a presentation at the October 1993 American Public Health Association (APHA) meeting. Site specific reports will be finalized and an article summarizing methods of identifying risk behaviors leading to condom failure will be completed.

Possible Problems, Barriers to Completion: None.

Initiation Date: August 1991
Projected End Date: September 1994
Funding Source: USAID/W
FY '94 Budget: \$14,326
Total Budget: \$106,886

Project Title: **Acceptability of the Female Condom Among
Commercial Sex Workers, Their Clients, and
Couples in the Nkhotakota and Salima Districts**

Country(s): Malawi
Division: CUE (Acceptability & Barrier Methods) FCO: 6382
Technical Monitor: Carol Joanis

Project Objectives: To assess the acceptability of the REALITY® female condom in two study populations: commercial sex workers (CSWs) and their clients and married or cohabiting couples. In addition, information will be gathered on male attitudes and opinions and the male's role in the decision to use/discontinue use of the device.

Project Description: The purpose of this study is to provide behavioral information on female condom use. Such information will assist health care providers, social workers, etc. in the provision of better interventions for the prevention of sexually transmitted disease, HIV and pregnancy. Approximately 120 women (60 commercial sex workers and 60 married women) will be enrolled in this study. For commercial sex workers (CSWs) in Malawi, the choices available if a client refuses to wear a condom are to risk acquiring a sexually transmitted disease or lose business. Thus, it is important for these women to experience using a method that is under their control. It is equally important for couples trying to avoid pregnancy to assess the acceptability of the female condom. Acceptability measures will include an assessment of how well women and men liked using the device, whether the device caused any discomfort in use and how well the female condom performed.

Implementing Agency: Salima Agricultural District Hospital, Nkhotakota District Hospital

FY'94 Planned Activities: Data collection will be completed; data will be analyzed and the final report will be issued.

Expected Outputs, FY '94: A final report, to be published in an African medical journal, will document the acceptability of the female condom among study populations in Malawi.

Possible Problems, Barriers to Completion: None.

Initiation Date: October 1993
Projected End Date: September 1994

Funding Source: USAID/W
FY '94 Budget: \$13,634
Total Budget: \$55,724

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Project Title: Acceptability of the REALITY® Female Condom Among Selected Females and Males in Mexico City

Country(s): Mexico
Division: CUE (Acceptability & Barrier Methods) FCO: 6382
Technical Monitor: Carol Joanis

Project Objectives: To assess the acceptability of the REALITY® female condom among a group of sexually active, mid-socioeconomic level couples and among commercial sex workers and their clients. A secondary objective is to examine male attitudes/opinions about use of the female condom in order to develop better interventions for women choosing to use the method.

Project Description: The purpose of this study is to provide behavioral information on female condom use. Such information will assist health care providers, social workers, etc. in the provision of better interventions for the prevention of sexually transmitted disease, HIV and pregnancy. The study will use interviews and focus groups to assess the acceptability of female condom use among mid-socioeconomic couples and CSWs and their clients in Mexico City. One hundred sixty (160) participants will be enrolled in the study.

Implementing Agency: IMIFAP (Instituto Mexicano de Investigacion de Familia y Poblacion, A.C.)

FY'94 Planned Activities: Study instruments will be developed. The study will be initiated, monitored and completed.

Expected Outputs, FY '94: The study final report will be completed and a publication will be drafted documenting female condom acceptability among a selected population of males and females in Mexico City.

Possible Problems, Barriers to Completion: None.

Initiation Date: March 1994
Projected End Date: September 1994

Funding Source: USAID/W
FY '94 Budget: \$74,083
Total Budget: \$74,083

Project Title: Dual Method Acceptability: Latex Condom vs. Choice of Latex Condoms and Nonoxynol-9 Film Among Oral Contraceptive Users

Country(s): United States
Division: CUE (Acceptability & Barrier Methods) FCO: 6010
Technical Monitor: Markus Steiner

Project Objectives: The primary objective is to assess if OC clients at increased risk of STDs, who are provided a choice between condoms and N-9 film to protect themselves from STDs, use barrier methods more consistently than their counterparts who are only provided condoms to protect themselves from STDs. A secondary objective is to assess the impact of additional barrier method use on OC compliance.

Project Description: In the absence of an ideal method that provides maximum protection against both pregnancy and STDs, family planning providers must decide on what method, or combination of methods, to recommend to clients who are both at risk of pregnancy and STDs. One option is to provide clients with two methods: a barrier method to protect against STDs and a non-barrier method to provide maximum protection against pregnancy. Aside from the increased cost, there is a possibility that clients will use one, or possibly, both methods less effectively than if they were using a single method.

A cohort of current OC users who have been identified as being at increased risk for STDs will be randomized into two groups. The first group will be provided the standard counseling on the importance of using condoms to prevent STDs. This first group (condom group) will be provided condoms along with their OCs during the 6-month study. The second group (choice group) will be provided the standard counseling on the importance of using condoms to prevent STDs. In addition, participants in the choice group will be told that for women who believe it difficult to convince their partners to use condoms, N-9 may provide barrier protection against STDs. The choice group will be provided both condoms and N-9 film during the first two months. At the 2-month and 4-month follow-up visit they will be asked with what barrier method(s) they want to be resupplied. Both groups will be provided with coital logs to record coital episodes and the barrier contraceptive method(s) used during the 6-month study. Pill compliance will be assessed with a series of questions on the follow-up questionnaires.

Implementing Agencies: Brazos Valley Community Action Agency/Family Planning Clinic, Bryan, Texas

FY'94 Planned Activities: Data collection will begin in November and is intended to last for one year; analysis of preliminary data will begin.

Expected Outputs, FY '94: Pilot compliance questionnaires; counseling strategy.

Possible Problems, Barriers to Completion: The possibility of slow enrollment could extend study period.

Initiation Date: July 1993
Projected End Date: April 1995

Funding Source: USAID/W
FY '94 Budget: \$87,854
Total Budget: \$144,202

126

Project Title: Prototype Condom Evaluation: Donning

Country(s): United States
Division: CUE (Acceptability & Barrier Methods) FCO: 6386
Technical Monitor: Carol Joanis

Project Objective: To select the best materials (structural integrity) and designs (acceptability) for prototype plastic condoms.

Project Description: The intent of a series of studies to be conducted under this protocol is to "explore the suitability of various condom designs and different polyurethane materials." The shapes sizes and methods of application of the prototype condoms which will be tested may vary considerably. A limited number of participants (up to 25) will be enrolled for each iteration (round) of the study. Condoms used in these studies will be donned only. Condoms will not be used for intercourse. The information gathered in this series of studies supports the development of the FHI polyurethane condom.

FY'94 Planned Activities: One study will be completed.

Expected Outputs, FY '94: Two final reports on materials and design of the prototype plastic condom will be available.

Possible Problems, Barriers to Completion: The timely delivery of study products are essential to completing these studies.

Initiation Date: March 1994
Projected End Date: April 1994

Funding Source: USAID/W
FY '94 Budget: \$30,780
Total Budget: \$165,900

127

Project Title: **Prototype Condom Evaluation: Acceptability and Feasibility for Use During Intercourse**

Country(s): United States
Division: CUE (Acceptability & Barrier Methods) FCO: 6386
Technical Monitor: Carol Joanis

Project Objective: To evaluate several different condoms to determine their feasibility for development into a marketable product. This investigation will assess device acceptability and rates of breakage and slippage (device function).

Project Description: The intent of a series of studies to be conducted under this protocol is to "explore the suitability of various condom designs and different polyurethane materials." The shapes, sizes and methods of application of the prototype condoms may vary considerably. The number of participants in any given study (round of study) will not exceed 350. These studies will be conducted with couples who are protected by an effective form of non-barrier contraceptive and are not at risk for STDs. Data from these studies will be used to support the FHI thermoplastic condom project.

FY'94 Planned Activities: Two studies will be completed.

Expected Outputs, FY '94: A final report will be available and a prototype for Phase Ia clinical studies will be selected.

Possible Problems, Barriers to Completion: None.

Initiation Date: May 1994
Projected End Date: December 1994

Funding Source: USAID/W
FY '94 Budget: \$71,821
Total Budget: \$387,100

128

Project Title: Acceptability of New Methods Working Group

Country(s): Worldwide

Division: CUE (Acceptability & Barrier Methods) FCO: 6373

Technical Monitor: Carol Joanis

Project Objective: To provide a forum for FHI staff for discussion and information sharing on current contraceptive acceptability research.

Project Description: The purpose of the Acceptability Working Group is to help FHI identify and anticipate problems in the introduction and use of contraceptives methods in developing countries. It is believed that early recognition of barriers related to product acceptability issues would assist in better service provision to family planning clients.

FY'94 Planned Activities: To gather company-wide information on acceptability research for the production of quarterly newsletters.

Expected Outputs, FY '94: Four quarterly newsletters will be produced, resulting in increased awareness of acceptability research issues by FHI staff and other interested professionals.

Possible Problems, Barriers to Completion: None.

Initiation Date: August 1990

Projected End Date: August 1995

Funding Source: USAID/W

FY '94 Budget: \$7,460

Project Title: Acceptability Paper Writing

Country(s): Worldwide
Division: CUE (Acceptability & Barrier Methods) **FCO:** 6006
Technical Monitor: Carol Joanis

Project Objective: To write and publish papers on completed acceptability studies.

Project Description: Following the completion of individual studies, research staff conduct further, in-depth analysis on specific topics, and draft papers for publications.

FY'94 Planned Activities: Four papers will be submitted for publication on areas such as the female condom, condom misuse and dual methods.

Expected Outputs, FY '94: Published papers on condom acceptability.

Possible Problems, Barriers to Completion: None.

Initiation Date: October 1991
Projected End Date: August 1995

Funding Source: USAID/W
FY '94 Budget: \$33,798

130

Project Title: Assessing the Acceptability, Service Delivery Requirements and Use Effectiveness of the Diaphragm in Some Developing Country Family Planning Settings

Country(s): Philippines, Chile, Dominican Republic, (African country to be determined)
Division: CUE (Acceptability & Barrier Methods) FCO: 6026
Technical Monitor: Carol Joanis

Project Objective: To assess the acceptability and efficacy of the diaphragm as a contraceptive method in populations where there has been limited or no availability.

Project Description: At a recent meeting organized by WHO's Special Programme of Research, Development and Research Training in Human Reproduction (HRP) strong support was expressed for promoting fertility regulation methods which: 1) are user-controlled; 2) provide protection against STDs including HIV; 3) have minimal or no side effects; and 4) foster knowledge about one's body. Specifically, one of the main recommendations made by women's health advocates was that more research needs to be conducted on the (re)introduction of barrier methods which emphasis on user and provider perspectives on safety, efficacy and acceptability of barrier contraception. Following this meeting, an interagency working group on barrier methods identified the diaphragm as the available, female-controlled method which closely meets these criteria.

This prospective study will follow for a minimum of 12 months a group of adequately counseled women who have chosen to use the diaphragm as their primary form of contraception. The study is intended to identify the factors influencing initial and continued acceptability, determine the service delivery requirements, and document the contraceptive use effectiveness of the diaphragm in several developing country settings. In addition, the study will gather information on reasons for discontinuation, method switching and use practices.

Implementing Agency: To be determined

Collaborating Agencies: World Health Organization, The Population Council

FY'94 Planned Activities: Study documents will be finalized; study sites will be identified, investigators and study staff will be trained and the study will be initiated and monitored.

Expected Outputs, FY '94: Greater understanding of factors related to the acceptability and use of the diaphragm, which is applicable to service delivery strategies in LDCs.

Possible Problems, Barriers to Completion: Poor acceptance of the diaphragm by clinic clients could lead to high study discontinuation.

Initiation Date: September 1993
Projected End Date: August 1995

Funding Source: USAID/W
FY '94 Budget: \$87,843
Total Budget: \$162,708

Project Title: Assessing Methods of Identifying Family Planning Clients at Increased Risk of Sexually Transmitted Disease

Country(s): To be determined.
Division: CUE (Acceptability & Barrier Methods) FCO: 6027
Technical Monitor: Alan Spruyt

Project Objective: To assess methods of identifying family planning clients at increased risk of STDs.

Project Description: As part of FHI research on the integration of family planning and STDs prevention, this study will test STDs risk assessment methods developed by FHI and others. In particular, preliminary results from a similar FHI study among U.S. family planning clients will be used to design STDs risk assessment methods. These methods will be tested in at least one international site.

Implementing Agency: To be determined

FY'94 Planned Activities: FHI will complete the study protocol and other study documents; site will be selected and the study will be initiated.

Expected Outputs, FY '94: A risk assessment document will be tested and finalized within the selected study populations.

Possible Problems, Barriers to Completion: None anticipated.

Initiation Date: September 1993
Projected End Date: March 1995

Funding Source: USAID/W
FY '94 Budget: \$48,263
Total Budget: \$98,263

132

Project Title: Feasibility of Female Condom Reuse

Country(s): United States
Division: CUE (Acceptability & Barrier Methods) FCO: 6029
Technical Monitor: Carol Joanis

Project Objective: To determine the feasibility of female condom reuse by testing the device for structural integrity (seam strength, peak pressure and material strength) after a single use. Further, microbial retention will be measured after a minimal washing regimen.

Project Description: A major drawback to widespread acceptance of the female condom is cost (currently about \$2.50 per use). This cost exceeds the amount most women are willing or able to pay for a single use product. This is especially true for poor women and those in developing countries. Even at subsidized cost, it is doubtful that the device would be cost competitive with latex condoms. Thus, device reuse appears to be an option to reduce cost. However, no data have been collected on reuse practice.

Approximately 60 women in the Research Triangle Park area of North Carolina will use the female condom in one act of intercourse. The used devices will be collected and tested for tensile strength, material strength and air burst values. These test values will then be compared to the test values of unused products from the same condom lot to determine if a change has occurred in the structural integrity of the device. Similarly, microbial retention will be measured after a minimal cleaning (warm water rinse) of the device. This study will assess the feasibility of reusing the female condom.

FY'94 Planned Activities: Study documents will be developed to establish baseline data to determine feasibility of reusing female condom. The first phase of the study will be initiated and completed.

Expected Outputs, FY '94: A final report on the first phase of the study will be completed.

Possible Problems, Barriers to Completion: None.

Initiation Date: September 1993
Projected End Date: November 1994

Funding Source: USAID/W, Mellon, AIDSCAP (USAID Office of Health)
FY '94 Budget: \$41,535
Total Budget: \$121,535

Project Title: Contraceptive Compliance: Development

Country(s): Worldwide
Division: CUE (Contraceptive Compliance) **FCO:** 6380
Technical Monitor: Linda Potter

Project Objectives: To provide tools for better measurement of contraceptive compliance; to develop strategies for increasing the use-effectiveness of the method, first by increasing correct knowledge among users and providers; and to better understand the relationship between problems with compliance and continuation of the method.

Project Description: This project includes a variety of small sub-projects and specific tasks designed to explore relationships between compliance and effective use of contraceptives, especially OCs; improve their use; inform, educate and provide technical assistance to USAID and the FDA, professional providers and pharmaceutical companies about compliance and how to improve it. The emphasis is on providing better tools for increasing the use-effectiveness of OCs.

Implementing Agencies: Various

Collaborating Agencies: FDA, pharmaceutical companies and various providers.

FY'94 Planned Activities: FHI plans to work with USAID, the FDA, pharmaceutical companies and providers to improve the labeling of COCs and POPs. We will do initial development of several other domestic and international projects to increase effective contraceptive use, such as a possible study of 21 v. 28 day oral contraceptive packaging in Mexico, studies of first year DMPA use, and correct use of spermicides and condoms. We will also continue to update our computerized, indexed bibliographies on contraceptive compliance; prepare research and position papers, review papers for journals, and serve as a resource to researchers at FHI and other agencies and organizations regarding their research on non-permanent contraceptive methods, and to prepare papers on issues of compliance across methods.

Expected Outputs, FY '94: As a result of research and recommendations by FHI along with other agencies, new simplified labeling for oral contraceptives is expected by the end of the year. Also, we will complete and distribute a fully indexed bibliography on oral contraceptive compliance and another on progestin-only pills; submit at least three papers to professional meetings, and two position papers for publication. A presentation will be made in November 1993 to the American Primary Care Research Group. Entitled "Oral Contraceptive Compliance as a Barrier to Family Planning", it discusses measures essential to correct compliance, and provides qualitative and anecdotal data which help to explain observed cultural differences in compliance behavior.

Possible Problems, Barriers to Completion: Barriers can vary with each project.

Initiation Date: August 1990
Projected End Date: August 1995
Funding Source: USAID/W
FY '94 Budget: \$78,462
Total Budget: \$284,243

134

Project Title: Further Testing of New OC Use Instructions

Country(s): To be determined.

Division: CUE (Contraceptive Compliance)

FCO: 6018

Technical Monitor: Linda Potter/Dorace Trotter

Project Objective: To test the USAID OC use instructions in at least two countries, and with different populations of lower literacy and education.

Project Description: As the first step in an effort to develop understandable and acceptable OC use instructions for USAID to include in the pill packs it distributes around the world, FHI has successfully completed a project with the Mexican Institute of Social Security (IMSS). These instructions were based on the FHI developed and FDA approved instructions, and were modified to fit the specific needs of the IMSS population. The current project seeks to expand the testing of the new instructions to an Asian site and an African site. Once the sites are determined, the instructions will be field-tested and modified to suit the different populations.

Implementing Agency: To be determined

Collaborating Agencies: Population Council, SOMARC

FY'94 Planned Activities: Explore further contacts with USAID/Dhaka, USAID/Niamey, Population Council and SOMARC to determine if and where the new oral contraceptive instructions should be tested further in order to be included in USAID pill packs.

Expected Outputs, FY '94: Concept proposals for one project in Asia and one project in Africa will be completed; project development of at least one of the proposals.

Possible Problems, Barriers to Completion: Mission priorities, availability of commodities and political unrest could all delay the development of this project.

Initiation Date: October 1992

Projected End Date: August 1995

Funding Source: USAID/W

FY '94 Budget: \$120,251

Total Budget: \$220,410

Project Title: Measuring OC Compliance Using the MEMS™ Device

Country(s): United States
Division: CUE (Contraceptive Compliance) FCO: 6003
Technical Monitor: Ruth Canamar

Project Objectives: 1) To validate the MEMS™ (Medication Event Monitoring System) as a tool to objectively measure daily pill taking in studies of OC compliance, and 2) to assess compliance and related factors among a sample population of OC users.

Project Description: The MEMS™ is a computerized pill dispenser that records the exact date and time a pill is dispensed from the pill pack. Two different types of populations, publicly-funded health clinic users and university health service users, make up the study sample. Both study sites are in North Carolina, with goal of 50 volunteers per site. Participants will be followed for 3 months. They will complete a questionnaire at each visit, and keep a daily diary card of OC use.

This study is also being piloted at two similar sites by the University of Michigan. This collaborative effort is intended to lead to a proposal to be submitted to NICHD for a multi-site study to measure OC compliance using the MEMS™ device in conjunction with diary cards.

This study is a pilot for future compliance studies in the U.S. and in developing countries to measure OC use behavior more rigorously than has previously been possible. Results should provide guidance on how to improve compliance among all types of OC users.

Implementing Agencies: Wake County Department of Health, Women's Health Center and the University of North Carolina Student Health Service

Collaborating Agency: University of Michigan's Center for Nursing Research

FY'94 Planned Activities: Data collection will be completed, and management, entry and analysis of data will be conducted. A proposal will be drafted for an NICHD multi-site study.

Expected Outputs, FY '94: A final report will be completed. A paper for presentation at a professional conference and publication will be generated.

Possible Problems, Barriers to Completion: None

Initiation Date: January 1993
Projected End Date: September 1994

Funding Source: USAID/W
FY '94 Budget: \$82,966
Total Budget: \$142,125

136

Project Title: Revision of Package Labeling for Progestin-Only OC Pills

Country(s): United States
Division: CUE (Contraceptive Compliance) FCO: 6472
Technical Monitor: Linda Potter

Project Objective: To develop package labeling and package insert information appropriate to progestin-only oral contraceptive pills (POPs), with simplified text for the patient labeling, and also to create an indexed POP bibliography/database.

Project Description: Labelling specifically for POPs is being developed by FHI for the FDA to replace the inappropriate COC labeling now found in POP pill packs.

POPs have special relevance to LDCs because they can be used during breastfeeding since they do not contain the estrogens found in COCs, which can decrease milk supply. The mislabeling of POPs causes much confusion and controversy about their use, especially in relation to breastfeeding. Most developing countries look to the FDA for the definitive word on the use and the safety of all contraceptives.

Collaborating Agency: U.S. Food and Drug Administration

FY'94 Planned Activities: A comprehensive review of the POP literature will be completed, on which the decisions about changes in labeling will be based. The FDA labeling itself will then be drafted by FHI. The FDA will then make its final revisions and provide the labeling guidance to the three U.S. pharmaceutical companies manufacturing POPs and USAID will be able to make the new labeling available to LDCs.

Expected Outputs, FY '94: FHI will complete the final version of the comprehensive review paper on POPs, which will then be submitted to the FDA and for publication. Upon approval of the paper's conclusions by the FDA, the text of the labeling will be completed and submitted to FDA.

Possible Problems, Barriers to Completion: Delays could occur in FDA revisions of new drug labeling guidelines.

Initiation Date: May 1992
Projected End Date: July 1994

Funding Source: USAID/W
FY '94 Budget: \$39,536
Total Budget: \$129,539

Project Title: Characteristics of Women Switching to DMPA

Country(s): United States
Division: CUE (Contraceptive Compliance) FCO: 6203
Technical Monitor: Ruth Cafiamar/Linda Potter

Project Objectives: 1) To determine characteristics of women who switch from OCs and other contraceptive methods to DMPA and why, and 2) to measure compliance and discontinuation of DMPA in a public health setting, and 3) to help design a computerized data collection program that will track DMPA users.

Project Description: This is a one year, retrospective pilot study of the characteristics of women who accepted DMPA during its first year of availability in the U.S. and their reasons for using this method. Compliance will be measured by the number and timing of follow-up injections. The reasons for discontinuation and, if applicable, the method switched to, will also be reported. The study will develop and test protocol and methodology for measuring compliance and discontinuation of DMPA which can be applied in LDC clinics providing DMPA to family planning clients.

Implementing Agencies: Wake County Department of Health, Women's Health Center

FY'94 Planned Activities: We will develop the study protocol and seek approval from the Protection of Human Subjects Committee (PHSC) and from the site. For this small pilot study, a student intern will be hired to write a simple computer program for tracking DMPA users, do the data collection, and work with FHI staff in writing the final report. We will then seek appropriate LDC sites for conducting similar studies.

Expected Outputs, FY'94: A DMPA user computer tracking program will be completed; and a final report written.

Possible Problems, Barriers to Completion: None

Initiation Date: October 1993
Projected End Date: September 1994

Funding Source: USAID/W
FY '94 Budget: \$10,459
Total Budget: \$10,459

138

Project Title: Risks and Benefits of Oral Contraceptive Use

Country(s): United States
Division: CUE (Contraceptive Benefits & Risks) FCO: 6216
Technical Monitor: Pam Schwingl

Project Objective: To evaluate the impact of known benefits and risks of OC use and other contraceptive methods on mortality.

Project Description: The purpose of this project is to develop methods of analysis to elucidate and update the impact of various contraceptive choices on the risk of mortality. The project encompasses several substudies, all of which assess the impact of the benefits and risks of contraceptive methods on mortality. The use of information generated by this activity will inform policy concerning the use of various methods for particular subgroups of women or women in particular countries.

Substudies include:

- 1) ongoing development and use of computer life-table model (OCRISK) software to assess the impact of risks and benefits of OC use on life expectancy in the U.S. and other countries. Users and nonusers of OCs are contrasted in this model.
- 2) Incorporation of U.S. data on smoking into the OCRISK model to compare mortality risk for groups characterized by different categories of OC use and smoking.
- 3) Development of a decision tree to compare mortality risks for a cohort of women who chose various contraceptive options. In this model, mortality risks of OC users, users of no method, users of barrier methods and users of sterilization will be contrasted.
- 4) Development of a decision tree which incorporates data on pre-existing conditions (smoking, diabetes, hypertension) to evaluate risk of mortality from various contraceptive methods compared to the risk of pregnancy among users of no method; this will be adapted for women in developing countries.

FY'94 Planned Activities: Using SMLTREE, a decision-tree analysis software package, a simulation model will be developed comparing the mortality risks and benefits associated with various forms of contraception versus no contraceptive use. Ongoing review of relevant literature and data sources will continue.

Expected Outputs, FY '94: Based on modeling analysis, a paper, along with a set of slides for presentation of results, will be produced and distributed to appropriate audiences - particularly USAID.

Possible Problems, Barriers to Completion: None.

Initiation Date: August 1990
Projected End Date: August 1995

Funding Source: USAID/W
FY '94 Budget: \$86,221
Total Budget: \$286,801

Project Title: Vasectomy and Prostate Cancer in a U.S. Screening Population

Country(s): United States
Division: CUE (Contraceptive Benefits & Risks) FCO: 6206
Technical Monitor: Pam Schwingl

Project Objective: To evaluate the putative association between vasectomy and subsequent prostate cancer by conducting a pilot case-control study within a population of men seeking screening for prostate cancer. This pilot will determine the feasibility of conducting a full case-control study within the prostate cancer screening population, and will be the basis for the submission of an NIH grant application.

Project Description: A positive relationship between vasectomy and prostate cancer has been noted in several U.S. studies. While there is no clear biologic mechanism for such a relationship, there is consensus that the small to modest elevation in risk groups among vasectomized men may be due to detection bias. That is, vasectomized men may be more likely to be detected since they may use urologic screening services more often and may be more medicalized. This phenomenon is likely to be confined to the peculiarities of the system in the U.S., since extensive screening for prostate cancer is common only here. However, the impact of this information has the potential to affect acceptance of vasectomy throughout the world. Our hypothesis is that a study of this relationship conducted among several populations in the U.S. will show no effect, since all men seeking screening may be "equally" likely to be medicalized. Should we see no effect, with sufficient numbers, these results would provide strong evidence for the existence of such a bias. This confirmation would help the scientific community interpret previous findings. In 1993 we conducted the first part of a pilot study in a screening population in 10 sites. A questionnaire was completed by approximately 2,000 men 50-70 years of age.

Implementing Agencies: Several clinics in the US.
Collaborating Agency: Prostate Cancer Education Council (PCEC)

FY'94 Planned Activities: Data from the pilot screening questionnaire will be coded, input and cleaned, merged with other PCEC data, and analyzed; 400 screened positives will be followed; and a vasectomy validation sub-study will be performed.

Expected Outputs, FY '94: A descriptive paper on vasectomy and screening behavior will be drafted; and an NIH grant application for a full study will be submitted.

Possible Problems, Barriers to Completion: None

Initiation Date: March 1993
Projected End Date: August 1995

Funding Source: USAID/W
FY '94 Budget: \$77,181
Total Budget: \$237,621

140

Project Title: Vasectomy and Prostate Cancer in Korea

Country(s): Korea
Division: CUE (Contraceptive Benefits & Risks) FCO: 6287
Technical Monitor: Jim Zhang

Project Objective: To ascertain if there is a relationship between vasectomy and prostate cancer in a non-Western population.

Project Description: Vasectomy is used for family planning by approximately 42 million couples worldwide, the majority of whom live in developing countries. It is a highly reliable and safe contraceptive method which has been extensively studied. Recently, renewed concerns have been raised about a possible adverse effect on cancer of the prostate many years after the procedure. These observations are based on research conducted in the United States of America (USA), a country where there is a high and rising incidence of prostate cancer. Overall incidence rates of prostate cancer in some developed countries, such as the USA, are fifty times higher than in some developing countries, such as the People's Republic of China. The majority of epidemiological studies on the relationship between vasectomy and prostate cancer have been based in the USA - the findings are inconsistent and the reported associations are weak. Therefore, although on the basis of currently available data it is concluded that no changes in family planning policies with regard to vasectomy are warranted, the concerns raised by these studies require that research into any possible association be undertaken in countries where vasectomy is widely practiced and, so far, accepted.

To address this research need, FHI will participate in supporting one site in a multicountry, multicentre hospital-based case-control study on the relationship between prostate cancer and vasectomy in developing countries (China, India, Korea and Nepal) and one developed country (New Zealand) where vasectomy has been extensively practiced for family planning.

Implementing Agency: Catholic Medical College, Seoul, Korea
Collaborating Agency: World Health Organization

FY'94 Planned Activities: A three-month pilot study to assess the logistics and test the questionnaire will be conducted. Next spring, WHO will hold a general meeting to summarize the pilot study, which is being carried out in all the participating countries, and to discuss the full-scale study. The main study will probably be launched next fall.

Expected Outputs, FY '94: Results from the pilot study will be used to plan the main study.

Possible Problems, Barriers to Completion: None.

Initiation Date: September 1991
Projected End Date: August 1995

Funding Source: USAID/W
FY '94 Budget: \$97,404
Total Budget: \$182,517

Project Title: Copper IUD Use and Tubal Infertility

Country(s): Mexico
Division: CUE (Contraceptive Benefits & Risks) FCO: 6205
Technical Monitor: Pam Schwingl/David Hubacher

Project Objective: To determine whether IUD use among nulliparous women increases their risk of developing tubal infertility.

Project Description: Previous research has shown an association between IUD use and tubal infertility among nulliparous women. Though the studies are widely cited, design flaws could have introduced biases which in turn resulted in spurious associations. This case-control study will use controls with male-mediated causes of infertility, and will be conducted at a site where copper IUD use is common.

Implementing Agency: National Perinatology Institute and perhaps IMSS (Mexican Social Security Institute)

Collaborating Agency: Pathfinder International.

FY'94 Planned Activities: Work will continue with Mexican counterparts to develop a study protocol; secure final approval from both Mexican institutions and FHI; finalize the data collection instruments and begin recruiting study subjects.

Expected Outputs, FY '94: None.

Possible Problems, Barriers to Completion: IMSS has not decided whether to participate in this study. If they agree, then the study will continue to be developed. If only the National Perinatology Institute agrees to participate, the feasibility of the whole study will be re-evaluated.

Initiation Date: October 1993
Projected End Date: August 1995

Funding Source: USAID/W
FY '94 Budget: \$29,127
Total Budget: \$58,859

142

Project Title: Norplant Use and Blood Pressure

Country(s): Worldwide

Division: CUE (Contraceptive Benefits & Risks)

FCO: 6207

Technical Monitor: Eilene Bisgrove

Project Objective: Examine the effects of Norplant use on women's diastolic and systolic blood pressure.

Project Description: The project will use data from the WHO Collaborative Postmarketing Surveillance Study (PMS) of Norplant to examine the effects of Norplant use on women's diastolic and systolic blood pressure. The investigator will work with the Clinical Trials Division to conduct a preliminary analysis of the relationship between Norplant use and blood pressure using premarketing clinical data. This analysis will set the groundwork for an analysis of the postmarketing data. Since the postmarketing study did not use a randomized design, appropriate methods will be required to account for contraceptive method selection bias.

Collaborating Agencies: WHO, The Population Council

FY'94 Planned Activities: Analysis of the premarketing data will be initiated; a short proposal for the analysis of postmarketing blood pressure data will be prepared and submitted to WHO and the Population Council for approval; if approved to use the blood pressure data, the investigator will proceed to model method selection and subsequently will proceed with the blood pressure analysis.

Expected Outputs, FY '94: Completed analysis of premarketing data and draft report; completed modelling of determinants of Norplant selection.

Possible Problems, Barriers to Completion: WHO and The Population Council may withhold permission to use blood pressure data from PMS study; the analytical approach required for analysis which appropriately deals with method selection bias is complicated.

Initiation Date: September 1993

Projected End Date: August 1995

Funding Source: USAID/W

FY '94 Budget: \$26,375

Total Budget: \$52,649

143

Project Title: Nonoxynol-9 Use and HIV

Country(s): To be determined

Division: CUE (Contraception & STD/HIV)

FCO: 6301

Technical Monitor: Ron Roddy

Project Objective: To assess the HIV prophylactic effect of N-9 film use among women.

Project Description: Recommendations for the prevention of sexually transmitted HIV infection include abstinence, monogamy with an uninfected partner, and condom use. These recommendations are inadequate for the protection of many women because sexual activity and condom use require the cooperation of their male partners. Women need a method of protection that they can control. N-9, a biodegradable approved for vaginal use as a spermicide, inactivates free and cell-associated HIV in less than 60 seconds, provides some protection from simian immunodeficiency virus in the monkey model, and has had mixed results in human studies. N-9 also can cause genital irritation, including epithelial disruption which theoretically may increase susceptibility to HIV infection. In vitro studies have shown that N-9 has an effect on bacteria known to be the usual vaginal flora. Neither the effect of N-9 on the microflora of female sex workers, nor what effect a change of the vaginal ecology will have on risk of HIV infection is known. We will test the hypothesis that N-9 film can affect the rate of HIV infection in high-risk women.

Implementing Agency: To be determined

Collaborating Agency: National Institutes of Allergy and Infectious Diseases, National Institutes of Health.

FY'94 Planned Activities: A site will be found for the study, local approval will be sought, and the study will be initiated.

Expected Outputs, FY '94: Study site found, all local approval obtained, and the study initiated.

Possible Problems, Barriers to Completion: It may not be possible to find a site for the study.

Initiation Date: August 1992

Projected End Date: August 1995

Funding Source: USAID/W (cost shared with the National Institutes of Health)

FY '94 Budget: \$80,816 (USAID funds)

Total Budget: \$193,810

144

Project Title: Condom Use and Cervical Infection

Country(s): Dominican Republic
Division: CUE (Contraception & STDs/HIV) FCO: 6304
Technical Monitor: Ron Roddy

Project Objective: To assess the effectiveness of N-9 lubricated condoms for prevention of gonorrhea and chlamydial infection compared with that of silicone lubricated condoms with a randomized controlled trial.

Project Description: Condoms are the foundation for programs and individuals attempting to prevent the spread of sexually transmitted infections (STI), including HIV. Several varieties of condoms are available and N-9 lubricated condoms have been promoted as providing extra protection because of the microbicidal activity of N-9. However, N-9 lubricated condoms are more expensive than condoms lubricated only with silicone. There are no human use data to determine if they afford more protection, or whether they are as non-irritating to women as silicone lubricated condoms. We will test the hypothesis that the addition of N-9 to silicone lubricant on latex male condoms can reduce the rate of gonorrheal and chlamydial cervicitis when compared with condoms lubricated only with silicone. We will also test the hypothesis that the N-9 lubricant has no increased effect on genital irritation in women who engage in frequent sexual intercourse when compared with silicone lubricant.

Implementing Agency: PROFAMILIA

FY'94 Planned Activities: The study will be initiated in January and at least 500 participants will be recruited and followed-up. Monitoring visits will be made to assure continued progress.

Expected Outputs, FY '94: Preliminary results may be available for the earliest enrollees.

Possible Problems, Barriers to Completion: Unknown problems with recruitment may slow the progress of the study.

Initiation Date: August 1992
Projected End Date: August 1995

Funding Source: USAID/W
FY '94 Budget: \$242,587
Total Budget: \$437,217

145

Project Title: Barrier Contraceptive Use Among Couples at High Risk of HIV Infection

Country(s): Zambia
Division: CUE (Contraception & STDs/HIV) FCO: 6305
Technical Monitor: Charles Morrison

Project Objectives: 1) To measure the long-term use of barrier contraceptives (female and male condoms, vaginal contraceptive film) among couples at high-risk for HIV infection; 2) to evaluate the acceptability of the female condom among women and men; 3) to identify factors predictive of long-term barrier contraceptive use.

Project Description: The goal of this study is to evaluate determinants and acceptability of long-term barrier contraceptive use among HIV-discordant couples, especially use of the female condom. Though there have been numerous short term acceptability studies of the female condom, there have been no long term acceptability studies among couples that should be well motivated to use a barrier method consistently. This study will recruit 100 couples at high-risk of HIV infection (HIV-discordant couples or couples with a partner with a diagnosed STDs), counsel them on use of the female and male condom and vaginal contraceptive film, and carefully measure long-term use of the methods (over 1 year period). In addition to behavioral variables, data on acceptability, psychosocial, and STDs variables are being collected.

Implementing Agency: University Teaching Hospital, Lusaka, Zambia

FY'94 Planned Activities: Recruitment of study participants; follow-up of couples.

Expected Outputs, FY '94: Short-term acceptability data on the female condom will be generated.

Possible Problems, Barriers to Completion: Recruitment is going slower than expected. FHI is discussing possible protocol changes to boost recruitment.

Initiation Date: January 1993
Projected End Date: April 1995

Funding Source: USAID/W
FY '94 Budget: \$82,344
Total Budget: \$195,175

146

Project Title: Barrier Methods Monograph

Country(s): United States

Division: CUE (Contraception & STDs/HIV)

FCO: 6030

Technical Monitor: Paul Feldblum

Project Objective: To improve the dissemination of research findings on barrier methods, contraceptive efficacy, and prophylactic efficacy for service providers.

Project Description: FHI will write, print and distribute a monograph on male and female barrier contraceptive methods. It will include the following sections: introduction to types of methods and historical aspects; contraceptive efficacy; prophylactic efficacy; acceptability; new barrier methods; research needs in barrier contraception; general bibliography; and appendices listing FHI barrier studies and FHI barrier publications. The audience for the monograph will be family planning service providers, USAID Missions, ministries of health, and women's health advocacy groups. The purposes in writing this monograph are several: to compile up-to-date information on barrier efficacy, safety and acceptability in a single document; to make the information accessible to non-researchers; and to highlight FHI's important contributions in the field.

FY'94 Planned Activities: FHI authors will write all sections of the monograph. Consultants and USAID/W staff will review the draft. A designer will be hired to lay out the publication which will be printed in North Carolina.

Expected Outputs, FY '94: Depending on the length, between 5,000 and 10,000 copies of the monograph will be printed and distributed around the world, including distribution at the Cairo International Conference on Population and Development.

Possible Problems, Barriers to Completion: None.

Initiation Date: September 1993

Projected End Date: September 1994

Funding Source: USAID/W

FY '94 Budget: \$69,345

Total Budget: \$69,345

Project Title: Short-term IUD Risk and HIV

Country(s): Kenya
Division: CUE (Contraception & STDs/HIV) FCO: 6204
Technical Monitor: Charles Morrison

Project Objective: To determine whether HIV+ women are at greater risk of short-term complications related to IUD use than HIV- women.

Project Description: Women, infected with HIV (HIV+), need safe, effective and long-lasting contraception. The current generation of IUDs fulfill these criteria and are also affordable. To date, it is unknown whether there is an increased risk of adverse effects in the early post-insertion period among HIV+ women. Despite the lack of data, the IPPF recently stated that an IUD should not be inserted in an HIV+ woman, and many providers are no longer inserting IUDs. Six hundred HIV- and two hundred HIV+ IUD users recruited from Kenyatta National Hospital in Nairobi, Kenya will be followed for four months to assess their rates of short-term complications related to IUD use, notably PID. It may also be possible to study HIV shedding before and after insertion, in collaboration with researchers from the University of Washington and the University of Manitoba.

Implementing Agency: University of Nairobi

FY'94 Planned Activities: Data collection instruments will be developed; recruitment will begin and the study will be initiated.

Expected Outputs, FY '94: Data collection instruments; study initiation.

Possible Problems, Barriers to Completion: None anticipated..

Initiation Date: September 1993
Projected End Date: August 1995

Funding Source: USAID/W, proposal submitted to AMFAR for partial support.
FY '94 Budget: \$70,356
Total Budget: \$200,732

Project Title: Clinical Trial of the Lactational Amenorrhea Method (LAM)

Country(s): Pakistan, Philippines
Division: CUE (Breastfeeding & Postpartum Contraception) FCO: 6389
Technical Monitor: Kathy Kennedy

Project Objective: To determine the efficacy of the lactational amenorrhea method when offered by trained counselors in two international settings.

Project Description: The LAM was developed based on prospective research which showed that the probability of conception during full breastfeeding and amenorrhea was extremely small during the first six months postpartum. However, few attempts have been made to teach women to use this information as a contraceptive method. In this sub-project, women volunteer to use LAM as a contraceptive. This study has been conducted at three centers in Karachi and one center in Multan, Pakistan. The same study was also conducted in Manila, Philippines. Data collection was completed in Pakistan in 1993.

Implementing Agencies: Jose Fabella Memorial Hospital (Philippines); National Research Institute for Fertility Control (Pakistan)

FY'94 Planned Activities: Data collection in the Philippines will be completed; FHI will complete querying and will begin data analysis.

Expected Outputs, FY '94: Preliminary analysis will be conducted and possibly papers will be drafted for publication.

Possible Problems, Barriers to Completion: New software innovations are needed for proper treatment of denominator cases.

Initiation Date: August 1990
Projected End Date: September 1994

Funding Source: USAID/W
FY '94 Budget: \$58,318
Total Budget: \$278,120

149

Project Title: Bellagio II: Further Assessment of the Lactational Amenorrhea Method

Country(s): Worldwide
Division: CUE (Breastfeeding & Postpartum Contraception) FCO: 6023
Technical Monitor: Kathy Kennedy

Project Objective: To organize and conduct a conference which evaluates new data relative to the Bellagio Consensus.

Project Description: The 1988 Bellagio Consensus stated that breastfeeding is 98% effective in preventing pregnancy during the first 6 months postpartum in fully breastfeeding, amenorrheic women. Since that time further research has been conducted by FHI, WHO and others on the recovery of fertility after childbirth and the use of the lactational amenorrhea method of family planning. A follow-up conference is warranted to evaluate the Consensus in light of the new research.

Collaborating Agency: World Health Organization, Institute for Reproductive Health

FY'94 Planned Activities: FHI plans to make an application to the Rockefeller Foundation to support the conference at Bellagio.

Expected Outputs, FY '94: FHI expects to secure funding from the Rockefeller Foundation and to negotiate an agenda and participant list with the collaborating agencies.

Possible Problems, Barriers to Completion: Plans for this conference have been postponed for at least two years in anticipation of completion of the WHO study.

Initiation Date: October 1992
Projected End Date: August 1995

Funding Sources: USAID/W, Rockefeller Foundation,
World Health Organization (possibly)
FY '94 Budget: \$10,746
Total Budget: \$44,721

150

Project Title: Switching from POCs to COCs: Guidelines for Breastfeeding Women

Country(s): Worldwide
Division: CUE (Breastfeeding & Postpartum Contraception) FCO: 6028
Technical Monitor: Cynthia Visness

Project Objective: To develop and disseminate guidelines for clinicians regarding whether and when breastfeeding women can or should switch from POCs to COCs for effective contraception.

Project Description: There is a need on the part of family planning professionals for more guidance about the use of progestin-only oral contraceptive (POC) use during breastfeeding. Specifically, there are no consistent guidelines regarding whether breastfeeding women who use POCs should switch to COCs at some point during lactation and what would be the best time for them to make this switch. FHI proposes to develop a set of guidelines regarding this issue by soliciting and compiling the opinions of a number of experts.

FY'94 Planned Activities: Expert opinions, and the scientific rationale upon which the opinions are based, will be solicited by correspondence -- possibly using dictaphones as well as written materials.

Expected Outputs, FY '94: A set of guidelines regarding pill switching during lactation will be drafted.

Possible Problems, Barriers to Completion: If the experts' opinions vary widely, FHI may not be able to develop guidelines which all will endorse.

Initiation Date: September 1993
Projected End Date: December 1994

Funding Source: USAID/W
FY '94 Budget: \$23,831
Total Budget: \$28,658

Project Title: Breastfeeding and NFP Paper Writing

Country(s): Worldwide

Division: CUE (Breastfeeding & Postpartum Contraception) FCO: 6462

Technical Monitor: Kathy Kennedy

Project Objective: To conduct primary and secondary analysis and preparation of manuscripts on breastfeeding, lactational amenorrhea, and natural family planning.

Project Description: FHI has collected data in the areas of breastfeeding and natural family planning for over 10 years. FHI also has access to data collected by colleagues. When an FHI study in the area of breastfeeding or natural family planning is completed, report writing and paper presentation or publication work is carried out under this sub-project.

FY'94 Planned Activities: In-depth analysis of data and preparation of papers from completed studies, plus presentation of results at professional meetings. Further investigation of LAM data, and of breastfeeding as a possible means of HIV transmission, will be special foci of study.

Expected Outputs, FY '94: FHI anticipates publications tentatively in the following areas:

- "The effects of breastfeeding on women's health";
- "Natural family planning use during breastfeeding";
- "The development and implementation of an NFP project in Lima, Peru"; and
- "Effect of day care on infant health".

FHI anticipates manuscript preparation on:

- "The effectiveness of LAM in Manila, The Philippines";
- "The effectiveness of LAM in Pakistan"; and
- "Breastfeeding as a mode of HIV transmission".

Possible Problems, Barriers to Completion: None.

Initiation Date: August 1990

Projected End Date: August 1995

Funding Source: USAID/W

FY '94 Budget: \$58,105

152

Project Title: Reproductive Health Paper Writing

Country(s): Worldwide

Division: Contraceptive Use and Epidemiology

FCO: 6352

Technical Monitor: Douglas Nichols

Project Objective: To conduct secondary analysis on data collected in completed CUE studies, and to write papers for presentations and publication based on these analyses.

Project Description: Following the completion of field research activities culminating in a project final report, CUE and other staff frequently are asked to continue to analyze data and/or prepare papers for publication in scientific journals to disseminate results of FHI-supported research. FCO #6352 supports staff time and travel costs related to these needs.

FY'94 Planned Activities: CUE staff will continue paper writing, using data generated as part of FHI field research (See Project Description above).

Expected Outputs, FY '94: Approximately 12 papers will be generated, among which the following have been specifically identified:

- "Analysis of Egyptian Demographic & Health Survey (DHS) Data on OC Compliance." (Trottier)
- "Knowledge, Attitudes, Practice and Provision of Family Planning Services Among Kenyan Medical Doctors." (Nichols)
- "Factors Associated with Copper-T IUD Removal for Bleeding/Pain: A Multivariate Analysis." (Zhang)
- "An Evaluation of Reproductive Health as an Approach to Family Planning in Ceará, Brazil." (Bailey)
- "Use of DMPA and the Risk of Cervical Carcinoma in Situ." (Bisgrove)

Possible Problems, Barriers to Completion: None.

Initiation Date: August 1990

Projected End Date: August 1995

Funding Source: USAID/W

FY '94 Budget: \$147,662

2. Service Delivery Research

The purpose of developing and introducing contraceptive technologies is to increase the options available to couples in the developing world who choose to control their fertility. Many factors help to determine whether family planning clients accept a method in the first place, whether they use it correctly, and whether they continue to use it. One important set of factors relates to the ways in which programs deliver contraceptive services to clients. Acceptance and continued use of contraception can be influenced profoundly by provider attitudes and official policies regarding various methods, by the quality of services provided, and by the cost of services. The Service Delivery Research Division carries out studies which seek to improve the delivery of family planning services, with the general goal of increasing access to contraception. SDR's research agenda includes projects that respond to interdivisional priorities such as contraceptive introduction, or improving provider practices which limit access to services; other projects respond directly to country-level needs as articulated by USAID Missions.

Currently, SDR's activities in service delivery research fall within the following four priority areas:

■ **Improving Resource Allocation and Financial Sustainability**

While demand for family planning services in developing countries has increased rapidly in recent years, funding from governments and donors has stagnated or even declined. SDR helps family planning programs to bridge this funding gap by carrying out research to find ways to improve the use of existing resources, and also to increase the financial resources generated locally through diversification of services and increased cost recovery.

■ **Improving Quality of Care**

As family planning programs expand beyond a clinic-based approach to service delivery, the quality of care (QOC) provided to clients is becoming a key program focus. SDR is engaged in a wide range of research activities related to improving the quality of services. These include assessing quality of care, estimating the impact on quality of removing barriers to family planning use, developing a model for service delivery improvement, and developing training materials.

■ **Improving Service Delivery Practices that Limit Access to Contraception**

SDR's programmatic research on service delivery barriers focuses on three types of studies: identifying and measuring barriers; measuring the impact of barriers on usage of staff and on client costs in both clinical and non-clinical settings; and evaluating the impact of introducing new service delivery guidelines which seek to improve practices.

■ **Evaluation of New Combinations of Methods and Delivery Systems**

A contraceptive service can be seen as consisting of two components: the contraceptive method itself, and the delivery system which channels the method to

users. SDR conducts research to evaluate different combinations of methods and delivery systems, and the factors which can determine whether specific method-delivery system combinations will succeed in attracting new clients in or encouraging continuation of use, or both.

FY'94 Program Objectives and Expected Outputs

The SDR division will continue to emphasize these four priority areas in research carried out under the Cooperative Agreement during the current year. SDR's key objective of increasing access to contraception will be pursued in several ways: by evaluating the impact of DMPA and Norplant introduction in selected countries in Latin America, Africa and Asia; by analyzing the impact of improving service practices in Ghana, Mexico and Cameroon; by continuing to develop methodologies to measure the quality of care, and field-testing these methodologies in Jamaica and other sites; and by carrying out economic analyses to increase program efficiency in Ecuador and Paraguay. SDR resources will continue to be leveraged through collaborative relationships with INOPAL II, International Planned Parenthood Federation (IPPF), the Pan American Health Organization (PAHO) and the Program for International Training in Health (INTRAH).

In addition to the activities mentioned above, SDR plans to proceed with the development of a new research area which focuses on the potential for adding STD services to existing family planning programs. This new priority area responds to an increasing emphasis on integrated reproductive health services. Research will be conducted to help family planning programs decide whether to add STD services to their programs, and if so, to provide guidance on which services to add, where to offer these services, and to whom to provide services.

The studies, ongoing and new, which the Service Delivery Research Division will implement in FY'94 are listed below:

■ **Improving Resource Allocation and Financial Sustainability**

Continuing Projects:

- Costs of Methods and Delivery Systems
- Technical Assistance in Sustainability
- Economic Analysis of ASHONPLAFA Programs

New Project:

- Costs of Family Planning Services provided by the Centro Paraguayo de Estudios de Poblacion (CEPEP)

■ **Improving Quality of Care**

Continuing Project:

- Improving Quality of Care

New Projects:

- Developing a Quality of Care Framework
 - Quality of Care of Norplant Services
- **Improving Service Delivery Practices that Limit Access to Family Planning**

Continuing Projects:

- Improving Service Delivery Practices: Development
- Improving Practices Among Private Physicians
- Measuring Provider Adherence to the National MCH/FP Service Policy and standards Document
- IUD Follow-up Visits
- 1991/92 Epidemiology and Family Health Survey

New Projects:

- Impact of Reducing IUD Follow-up Visits
 - Improving Service Delivery Practices in Ghana
- **Evaluation of New Combinations of Methods and Delivery Systems**

Continuing Projects:

- Introduction of an Injectable Contraceptive in an Ecuadoran Family Planning Program
- Programmatic Evaluation of Norplant Introduction in Mali
- Evaluation of Immediate Postplacental IUD Insertion In Mali
- Evaluation of Postplacental IUD Insertion In Kenya
- Introductory Study of Postdelivery IUD Insertion in Niger

New Projects:

- Introduction of DMPA in Latin America
 - Programmatic Research on Introduction of DMPA in the Philippines
 - Impact of Norplant Expansion in Haiti
- **Adding STD Services to Existing Family Planning Programs**

New Project:

- Family Planning and STD Service Integration

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Project Title: Costs of Methods and Delivery Systems

Country(s): Bangladesh
Division: Service Delivery Research FCO: 9713
Technical Monitor: Barbara Janowitz

Project Objective: To estimate the cost per couple year of protection (CYP) for various combinations of methods and delivery systems and to determine reasons for variations.

Project Description: This study (funded by USAID/Bangladesh) will estimate the cost of services for combinations of delivery systems and contraceptive methods. While Bangladesh has made impressive gains in raising the level of contraceptive use, there are concerns about the growing costs of maintaining and expanding family planning services. Therefore the rationale for the study is to determine whether there are more cost effective ways of providing services so that contraceptive use can be expanded at reasonable cost.

The study covers both government and non-government programs, including some innovative programs of both the government and of non-governmental organizations (NGOs). Within the government program, the major emphasis is on the outreach program which employs approximately 23,000 outreach workers and 5,000 supervisors. What are the current inefficiencies in this delivery mode? NGOs also run outreach programs. Should greater reliance be placed on some of the innovative attempts to substitute lower paid part-time workers for these full-time workers? As to the fixed service delivery points, there is concern that this delivery system is not heavily used, and that costs may be high because of this low usage.

Implementing Agencies: Associates for Community and Population Research and the Population Development and Evaluation Unit

FY'94 Planned Activities: Data collection for government field workers will be completed. Data collection in NGO programs will be implemented and completed. In all fixed-site facilities, data collection forms will be designed, pre-tested, and all data will be collected. Data will be analyzed.

Expected Outputs, FY '94: Information on costs per CYP for various method-delivery system combinations will be provided. An analysis of reasons for differences in costs of given method-delivery system combinations including salaries and credentials of staff, the time spent to perform tasks, differences in tasks performed and capacity utilization will be carried out. Costs per CYP for each of the innovative programs will be calculated. A report detailing study findings including an analysis of how costs could be reduced through changes in service delivery will be prepared. Results will be presented at a workshop.

Possible Problems, Barriers to Completion: Slowdowns in data collection may result in delay of report until FY '95

Initiation Date: April 1992
Projected End Date: September 1994
Funding Source: USAID/Bangladesh
FY '94 Budget: \$203,510 (an additional \$22,000 is being requested)
Total Budget: \$352,000

157

Project Title: Technical Assistance in Sustainability

Country(s): Ecuador
Division: Service Delivery Research FCO: 9309
Technical Monitor: John Bratt

Project Objective: To provide training and technical assistance to CEMOPLAF (Family Planning Medical Centers) in the areas of cost containment, cost recovery and income generation.

Project Description: CEMOPLAF, an Ecuadoran family planning PVO, is interested in strengthening its ability to conduct programmatic research that will improve agency cost-control, cost-recovery, and income generation. USAID/Ecuador is helping CEMOPLAF achieve these aims, with the assistance of the Population Council's INOPAL II Project and FHI. Staff from INOPAL II and FHI have coordinated several training courses in research methodology for CEMOPLAF staff and will provide technical assistance to CEMOPLAF researchers as they apply their skills in a series of costing, pricing and market research studies.

Implementing Agency: CEMOPLAF

Collaborating Agency: INOPAL II (Population Council)

FY'94 Planned Activities: Several sub-projects will be designed and initiated. These will include a study of CEMOPLAF clients' ability to pay for family planning services, an experimental study examining the impacts of a price increase in CEMOPLAF clinics, and studies of the costs of laboratory services, clinic-based pharmacies and CEMOPLAF's community based distribution (CBD) program.

Expected Outputs, FY '94: The final report for the ability-to-pay study will be completed by June 30, 1994. The results of other studies should be available in early FY '95.

Possible Problems, Barriers to Completion: None foreseen

Initiation Date: April 1993
Projected End Date: August 1995

Funding Source: USAID/W, USAID/Ecuador, INOPAL II
FY '94 Budget: \$27,165
Total Budget: \$75,000

158

Project Title: Economic Analysis of ASHONPLAFA Programs

Country(s): Honduras
Division: Service Delivery Research FCO: 9712
Technical Monitor: John Bratt

Project Objective: To use economic criteria to evaluate various aspects of ASHONPLAFA's family planning service delivery.

Project Description: This study was conducted at ASHONPLAFA (Family Planning Association of Honduras), the Honduran IPPF affiliate, and was funded with an add-on from USAID/Honduras. ASHONPLAFA and USAID/Honduras were interested in conducting this study to provide ASHONPLAFA with information to control costs and to establish a fee structure.

Results and recommendations were presented to ASHONPLAFA senior management and to USAID/Honduras in June, 1993. The results showed that utilization of ASHONPLAFA's smaller clinics is very low, resulting in much higher average costs for clinic services. In terms of cost per CYP, female sterilization is the least costly method, while the costliest methods are condoms distributed through the community based distribution (CBD) program. Cost recovery is highest in the social marketing program, and lowest in the clinics; cost recovery for female sterilization is especially low, with clients paying US\$0.75 per year of protection. Recommendations were made to ASHONPLAFA senior management on ways to improve cost recovery, to increase utilization of smaller clinics, and to track costs more effectively.

Implementing Agency: ASHONPLAFA

FY'94 Planned Activities: Complete final report

Expected Outputs, FY '94: Final Report

Possible Problems, Barriers to Completion: None

Initiation Date: January 1992
Projected End Date: December 1993

Funding Source: USAID/Honduras
FY '94 Budget: \$437
Total Budget: \$48,000

Project Title: Costs of Family Planning Services provided by
CEPEP

Country(s): Paraguay
Division: Service Delivery Research FCO: 9333
Technical Monitor: John Bratt

Project Objective: To estimate the costs of all family planning services and products currently provided by the Centro Paraguayo de Estudios de Poblacion (CEPEP), the Paraguayan affiliate of the International Planned Parenthood Federation.

Project Description: CEPEP is interested in receiving technical assistance to estimate the costs of producing family planning services through its network of clinics, associated physicians and CBD distributors. CEPEP is currently in the midst of an ambitious expansion program, and plans to use the information generated by the cost study to help set fees for services as well as to identify areas to control costs.

Implementing Agency: CEPEP (Centro Paraguayo de Estudios de Poblacion)
Collaborating Agency: IPPF/WHR

FY'94 Planned Activities: A protocol and subagreement will be written, data collection forms will be developed, CEPEP staff will be trained in cost analysis, cost data will be collected and analysis will begin.

Expected Outputs, FY '94: Not applicable

Possible Problems, Barriers to Completion: None foreseen

Initiation Date: February 1994
Projected End Date: December 1994

Funding Source: IPPF/WHR and USAID/W
FY '94 Budget: \$15,787
Total Budget: \$25,000

160

Project Title: Improving Quality of Care

Country(s): Worldwide

Division: Service Delivery Research

FCO: 9318

Technical Monitor: Karen Hardee

Project Objectives: To promote the concepts of quality of care and service quality improvement (SQI) in family planning programs. To develop a training curriculum on quality of care assessment and the processes and tools of SQI.

Project Description: Increasingly, family planning programs are realizing that to make further gains in family planning, programs must focus on improving the quality of care given to clients. Improved quality is also a key consideration as programs shift their emphasis from meeting demographic objectives to meeting the reproductive health needs of individual clients. However, confusion remains regarding the definition and measurement of quality, and most importantly, how to make improvements in quality of care. FHI has played a lead role in assessing and promoting processes, tools and methods for improving quality of care.

FY'94 Planned Activities: FHI will continue to respond to requests for assistance with training and assessments in service quality improvement. Staff will develop two quality of care research studies by identifying relevant issues, reviewing literature, making site visits and preparing concept proposals. Potential study topics include the dimensions of quality from the user's perspective in public sector clinics in Jamaica and the needs of family planning workers to provide quality care in family planning programs.

Expected Outputs, FY '94: Expected outputs include: refined training tools for SQI, a research study of quality of care in the public sector in Jamaica, and a research design for assessing family planning workers' perspectives on quality of care in a selected site.

Possible Problems, Barriers to Completion: Site selection for studies. Interest of Missions in studies.

Initiation Date: September 1992

Projected End Date: August 1995

Funding Source: USAID/W

FY '94 Budget: \$ 42,171

Total Budget: \$184,097

Project Title: Developing A Quality of Care Framework

Country(s): Latin America
Division: Service Delivery Research **FCO:** 9302
Technical Monitor: Laurie Fox

Project Objective: To develop and field test an integrated framework for assessing quality of care in reproductive health, including family planning, maternal health and HIV/STDs in Latin America.

Project Description: In a memorandum of understanding between the PAHO and FHI, PAHO requested the participation of FHI in developing a framework for an integrated model of quality of care in reproductive health. Since hosting a workshop in March 1993 to lay the foundation of the model, PAHO, FHI and International Projects Assistance Services (IPAS) have continued to expand on the meeting's output. A draft model is being widely reviewed at the country level in Latin America, and by experts in the field of quality of care and reproductive health. The framework will be presented at three regional meetings to obtain input from public and private institutions working in reproductive health services and groups advocating for women's health rights in the region. An outgrowth of this project is PAHO's proposal to establish a clearinghouse on QOC in reproductive health.

Implementing Agency: Pan American Health Organization
Collaborating Agencies: PAHO and IPAS

FY'94 Planned Activities: FHI will participate in at least one of the three regional meetings (Bolivia, Honduras and Trinidad/Tobago). Staff will collaborate on the drafting of an instrument to measure the framework and on the evaluation of its applicability. FHI will also assist in the development of a clearinghouse for information about QOC in reproductive health services, based at PAHO, in Washington, D.C.

Expected Outputs, FY '94: Outputs will include: an instrument to measure the three components of the QOC framework; technical assistance provided in the field testing of the framework; and provision of material for and incorporation into the QOC clearinghouse.

Possible Problems, Barriers to Completion: Delays in coordinating input on the instrument, or in establishing field test sites with in-country agencies.

Initiation Date: October 1993
Projected End Date: August 1995
Funding Source: USAID/W
FY '94 Budget: \$28,523
Total Budget: LOP budget not yet determined.

162

Project Title: Quality of Care of Norplant Services

Country: Haiti

Division: Service Delivery Research

FCO: 9716

Technical Monitor: Andy Thompson

Project Objective: To evaluate the quality of Norplant clinical and counseling services in Haiti.

Project Description: In order to assess the success of the Norplant expansion phase and guide future programming, evaluation components will be built into the training program to insure that the needs of both service providers and acceptors are being met. FHI and a collaborating Haitian research organization will conduct research activities related to the quality of care of Norplant services.

The research will focus on assessing the quality of Norplant clinical and counseling service provisions, particularly in regards to access to removal. This activity will be implemented in coordination with the Institut Haitien de Santé Communautaire (INHSAC) follow-up program to assure proficiency of its training.

Implementing Agency: To be determined

FY'94 Planned Activities: Identify a Haitian research organization, develop a research protocol, finalize subagreement, and begin data collection.

Expected Outputs, FY '94: Research protocol developed, subagreement finalized, and data collection instruments created and pre-tested.

Possible Problems, Barriers to Completion: Political instability

Initiation Date: April 1994

Projected End Date: August 1995

Funding Source: USAID/Port au Prince

FY '94 Budget: \$23,067

Total Budget: \$61,000

Project Title: Improving Service Delivery Practices: Development

Country(s): Worldwide
Division: Service Delivery Research FCO: 9320
Technical Monitor: Barbara Janowitz

Project Objectives: 1) To develop projects to assess the impact of interventions to improve service delivery practices, such as the introduction of service delivery guidelines; 2) to develop projects to document the extent of poor service practices; and 3) to develop projects to determine the impact of specific barriers on reducing access to family planning.

Project Description: Approximately two programmatic research projects on barriers to access will be developed. They could consist of assessments to identify specific barriers, assessments of interventions to improve practices, and cost/benefit analyses of the impact of improving service practices.

FY'94 Planned Activities: Protocols will be designed and discussed with potential investigators. Site visits will be made.

Expected Outputs, FY '94: Up to two research projects will be developed which highlight two of the three objectives listed above.

Possible Problems, Barriers to Completion: Lack of interest on the part of USAID Missions or in-country collaborating agencies.

Initiation Date: August 1993
Projected End Date: August 1995
Funding Source: USAID/W (other funding will be sought)
FY '94 Budget: \$ 62,524
Total Budget: \$100,000

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Project Title: Improving Practices among Private Physicians

Country(s): Jamaica
Division: Service Delivery Research **FCO:** 9314
Technical Monitor: Michele Villinski

Project Objective: To assess current practices of private physicians in order to help design a pilot project to involve private physicians in family planning.

Project Description: To prepare for USAID's withdrawal in 1998, the National Family Planning Board (NFPB), through the University of the West Indies (UWI) and in collaboration with the Futures Group OPTIONS II project and FHI, is conducting a mapping study of all service delivery outlets in Jamaica and an in-depth study of the service delivery practices of private physicians who offer family planning. A pilot project will be developed to help expand private sector provision of family planning. Results of the study will be used by FHI to prepare and conduct a series of contraceptive technology update seminars (CTUs) throughout Jamaica (through PRU).

Implementing Agency: University of the West Indies
Collaborating Agencies: The Futures Group, National Family Planning Board

FY'94 Planned Activities: FHI, the Futures Group and the University of the West Indies will complete the data analysis and work together to interpret the data in the Jamaican context. FHI will also participate in the dissemination seminar.

Expected Outputs, FY '94: Expected outputs include a final study report with recommendations for improving clinical practices of private doctors providing family planning and findings that will be used in the design of CTUs.

Possible Problems, Barriers to Completion: None anticipated.

Initiation Date: March 1993
Projected End Date: April 1994

Funding Source: USAID/W
FY '94 Budget: \$56,768
Total Budget: \$67,098

Project Title: Measuring Provider Adherence to the National MCH/FP Service Policy and Standards Document

Country(s): Cameroon
Division: Service Delivery Research **FCO:** 9315
Technical Monitor: Andy Thompson

Project Objective: To measure the impact of introduction of the *National Family Planning Policy and Standards Guidelines* on improving practices to maximize access to family planning.

Project Description: FHI and INTRAH are working together to reduce restrictive practices which limit access to family planning through the development, introduction and evaluation of policies, standards and guidelines in family planning. INTRAH is mainly responsible for the development of guidelines and for training to implement them, while FHI has taken the lead in dissemination of information about contraceptive technology and in measuring the impact of guidelines in service delivery practices.

The impact of policies on service delivery practices will be measured using a number of different approaches. These include data currently obtained at ten participating clinics, as well as interviews with service providers and clients. The study will focus on seven primary criteria including age and parity restrictions on provision of injectables and lab tests for hormonal methods. It is expected that the results of the data analysis will indicate two primary outcomes. 1) Among family planning service providers there should be quantifiable changes in practices. These changes should reflect the medical guidelines outlined in the MCH/FP Policy and Standards document. Reasons for non-adherence to the document will be determined through service provider interviews. 2) Adherence to the document should improve client access to family planning services and increase contraceptive use. Providers complying with the *Policy and Standards* document are expected to be associated with clinics showing an increase in the number of women receiving contraception.

Implementing Agency: The Pan-African Association of Anthropologists (PAA)
Collaborating Agency: INTRAH

FY'94 Planned Activities: With assistance from FHI, the PAA will collect and record data obtained from questionnaires and client records and conduct the data analysis.

Expected Outputs, FY '94: The final report will be disseminated to USAID, INTRAH, and the Ministry of Public Health (MOPH).

Possible Problems, Barriers to Completion: Because FHI has been requested by USAID/Cameroon to cease field activities by July 30, 1994, delay in the dissemination of the MCH/FP *Policy and Standards* document will jeopardize data collection.

Initiation Date: July 1993
Projected End Date: January 1995

Funding Source: USAID/W
FY '94 Budget: \$101,121
Total Budget: \$195,000

166

Project Title: IUD Follow-up Visits

Country(s): Mexico

Division: Service Delivery Research

FCO: 9301

Technical Monitor: David Hubacher

Project Objective: To determine whether a follow-up regimen of two scheduled visits for IUD acceptors is as safe as the four-visit regimen, and to estimate the cost savings of adopting a two-visit scheme.

Project Description: The IUD is the most commonly used temporary contraceptive method in Mexico. Since many providers ask their clients to make four follow-up visits in the first year of use, a significant portion of clinic resources is spent on appointments for perfectly healthy and satisfied users; these resources might be better spent servicing those with greater needs. This is a prospective study designed to examine costs and benefits of frequent follow-up schedules. It will compare the incidence of medical problems among an IMSS (Mexican Social Security Institute) study population of 1,713 new IUD users. Half of these users were told to return for check-ups four times in the first year and the other half were told to return only twice. All recruits have now completed one full year of use, and the costs of providing follow-up care have been estimated.

Implementing Agencies: Academia Mexicana de Investigacion Demografia Medica (AMIDEM) and IMSS

FY'94 Planned Activities: Women lost to follow-up will be contacted and interviewed, to simulate the kind of data that would have been collected if they had made a clinic visit; data collection instruments will be finalized and field work will be completed. The data will be analyzed to check some key assumptions about incidence of IUD complications. In collaboration with Mexican counterparts, the analysis plans, data processing, and interpretation of results will be completed. The final report will be written in Spanish and the production will be managed by IMSS. Plans for dissemination of study results will be finalized.

Expected Outputs, FY '94: A final report will be written and distributed. It will provide estimates for the costs of four combinations of follow-up visits: scheduled/unscheduled and normal/abnormal. In addition, the report will evaluate the safety of a two-visit schedule, and estimate the additional costs to IMSS of a four-visit scheme. The study will also determine to what extent IUD users can recognize potential problems and seek treatment on their own initiative.

Possible Problems, Barriers to Completion: None foreseen.

Initiation Date: February 1992

Projected End Date: September 1994

Funding Source: USAID/W

FY '94 Budget: \$24,733

Total Budget: \$78,000

Project Title: 1991/92 Epidemiology and Family Health Survey

Country(s): Honduras

Division: Service Delivery Research

FCO: 9719

Technical Monitor: David Hubacher

Project Objective: To estimate key national and subnational fertility and health indicators and compare these results with previous findings to better understand the national health picture.

Project Description: This is the third major cross-sectional survey in which FHI has provided technical assistance to Honduras. FHI's participation in this project is funded by USAID/Honduras; the Honduran Ministry of Health and ASHONPLAFA (Family Planning Association of Honduras) are the local institutions. Over 8,000 women aged 15-49 were interviewed on a variety of family health topics, including fertility, mortality, pre- and postnatal care, breastfeeding, other feeding practices, family planning, child health (diarrhea, acute respiratory infections, vaccination status), and knowledge about AIDS. The 1991/92 survey provides important national and subnational estimates for key health indicators; when compared with results from the previous surveys (1984 and 1987), they can help identify strengths and weaknesses in the Honduran health care system. The results of the survey show that contraceptive use has increased from 41% (1987) to 47%. Most of this increase has been in the use of traditional methods.

Implementing Agency: Ministry of Health and ASHONPLAFA

FY'94 Planned Activities: Final revisions on the English summary report will be made. Secondary analysis of the data set will be conducted to explore the rise in prevalence of traditional methods; a paper written in English will be drafted and shared with Honduran counterparts for their comments. FHI will provide additional technical assistance to support secondary analysis of other topics as requested.

Expected Outputs, FY '94: The English summary report will be printed and distributed. FHI will collaborate with Honduran counterparts and submit a paper examining the increase in traditional methods to a peer-reviewed journal. A second paper on breastfeeding trends might also be written.

Possible Problems, Barriers to Completion: None foreseen.

Initiation Date: June 1991

Projected End Date: June 1994

Funding Source: USAID/Honduras

FY '94 Budget: \$14,193

Total Budget: \$179,000

163

Project Title: Impact of Reducing IUD Follow-up Visits

Country(s): Honduras
Division: Service Delivery Research **FCO:** 9721
Technical Monitor: Andrew Thompson

Project Objective: To determine whether the current four-visit follow-up regimen for IUD users has safety advantages over a one-visit regimen; to estimate the cost savings of adopting a one-visit regimen.

Project Description: ASHONPLAFA, the Honduran IPPF affiliate, is an important provider of IUDs in Honduras. Current ASHONPLAFA norms stipulate that clients should make four follow-up visits in the first year of use; consequently, IUD follow-up visits account for 42 percent of all family planning visits. ASHONPLAFA is considering whether to reduce the number of required follow-up visits, in order to use its scarce resources to provide services to clients with greater needs.

This is a prospective study designed to examine costs and benefits of frequent follow-up schedules. It will compare the incidence of medical problems among a study population of approximately 1,800 new IUD users in two ASHONPLAFA clinics. Half of these users will be told to return for check-ups four times in the first year and the other half will be told to return only once. Method-related problem rates in the two groups will be compared, and the cost savings of adopting the less-stringent norm will be estimated.

Implementing Agency: ASHONPLAFA

FY'94 Planned Activities: The study protocol and subagreement will be written. The study design and data collection forms will be finalized, and client recruitment will commence.

Expected Outputs, FY '94: Not applicable

Possible Problems, Barriers to Completion: None

Initiation Date: February 1994
Projected End Date: November 1995

Funding Source: USAID/Honduras
FY '94 Budget: \$32,993
Total Budget: \$94,081

Project Title: Improving Service Delivery Practices in Ghana

Country(s): Ghana

Division: Service Delivery Research

FCO: 9322

Technical Monitor: Barbara Janowitz/John Stanback

Project Objectives: 1) To provide baseline data on service practices that limit access to family planning and to use this information to draft policies and guidelines for improving access to family planning, and 2) to measure the impact on access to family planning of introduction of service delivery guidelines.

Project Description: This project complements activities in PRU and is being carried out in collaboration with INTRAH. SDR activities will include the following: 1) a survey of family planning providers from different service delivery organizations (most likely including the Ministry of Health, Planned Parenthood Association of Ghana, and the Ghana Registered Midwives Association) to determine service delivery practices that limit access to family planning, 2) a survey of clients to show how access to family planning is limited by restrictive practices of providers, and 3) follow-up surveys of both providers and clients to show the impact on access of introduction of service delivery guidelines.

Implementing Agency: To be determined

Collaborating Agency: INTRAH

FY'94 Planned Activities: A sub-agreement will be drafted which will include the project design, timetable and designated sub-contracting research company. The questionnaires will be drafted, pre-tested and the data collection will be implemented. The data for the baseline surveys will be analyzed.

Expected Outputs, FY '94: Information on the extent of poor service delivery practices, why they are practiced and how they limit access to family planning will be available from the analysis.

Possible Problems, Barriers to Completion: Difficulty in obtaining in-country funding for project activities.

Initiation Date: August 1993

Projected End Date: August 1995

Funding Source: USAID/Washington for in-house costs and USAID/Accra for in-country costs

FY '94 Budget: \$76,817

Total Budget: \$150,000

170

Project Title: Introduction of an Injectable Contraceptive in an Ecuadoran Family Planning Program

Country(s): Ecuador
Division: Service Delivery Research **FCO:** 9323
Technical Monitor: John Bratt

Project Objective: To assess the clinical performance, acceptability and method continuation of DMPA, and to test the efficiency and cost-effectiveness of different systems of supply and resupply of DMPA.

Project Description: FHI is collaborating with the Population Council to carry out a comprehensive analysis of DMPA introduction through three delivery channels: 1) physicians in clinics; 2) non-physicians in clinics; and 3) community outreach workers making home visits. A total of approximately 1000 women will be recruited in clinics operated by CEMOPLAF, an Ecuadoran family planning PVO. Women will be assigned to one of three resupply groups: physician, non-physician, or community outreach worker. Acceptability, continuation, and costs of provision will be compared among the three groups. The Ecuadoran Ministry of Health will use the results of this study to decide whether and how to introduce DMPA through its extensive network of health facilities.

Implementing Agency: CEMOPLAF
Collaborating Agency: INOPAL II (Population Council)

FY'94 Planned Activities: Recruitment of clients will be completed, and follow-up of DMPA and OC acceptors will continue. Data collection forms will be developed for the study of the costs of DMPA resupply, and collection of cost data will be completed. Estimates of the costs of DMPA resupply will be calculated.

Expected Outputs, FY '94: Estimates of the costs of DMPA resupply

Possible Problems, Barriers to Completion: None

Initiation Date: April 1993
Projected End Date: December 1994

Funding Source: USAID/W, USAID/Ecuador, INOPAL II
FY '94 Budget: \$35,547
Total Budget: \$50,000

171

Project Title: Programmatic Evaluation of Norplant Introduction in Mali

Country(s): Mali
Division: Service Delivery Research FCO: 9714
Technical Monitor: Karen Katz

Project Objective: To evaluate the acceptability of Norplant as a long-term contraceptive method to Malian women.

Project Description: In February, 1993, FHI began work with the Family and Community Health Division (DSF) of the Ministry of Health, Solidarity and Aged Persons (MSSPA) to develop a research study to evaluate programmatic and clinical outcomes associated with Norplant introduction into five family planning clinics in Bamako. The results obtained in this study will be used to improve the Norplant program and assist in developing the expansion phase. Outcomes to be examined include the factors which could influence a woman's decision to accept Norplant, the quality of counseling, client satisfaction, program costs, impact on contraceptive use, experience with side effects and requests for removal.

Implementing Agency: Ministry of Health, Solidarity and Aged Persons
Collaborating Agencies: Johns Hopkins Programs for International Education in Gynecology and Obstetrics (JHPIEGO) and AVSC

FY'94 Planned Activities: The subagreement will be completed and data collection instruments finalized. Interviewers and data entry staff will be trained. The questionnaires will be pre-tested and data collection will begin.

Expected Outputs, FY '94: Information will be generated on why women are accepting Norplant and the quality of family planning counseling that they received will be provided.

Possible Problems, Barriers to Completion: None foreseen

Initiation Date: May 1993
Projected End Date: August 1995

Funding Source: USAID/Mali
FY '94 Budget: \$56,576
Total Budget: \$131,000

172

Project Title: Evaluation of Immediate Postplacental IUD Insertion

Country(s): Mali
Division: Service Delivery Research FCO: 9311
Technical Monitor: Charles Morrison

Project Objective: To promote the use of IUDs as an appropriate postpartum contraceptive method through support of provider training programs, implementation of clinical and programmatic research studies to increase IUD acceptability, development of information and educational materials, and assessment of the costs of postpartum IUD programs. This subproject assesses the clinical and programmatic impact of immediate postplacental IUD insertion introduction on contraceptive use.

Project Description: A study to assess clinical and programmatic outcomes related to immediate postplacental IUD insertion and postpartum IUD insertion before hospital discharge was initiated in Mali in 1992. Data were collected from 110 women who chose to have an IUD inserted after delivery. Similar samples of nonacceptors who delivered in the same hospital where the IUD insertions were performed were also interviewed to determine factors relevant to the acceptance of an IUD during this period.

Implementing Agency: Maternité Hamdallaye
Collaborating Agency: AVSC

FY'94 Planned Activities: Data analysis will be completed.

Expected Outputs, FY '94: The programmatic and clinical results of the study will be presented to USAID and Ministry of Health officials. A paper describing the postpartum IUD introduction programs in Mali and Kenya will be submitted for publication.

Possible Problems, Barriers to Completion: None

Initiation Date: February 1992
Projected End Date: December 1993

Funding Source: USAID/W
FY '94 Budget: \$9,386
Total Budget: \$100,000

173

Project Title: Evaluation of Postplacental IUD Insertion

Country(s): Kenya
Division: Service Delivery Research **FCO:** 9306
Technical Monitor: Cindy Waszak

Project Objective: To promote the use of IUDs as an appropriate postpartum contraceptive method through support of provider training programs, implementation of clinical and programmatic research studies to increase IUD acceptability, development of information and educational materials and assessment of the costs of postpartum IUD programs. This project assesses the clinical and programmatic impact of immediate post-placental IUD insertion introduction on contraceptive use and service delivery costs.

Project Description: A study to assess clinical and programmatic outcomes related to immediate postplacental IUD insertion and postpartum IUD insertion before hospital discharge was initiated in Nyeri, Kenya in 1992. Data were collected from 224 women who chose to have an IUD inserted after delivery. Similar samples of nonacceptors who delivered in the same hospital where the IUD insertions were performed were also interviewed to determine factors relevant to the acceptance of an IUD during this period. In a separate component of the project, the costs of delivering postpartum IUD services were compared to those for interval insertions.

Implementing Agency: Provincial General Hospital of Nyeri
Collaborating Agency: AVSC

FY'94 Planned Activities: Data analysis will be completed.

Expected Outputs, FY '94: A paper describing the clinical and programmatic results of the postpartum IUD introduction programs in Mali and Kenya will be submitted for publication.

Possible Problems, Barriers to Completion: None foreseen.

Initiation Date: October 1991
Projected End Date: December 1993

Funding Source: USAID/W
FY '94 Budget: \$ 3,102
Total Budget: \$139,000

574

Project Title: Introduction of DMPA in Latin America

Country(s): To be determined

Division: Service Delivery Research

FCO: 9334

Technical Monitor: John Bratt

Project Objective: To conduct programmatic research and dissemination activities which support the introduction of DMPA in selected Latin American countries.

Project Description: By mid-1994, USAID expects to be able to make DMPA widely available throughout the developing world. Few programs in Latin America have had experience with the method, and appropriate, efficient delivery systems for the method may not exist. This project will bring together FHI and the Population Council, whose complementary skills and resources will enable the two organizations to collaborate on research and dissemination efforts ranging from improving service practices to sustainability and quality of care.

Implementing Agency: To be determined

Collaborating Agencies: The Population Council; one or more service delivery CAs such as IPPF, AVSC, Pathfinder or JHPIEGO.

FY'94 Planned Activities: A half-day meeting will be organized to coincide with the 1994 CAs meeting in February. The purposes of this meeting will be to establish programmatic research priorities for DMPA introduction in Latin America, and to enlist the cooperation of one or more of the service delivery CAs. Details of FHI/Population Council collaboration will be finalized, and the first programmatic research study will be designed.

Expected Outputs, FY '94: Research priorities will be set, and the first study protocol and subagreement will be written.

Possible Problems, Barriers to Completion: Availability of DMPA, interest of service delivery CAs.

Initiation Date: December 1993

Projected End Date: September 1995

Funding Source: USAID/W, Mission add-ons

FY '94 Budget: \$53,482

Total Budget: \$200,000

176

Project Title: Programmatic Research on Introduction of DMPA in the Philippines

Country(s): The Philippines
Division: Service Delivery Research FCO: 9310
Technical Monitor: Michele Villinski

Project Objective: To develop a strategy for the introduction of DMPA use in the Philippines, and to assist with the introduction.

Project Description: In August 1993, USAID/Manila and the Philippine government requested FHI's assistance in the development of a strategy to introduce DMPA in their country. A team of three FHI staff traveled to the Philippines and developed a strategy document in collaboration with Pathfinder. This project will fund programmatic research to facilitate the introduction of DMPA in the Philippine national family planning program. Potential topics for research include quality of care in clinic-based provision of DMPA and quality of care in social marketing of DMPA.

Implementing Agency: To be determined

FY'94 Planned Activities: Staff from FHI will work with the Department of Health to identify key research issues relating to DMPA introduction and to develop studies. FHI staff will travel to the Philippines to help design the research studies and will write subagreements and provide technical assistance in survey design and interviewer training as necessary.

Expected Outputs, FY '94: Expected outputs include one or two research studies to examine the quality of care provided during introduction of DMPA.

Possible Problems, Barriers to Completion: Research activities will depend on the pace of introduction of DMPA in the Philippines.

Initiation Date: July 1993
Projected End Date: August 1995

Funding Source: USAID/W
FY '94 Budget: \$30,957
Total Budget: \$100,461

177

Project Title: Impact of Norplant Expansion

Country(s): Haiti

Division: Service Delivery Research

FCO: 9715

Technical Monitor: Andy Thompson

Project Objective: To evaluate the impact of Norplant expansion on program costs and contraceptive use in Haitian family planning programs. This study will assess the economic advantages and disadvantages of introducing this new method given the various environments in which services are delivered.

Project Description: FHI and a collaborating Haitian research organization will conduct study activities related to the impact of Norplant expansion on contraceptive use and its costs. The following research activities are proposed:

- 1) Impact of Norplant introduction on the demand for other methods of contraception. Patterns of method acceptance at facilities where Norplant is available will be compared to method acceptance at facilities where Norplant is not available.
- 2) Determinants of the client's decision to choose. Norplant acceptors will be interviewed at a sample of facilities offering this method. The interviews will focus on the factors that influence decisions to accept the method.
- 3) Costs of providing Norplant. The marginal costs of providing Norplant and other methods at each facility will be measured. Cost estimates will be used to determine (a) the incremental costs of providing Norplant compared with other methods; and (b) how and why the costs of providing Norplant differ across the facilities providing the method.

Implementing Agency: To be determined

FY'94 Planned Activities: FHI will identify a Haitian research organization, develop a research protocol, finalize the subagreement, and begin data collection.

Expected Outputs, FY '94: Research protocol developed, subagreement finalized, and data collection instruments created and pre-tested.

Possible Problems, Barriers to Completion: Political instability

Initiation Date: April 1994

Projected End Date: August 1995

Funding Source: USAID/Port au Prince

FY '94 Budget: \$21,805

Total Budget: \$61,000

178

Project Title: Family Planning and STD Service Integration

Country(s): Worldwide

Division: Service Delivery Research

FCO: 9316

Technical Monitor: Laurie Fox

Project Objective: This project funds the development of projects on family planning and STD integration until country-specific projects are developed, and initiated. Projects may include one of the following objectives: 1) to determine the appropriate level of integration of Family Planning and STD/HIV services at service delivery points; 2) to develop methodology to assist family planning service delivery points to assess the risk level of their clientele; 3) to evaluate the usefulness of the syndromic approach for STD diagnosis in family planning settings. 4) to assess the costs of adding STD services to family planning programs.

Project Description: It is anticipated that two programmatic research projects on family planning and STD service integration will be developed. They may include data collection to determine the extent of existing STD service provision in family planning programs, testing STD risk assessment methodologies; and cost-benefit analyses.

Implementing Agency: To be determined.

FY'94 Planned Activities: Two projects will be developed and initiated.

Expected Outputs, FY '94: Initiation of two new projects in family planning and STD service integration research which highlight two of the three objectives listed above.

Possible Problems, Barriers to Completion: Lack of interest on the part of USAID Missions or in-country collaborating agencies.

Initiation Date: August 1993

Projected End Date: August 1995

Funding Source: USAID/W (other funding will be sought for projects)

FY '94 Budget: \$54,735

Total Budget: LOP budget not yet determined

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3. Policy and Research Utilization

The Policy and Research Utilization Division ensures that the work of FHI and the latest important research findings in reproductive health are made available to policymakers, program managers and service providers in the field. Unless current information is made available and utilized in programs it is of little use. For this purpose, FHI has developed a strong in-house capacity in publications and media, educational design, and health communication and training. In doing this work, the Policy and Research Utilization Division works closely with all divisions at FHI.

Currently, FHI's work in this area falls into four major categories:

■ Information Dissemination

Activities in this area focus on the dissemination of information on reproductive health to the field and collaborating organizations through a quarterly bulletin, Network, published in French, Spanish, English and Russian; a new working paper series; and reprints of articles by FHI staff and collaborators. The priority topics for FY'94 dissemination include injectables, costing and sustainability, improving access to contraception, family planning and STDs, and barrier methods. In FY'94, the Information Dissemination Unit will expand the circulation of Network, disseminate information through policy forums such as the International Conference on Population and Development, and provide timely information on controversial issues in reproductive health to service providers, policy makers, and the media.

■ Health Communication and Training

One of the greatest challenges facing the field of reproductive health today is how to translate and transfer knowledge, information, and related skills into action. The Health Communication and Training Program (HCTP) tries to address those challenges through an integrated and comprehensive array of services available to FHI divisions and other collaborating organizations working in the field of family planning, reproductive health, and STD prevention. HCTP provides training and health communication assistance first by designing, implementing, and evaluating training programs that emphasize participatory, competency-based techniques and skills acquisition. Assistance to collaborators developing targeted, culturally-appropriate educational materials on various reproductive health topics utilizes a multi-phase approach that emphasizes audience research and field testing. In collaboration with governments and private organizations, HCTP plans integrated communication programs. These communication programs are multifaceted and capitalize on a range of innovative strategies including peer education, mass media, interpersonal communication and outreach. Our approach is based on assessment of local needs and emphasizes collaboration in order to ensure long-term sustainability.

■ Improving Service Practices

During much of its history, FHI has been committed to improving client access to family planning. In the past two years, that commitment has been reinforced by USAID's desire for FHI to take a lead in the movement to increase client access through the improvement of service practices that impede delivery of quality contraceptive services. Specifically, PRU has allocated resources to support this continued effort. Below is a description of principal areas of activity.

- 1) PRU is engaged in the development of a series of contraceptive technology modules for use by family planning colleagues at in-service and/or pre-service training events. These packaged informational modules contain slides, narratives, scientific articles, audience handouts, and a fact sheet. Created for a wide provider audience, these tools are intended to update family planning workers' knowledge of methods and issues.
- 2) PRU is working in collaboration with FHI's Service Delivery Research Division and INTRAH to examine the impact that national service delivery guidelines have on provider practices. Working jointly in Cameroon and Ghana, FHI and INTRAH hope to provide valuable information about the role of national service policies and standards on improving service practices and increasing clients' access to family planning.
- 3) Improving service practices involves updating providers and policymakers about current scientific information regarding service provision and contraceptive methods. PRU has added a conference coordinator to the division to help meet the needs of various demands to conduct educational activities.

■ Policy

PRU works to ensure that reproductive health research findings are made available to policymakers through conferences, workshops, and publications. It also supports direct technical assistance to ministries and governments in policy development in research and family planning service delivery.

FY 94 Program, Objectives, and Expected Outputs

Priorities for Policy and Research Utilization under the Cooperative Agreement in FY'94 continue to emphasize the utilization of the latest information from research results to strengthen population programs. This work will include both written dissemination through publications and educational materials and training and technical assistance to developing world collaborators. In FY'94, PRU will work closely with other cooperating agencies including the Population Council, WHO, and IPPF.

The projects, ongoing and new, which the Policy and Research Utilization Division will implement in FY'94 are listed below:

■ **Information Dissemination**

Continuing Projects:

- English Network
- Network en espanol
- Network en français
- Russian Network
- Information Dissemination
- Publications Catalog
- Library & Information Services
- Graphic Image Database Development

■ **Health Communication and Training**

Continuing Projects:

- Health Communication and Training: Development
- East and Southern Africa Editors Seminar
- International Workshop on Postpartum & Postabortion Contraception

New Projects:

- Postpartum and Postabortion Family Planning
- Journalists Training Workshop
- Interagency Working Group on Barrier Methods
- Health Communication and Training for Contraceptive Introduction in the Philippines
- Norplant Information, Education and Communication (IEC)/Training in Haiti

■ **Improving Service Practices**

Continuing Projects:

- Improving Service Practices: Development
- Contraceptive Technology Update Meetings: Development
- Contraceptive Technology Update Modules Series
- Expert Slide Sets: CTUs
- Latin America Regional Experts Meeting: Improving Service Practices
- Asia Regional Experts Meeting: Improving Service Practices
- Activities to Improve Service Practices in Jamaica
- Service Guidelines Dissemination Workshops in Cameroon
- FHI Fellow - USAID/W

New Projects:

- Consensus Building Activities in Ghana

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■ **Policy**

Continuing Projects:

- Policy Implementation

New Projects:

- MIS Workshop in Nepal

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Project Title: English Network

Country(s): Worldwide

Division: Policy and Research Utilization

FCO: 3502

Technical Monitor: William Finger

Project Objective: To disseminate important research results and provide timely information on contraceptive technologies and reproductive health issues to family planning providers, health policy makers and developing country media.

Project Description: Through this quarterly bulletin, FHI distributes the latest scientific and programmatic information on reproductive health issues in a timely manner to readers around the world. Articles synthesize a broad range of information in an attractive, easy-to-understand format, involving overseas journalists and international experts as contributors. English Network is translated into French and Spanish four times a year, yielding a combined subscription list of more than 40,000. Many more copies are distributed for special needs, and translation projects in other languages are also undertaken.

FY'94 Planned Activities: Publication and distribution of four issues of Network, 24-36 pages each, to inform physicians, researchers, ministries, health-care providers, developing country media and others on new contraceptive technologies, women and development, family planning and STDs, maternal health, and contraceptive introduction of barrier methods, injectables and other methods. About 20,000 of each will be printed, with about 2,000 going to media representatives worldwide. Increased numbers may be printed for targeted purposes as needed, such as the International Conference on Population and Development.

Expected Outputs, FY '94: Four issues of Network will be published and disseminated through many channels so as to maximize the impact on policies and practices. When translated, an estimated 200,000 copies in all three languages will be distributed.

Possible Problems, Barriers to Completion: None anticipated

Initiation Date: August 1990

Projected End Date: July 1995

Funding Source: USAID/W

FY '94 Budget: \$358,114

Total Budget: \$1,278,000

1484

Project Title: Network en español

Country(s): Spanish-speaking/Worldwide
Division: Policy and Research Utilization
Technical Monitor: Marina McCune

FCO: 3528

Project Objective: To provide current and comprehensive information in a non-technical but scientifically credible and timely way to health providers, ministries, USAID Missions, policymakers, and media in Latin America and the Caribbean.

Project Description: To produce and disseminate a quarterly publication of 32-36 pages in Spanish on FHI's reproductive health and family planning research.

FY '94 Planned Activities: Production of four issues of volume 9 of Network en español on: (1) Adolescents, (2) Family Planning and Maternal Health, (3) Family Planning and STDs, and (4) Women and Family Planning with a print run of 25,000 copies. Press releases on each issue will be sent to journalists in Latin America. Work to increase circulation of the bulletin will continue.

Expected Outputs, FY '94: Publication and distribution of four issues of Network en español, resulting in an increased flow of accurate and timely information to readers in Latin America and the Caribbean. More than 16,000 copies of each issue will be sent to regular subscribers and copies will be available to USAID Missions and health agencies upon request. Press releases on each issue will be sent to journalists in Latin America, resulting in greater news coverage of the family planning topics covered in Network en español.

Possible Problems, Barriers to Completion: none

Initiation Date: August 1990
Projected End Date: July 1995

Funding Source: USAID/W
FY '94 Budget: \$211,751
Total Budget: \$642,000

Project title: Network en français

Country(s): French-speaking/Worldwide

Division: Policy and Research Utilization

FCO: 3550

Technical Monitor: Mary Bean

Project Objective: To provide current and comprehensive information in a non-technical but scientifically credible and timely way to health providers, ministries, USAID Missions, policymakers, and media in francophone developing countries.

Project Description: FHI produces a quarterly magazine of 32-36 pages on reproductive health and family planning for francophone health providers, policymakers, USAID Missions, ministries and news media around the world.

FY '94 Planned Activities: Production of four issues of Volume 9 of Network en français on: (1) Adolescents, (2) Family Planning and Maternal Health, (3) Family Planning and STDs, and (4) Women and Family Planning. Articles used in each issue will require translation, careful editing, production and distribution. Press releases in French will be disseminated to francophone media with each issue.

Expected Outputs, FY '94: Publication and distribution of four issues of Network en français, resulting in an increased flow of accurate and timely information to readers in francophone Africa and Haiti. More than 11,500 copies of each issue will be sent to regular subscribers and copies will be available to USAID Missions and health agencies upon request. Press releases on each issue will be sent to francophone journalists, resulting in greater news coverage of the family planning topics covered in Network en français.

Possible Problems, Barriers to Completion: none expected

Initiation Date: August 1990

Projected End Date: July 1995

Funding Source: USAID/W

FY '94 Budget: \$178,212

Total Budget: \$542,000

186

Project Title: Russian Network

Country: Russian Speaking/Worldwide

Division: Policy and Research Utilization

FCO: 3513

Technical Monitor: Beverly Tucker

Project Objective: To produce a 36-page issue of FHI's reproductive health and family planning bulletin, Network, in Russian. The Russian issue will provide current comprehensive information in a non-technical, but scientifically credible way to health providers, ministries, media, policymakers and non-government organizations in the Former Soviet Union.

Project Description: Current and accurate material in Russian on family planning is scarce but in demand throughout the Former Soviet Union. The translation of Network into Russian will serve as a resource for organizations and institutions working in the area of reproductive health. In FY'94, funds will be used to translate, print and distribute 20,000 copies of a second issue of Network in Russian and bulk mail copies of the first issue.

FY'94 Planned Activities: The first issue of Network in Russian was on improving access to contraceptive use and will be distributed during FY'94. The topic of the second issue will be determined.

Expected Outputs, FY '94: Bulk mailing to the Former Soviet Union of the first issue will be completed in FY'94. The second issue will be translated and printed. Bulk mailing of the second issue to the Former Soviet Union will also be completed.

Possible Problems, Barriers to Completion: Difficulty in finding an appropriate translator or a poor initial translation which would require significant review of publication might delay completion. Reduction of funding.

Initiation Date: June 1993

Projected End Date: July 1995

Funding Source: USAID/W

FY '94 Budget: \$35,623

Total Budget: \$116,000

Project Title: Information Dissemination

Country(s): Worldwide

Division: Policy and Research Utilization

FCO: 3505

Technical Monitor: Elizabeth Robinson

Project Objective: To increase acceptance of family planning by increasing knowledge of family planning research and service delivery personnel, policymakers and media, directly and through funding agencies, especially USAID/W and USAID Missions.

Project Description: FHI information programs: 1) provide information on recent findings to health care professionals; 2) respond to controversies and disseminate information to providers, USAID Missions, and media; 3) encourage developing country news media to cover reproductive health issues; and 4) support development of information dissemination capacity among reproductive health agencies in priority countries.

Collaborating Agencies: FHI works on information dissemination activities with numerous in-country organizations, international health agencies, and USAID collaborating agencies.

FY'94 Planned Activities: Activities to be carried out under this program include: publication of the FY'94 FHI Working Paper Series on contraceptive technologies, organization of three media panels in conjunction with CTUs, rewriting of Network articles on contraceptive technology for placement in other publications, dissemination of recent contraceptive technology research findings and contraceptive introduction initiatives, management of overall information programs, and marketing of FHI's technical assistance capacity in information dissemination targeted at health providers. Also, expansion of media and provider mailing lists in all languages will continue.

Expected Outputs, FY '94: Two information campaigns and targeted mailings on family planning topics targeted at health providers, USAID Missions, ministries of health, and donor agencies; three media panels in conjunction with CTUs; placement of 5-10 articles on contraceptive technology in major news magazines in developing countries; distribution in three languages of 20 press releases; and publication of three brochures on information programs.

Possible Problems, Barriers to Completion: none

Initiation Date: August 1990

Projected End Date: July 1995

Funding Source: USAID/W

FY '94 Budget: \$205,119

Total Budget: \$921,000

186

Project Title: Publications Catalog

Country: Worldwide

Division: Policy and Research Utilization

FCO: 3521

Technical Monitor: Marguerite Rogers

Project Objective: To publish and distribute a catalog of current FHI scientific publications in order to facilitate dissemination of research findings on reproductive health.

Project Description: This publication provides a listing of current FHI scientific publications. FHI publications described in the catalog are offered to an audience of about 10,000 health care providers, USAID Missions, ministries and researchers. Publications listed include journals, articles, monographs, and the translation series articles.

FY'94 Planned Activities: Staff will compile information for the 1994 catalog on a PROCITE database, edit and typeset the material and print approximately 10,000 copies of the catalog.

Expected Outputs, FY '94: 10,000 copies of the 1994 Publications Catalog.

Possible Problems, Barriers to Completion: None

Initiation Date: August 1990

Projected End Date: July 1995

Funding Source: USAID/W

FY '94 Budget: \$21,255

Total Budget: \$66,000

189

Project Title: Library and Information Services

Country: United States
Division: Policy and Research Utilization **FCO:** 3560
Technical Monitor: William Barrows

Project Objective: To provide information services to FHI staff, consultants, visitors and projects; to assist in the dissemination of information on contraceptive research.

Project Description: This project operates the FHI Library, provides information services to FHI staff, investigators and others; and supports the dissemination of information on contraceptive research.

FY'94 Planned Activities: Staff will complete conversion of records from the Library of Congress and the National Library of Medicine to an in-house computerized database. Cataloging guidelines for non-standard publications will be completed. A users' group of FHI staff will be included in planning and policy making for company-wide implementation. A network version of PROCITE will be installed. A plan for integrating PROCITE databases and CD-ROM databases with the Online Public Access Catalog (OPAC) will be developed. FHI Serials list and the Selected List of Journals for Population Libraries will be updated. Staff will finalize procedures for proposals, review and recording papers in the new Working Paper series. Maintenance and development of Library collections and provision of services to FHI staff will continue.

Expected Outputs, FY '94: The retrospective conversion of FHI monograph cataloging records will be largely completed. All FHI staff will have access to the OPAC. PROCITE database management capabilities will be enhanced. Library resource guides will be updated. Library and information services will be provided to FHI staff, USAID/W, investigators, other cooperating agencies, and others.

Possible Problems, Barriers to Completion: Insufficient staff may slow conversion process. Software developed by vendor for integration of databases with library OPAC may not be completed or may not be available.

Initiation Date: August 1990
Projected End Date: July 1995

Funding Source: USAID/W
FY '94 Budget: \$270,738
Total Budget: \$1,153,000

190

Project Title: Graphic Image Database Development

Country: United States
Division: Policy and Research Utilization **FCO:** 3511
Technical Monitor: William Barrows

Project Objective: To develop an efficient, effective means to store, organize, transmit and reproduce graphic images such as slides for use in training and scientific presentations.

Project Description: This project explores the feasibility of developing a database to store, organize and retrieve graphic images. The project team has reviewed readily available hardware and software to improve access to graphic images such as slides, charts and illustrations produced to support Contraceptive Technology Update seminars, the initiative for improving service practices and other training/information dissemination activities.

FY'94 Planned Activities: The software will be tested and installed on a computer that is generally accessible. Additional hardware and the network version of the software will be purchased. Relevant data elements will be defined and a record form developed. A strategy for implementation will be designed, including additional staffing needs. After a sample database is input, revisions made and demonstrations conducted, FHI graphic databases will be input.

Expected Outputs, FY '93: Completion of testing. Demonstrations of a sample database. A strategy for general implementation with FHI staff, including hardware purchases and staffing needs. Input of highest priority images and descriptive records.

Possible Problems, Barriers to Completion: None

Initiation Date: June 1993
Projected End Date: July 1995

Funding Source: USAID/W
FY '94 Budget: \$32,960
Total Budget: \$64,000

Project Title: Health Communication and Training: Development

Country(s): Worldwide
Division: Policy and Research Utilization **FCO:** 3011
Technical Monitor: LaHoma Smith Romocki

Project Objective: To translate scientific information and research findings into educational and training programs.

Project Description: The Health Communication and Training Unit develops and implements health communication and training activities, specifically 1) national strategies for the introduction of contraceptive methods, 2) training of ministry officials and representatives from nongovernmental organizations on contraceptive methods and other reproductive health issues, and 3) development of educational materials and training manuals designed for specific target audiences on a variety of reproductive health issues.

Collaborating Agencies: FHI works closely with many U.S., international, and host country organizations in the design and implementation of activities.

FY'94 Planned Activities: The Health Communication and Training Unit will expand the reproductive health materials and training manuals database, provide technical assistance in the development of educational materials for health care providers and users of family planning methods, manage the overall health communication and training programs, develop two national level strategies for the introduction of contraceptive methods, and provide technical assistance in the design and implementation of four CTU seminars.

Expected Outputs, FY '94: A comprehensive list of reproductive health educational materials and training manuals will be completed, two educational materials and two training manuals targeting health care providers and users of family planning services will be produced and distributed, two national communication programs will be developed, and staff participation in four CTUs completed.

Possible Problems, Barriers to Completion: None

Initiation Date: January 1993
Projected End Date: July 1995

Funding Source: USAID/W
FY '94 Budget: \$86,539
Total Budget: \$214,000

YR

Project Title: East and Southern Africa Editors Seminar

Country(s): Regional (East and Southern Africa)
Division: Policy and Research Utilization FCO: 3201
Technical Monitor: Julie Beamish

Project Objective: To improve news coverage of reproductive health in East and Southern Africa by increasing editors' awareness of the importance of covering reproductive health and motivating them to make a commitment to improve and increase this coverage.

Project Description: The seminar, organized in collaboration with the African Council on Communication Education (ACCE), will take place November 9-12, 1993 in Naivasha, Kenya. Twenty-two participants will represent nine countries: Botswana, Eritrea, Kenya, Malawi, Swaziland, Tanzania, Uganda, Zambia and Zimbabwe. Work in the seminar will include establishing the need for reproductive health coverage, evaluating coverage of reproductive health, and defining the role of the journalist in reproductive health. Approximately 12 reproductive health professionals will serve as resource persons for the workshop.

Implementing Agency: African Council for Communication Education, Kenya Chapter

FY'94 Planned Activities: The editors seminar will be held in November 1993. Based on needs of seminar participants, follow-on activities will be planned and conducted, including needs assessments of media and health sector reporting in specific countries in the region.

Expected Outputs, FY '94: Editors will be made aware of and become committed to reproductive health issues. This will increase the dissemination of health information to the public, policymakers and the health sector; long-term capacity for media to report on health and work with the health sector will also be strengthened. A regional committee will be formed to monitor and evaluate reproductive health coverage.

Possible Problems, Barriers to Completion: Sufficient funding for follow-on activities.

Initiation Date: June 1993
Projected End Date: July 1994

Funding Source: USAID/W
FY '94 Budget: \$58,516
Total Budget: \$65,000

193

Project Title: International Workshop on Postpartum and Postabortion Contraception

Country(s): Regional (Latin America)
Division: Policy and Research Utilization **FCO: 3019**
Technical Monitor: Julie Beamish

Project Objective: In 1994, the objectives are to disseminate the findings of the July 1993 Quito Workshop and to evaluate the national strategies for integrating postpartum and postabortion family planning in the reproductive health services of the Latin American countries that were represented at the Quito Workshop.

Project Description: FHI and PAHO conducted a 4-day workshop in Quito, Ecuador, in July 1993. Eighty-seven participants, including the two facilitators/presenters from FHI, Dr. Mora of PAHO and several presenters from around the region -- altogether representing 13 Latin American countries and the U.S. -- attended the workshop. FHI and PAHO identified nine countries as having the greatest need in the region to develop or improve postpartum and postabortion family planning services. FHI will design follow-through programs in up to two countries represented in the workshop; these programs could serve as models to be used and adapted by the other countries and agencies that were at the workshop.

Collaborating Agencies: PAHO, AVSC, IPAS, JHPIEGO, UNFPA, the Population Council and Pathfinder International.

FY'94 Planned Activities: FHI will help review, revise and disseminate the workshop proceedings; write and disseminate guidelines based on the workshop findings; assess needs for and possibilities of following through the work started at the workshop; and write a plan for long-term follow-through and evaluation.

Expected Outputs, FY'94: Proceedings from the workshop; published written guidelines based on the workshop proceedings; written plan for following through and evaluating the workshop.

Possible Barriers to Completion: Limited funding.

Initiation Date: January 1993
Projected End Date: September 1995

Funding Source: USAID/W
FY '94 Budget: \$25,612
Total Budget: \$92,000

194

Project Title: Postpartum and Postabortion Family Planning

Country(s): Honduras and/or Paraguay

Division: Policy and Research Utilization

FCO: 3218

Technical Monitor: Julie Beamish

Project Objective: Provide technical assistance in the implementation and evaluation of national strategies designed to integrate postpartum and postabortion family planning in the existing reproductive health services of Honduras and/or Paraguay.

Project Description: This follows through the International Workshop on Postpartum and Postabortion Family Planning held in Ecuador in July 1993. FHI plans to help finalize up to two national strategies that the country teams developed at the workshop, implement various components of those strategies (for example, in training, communication and information dissemination), and evaluate the strategies. FHI's follow-through program can serve as a model to be adapted by the other countries and international agencies represented at the Ecuador workshop. Of the countries represented in Ecuador, Paraguay has expressed the greatest interest in and need for technical assistance and support from FHI; the team also represents local institutions with which FHI could collaborate to implement follow-through activities. The Honduran team has already begun implementation of the country strategy with assistance from other agencies.

Implementing Agency: Ministry of Public Health and Social Welfare of Paraguay, and/or Instituto Hondureño de Seguridad Social.

Collaborating Agencies: PAHO, UNFPA.

FY'94 Planned Activities: FHI plans to help finalize country strategies, assess needs for technical assistance in specific program (strategy) components, identify in-country resources and donors for implementation of components, write implementation workplan, provide technical assistance as needed and appropriate, and evaluate strategies.

Expected Outputs, FY '94: At least one country strategy will have been finalized, needs for technical assistance in implementation identified, an implementation workplan written, local resources and donors named, health care providers and trainers trained, appropriate materials produced, and policy guidelines developed and disseminated.

Possible Problems, Barriers to Completion: Limited funding

Initiation Date: October 1993

Projected End Date: July 1995

Funding Source: USAID/W

FY '94 Budget: \$72,449

Total Budget: \$158,000

Project Title: Journalists Training Workshops

Country(s): Asia, Africa and/or Latin America
Division: Policy and Research Utilization **FCO:** 3220
Technical Monitor: Julie Beamish

Project Objective: To increase and improve news coverage of reproductive health in Asia, Africa and/or Latin America.

Project Description: Up to three training workshops to increase journalists' knowledge of reproductive health; build their skills for reporting on reproductive health topics in ways that are in-depth, accurate, relevant in the local context, and timely; and foster their commitment to covering reproductive health more extensively and effectively. In addition, these workshops will bring in leaders from the reproductive health sector to begin to establish long-term working relationships with the news media.

This project is part of FHI's ongoing journalism training program. The workshops that are tentatively planned for FY '94 include a joint workshop for health professionals and journalists in Bangladesh and a workshop for reporters in East or Southern Africa (to follow through the East and Southern African Editors Seminar on News Coverage of Reproductive Health).

Collaborating Agencies: WHO/HRP, IPPF and JHU/PCS (Bangladesh), ACCE (Africa), PAHO and the Mexican Ministry of Health.

FY'94 Planned Activities: FHI will conduct pre-workshop needs assessments, design workshop objectives and curricula, facilitate and evaluate workshops, and plan follow-through programs.

Expected Outputs, FY '94: Up to 75 journalists will have the knowledge and skills to write effectively on reproductive health issues. This will increase the dissemination of up-to-date information on reproductive health to the public, policymakers and the health sector through the news media. In addition, three to six local communication and/or reproductive health professionals will have acquired the skills to conduct similar training independently of FHI.

Possible Problems, Barriers to Completion: Concurrence by USAID Missions is not certain. The number of workshops undertaken will depend on the availability of funds.

Initiation Date: October 1993
Projected End Date: September 1994

Funding Source: USAID/W
FY '94 Budget: \$114,563 (for up to three workshops)
Total Budget: \$114,563

196

Project Title: Interagency Working Group on Barrier Methods

Country(s): Multiple
Division: Policy and Research Utilization **FCO:** 3225
Technical Monitor: Susan Palmore

Project Objective: To coordinate with other organizations in the development of studies to assess the acceptability and efficacy of the diaphragm as a contraceptive method in populations where its use has been limited or unavailable.

Project Description: At a recent meeting organized by WHO/HRP, strong support was expressed for promoting fertility regulation methods which: 1) are user-controlled; 2) provide protection against STDs including HIV; 3) have minimal or no side effects; and 4) foster knowledge about one's body. Specifically, one of the main recommendations made by women's health advocates was that more research needs to be conducted on the (re)introduction of barrier methods with emphasis on user and provider perspectives on safety, efficacy and acceptability of barrier contraception. Following this meeting, an interagency working group on barrier methods identified the diaphragm as the available, female-controlled method which most closely met these criteria.

An interagency group is designing a prospective study that will follow, for a minimum of 12 months, a group of adequately counseled women who have chosen to use the diaphragm as their primary form of contraception. The study is intended to identify the factors influencing initial and continued acceptability, determine the service delivery requirements, and document the use effectiveness of the diaphragm in several developing country settings. In addition, the study will gather information on reasons for discontinuation, method switching and use practices. Each agency will conduct studies in specified countries. FHI's CUE Division will be responsible for implementation of the study in one or more countries. PRU staff will coordinate activities with other members of the interagency working group and will develop and implement training and IEC activities related to the study.

Collaborating Agencies: WHO, The Population Council

FY'94 Planned Activities: Study documents will be finalized; study sites will be identified, investigators and study staff will be trained and the study will be initiated and monitored. Training and IEC plan will be completed.

Possible Problems, Barriers to Completion: Poor acceptance of diaphragm by clinic clients could lead to difficulty in recruitment and high study discontinuation.

Initiation Date: October 1993
Projected End Date: July 1995

Funding Source: USAID/W
FY '94 Budget: \$50,958
Total Budget: \$107,000

197

**Project Title: Health Communication and Training for
Contraceptive Introduction**

Country: Philippines
Division: Policy & Research Utilization **FCO:** 3529
Technical Monitor: Anne Phillips

Project Objective: To provide technical assistance to the Philippine Department of Health, Family Planning Service (DOH/FPS) on the development of information, education and communication and training materials for the introduction of DMPA.

Project Description: FHI will assist in the planning and implementation of a 2-day DMPA workshop at which trainers from the DOH and local non-governmental organizations will receive an orientation on DMPA and develop a 2-day training design on DMPA. This training design will be used by these trainers to train both DOH and NGO service providers, following a pre-test in two regions of the country.

FY 94 Planned Activities: Plan and implement workshop for DOH staff on materials development; develop and review training manual for use by DOH.

Expected Outputs FY'94: Completion of workshop and training manual

Initiation Date: October 1993
Project End Date: January 1994

Funding Source: USAID/W
FY'94 budget: \$12,332
Total budget: \$12,332

198

Project Title: Norplant IEC/Training

Country: Haiti
Division: Policy and Research Utilization FCO: 3721
Technical Monitor: Anne L. Phillips

Project Objective: To increase awareness and access to Norplant through effective IEC and training activities.

Project Description: Because of initial success with Norplant introduction activities and in response to increasing demand among potential family planning clients, FHI will provide technical assistance to the Institut Haitien de Santé Communautaire to reinforce Norplant IEC and training activities. Training activities will focus on increasing the number of physicians, nurses and midwives trained to provide Norplant services, and the development of a training of trainers program that will ensure continued expansion of services. IEC activities will include the development of culturally appropriate client education materials in Creole targeting the general public, potential acceptors and current users.

Implementing Agency: Institut Haïtien de Santé Communautaire.

FY'94 Planned Activities: In collaboration with appropriate medical experts, FHI staff will adapt current clinical guidelines for Norplant service provision, including counseling; develop IEC materials for health care providers, clients, and their partners; develop and implement training programs in both clinical and counseling services for health care providers.

Expected Outputs, FY '94: Clinical guidelines developed; IEC materials in Creole developed and disseminated; 20 physicians and 40 midwives/nurses trained in Norplant service provision; training of trainers program developed for midwives, nurses and community health workers.

Possible Problems, Barriers to Completion: Unstable political situation

Initiation Date: October 1993
Projected End Date: July 1995
Funding Source: USAID/Port-au-Prince
FY '94 Budget: \$74,186
Total Budget: \$143,000

Project Title: Improving Service Practices: Development

Country(s): Worldwide
Division: Policy and Research Utilization **FCO:** 3021
Technical Monitor: Susan Palmore

Project Objective: To improve contraceptive service practices in developing countries; and to encourage collaborating agencies to include a focus on improving access to contraception.

Project Description: Funds will be used to develop opportunities for FHI to conduct work in developing countries, to participate in USAID/W working groups and other meetings and for the FHI working group aimed at improving contraceptive services.

Collaborating Agencies: AVSC, JHPIEGO, INTRAH, Futures Group, The Population Council, PCS, Pathfinder, IPPF

FY'94 Planned Activities: Participate in USAID Steering Committee and related working groups and meetings; regular meetings of FHI working group on Improving Access to Contraception and development of two new activities; travel to countries, as yet unidentified.

Expected Outputs, FY '94: At least two project opportunities will be identified and FHI strategy will be revised.

Possible Problems, Barriers to Completion: None

Initiation Date: October 1992
Projected End Date: July 1995

Funding Source: USAID/W
FY '94 Budget: \$55,768
Total Budget: \$353,000

200

Project Title: Contraceptive Technology Update Meetings:
Development

Country(s): Worldwide
Division: Policy and Research Utilization FCO: 3208
Technical Monitor: Lynn Krueger Adrian

Project Objective: To provide technical assistance to host countries or regions that wish to conduct educational/training events on issues relating to reproductive health, population, and family planning.

Project Description: FHI will work to identify regional and country needs and investigate opportunities to assist in the logistical, administrative and financial facilitation of CTU meetings.

Implementing Agency: To be determined.
Collaborating Agencies: To be determined, as appropriate.

FY '94 Planned Activities: FHI plans to use these funds to collaborate with INTRAH and JHPIEGO in conducting a seminar in francophone West Africa on improving client access to contraception. This activity will take place in the spring of 1994. In addition, funds will be used to enhance a series of CTUs being planned for Jamaica.

Expected Outputs, FY '94: One to two additional CTU meetings.

Possible Problems, Barriers to Completion: None

Initiation Date: October 1993
Projected End Date: September 1994

Funding Source: USAID/W
FY '94 Budget: \$98,748
Total Budget: \$98,748

201

Project Title: Contraceptive Technology Update Modules Series

Country(s): Worldwide (English, Spanish, French)
Division: Policy and Research Utilization **FCO:** 3210
Technical Monitor: Lynn Krueger Adrian

Project Objective: The objective of the CTU modules series is to provide a comprehensive, user-friendly packet of informational materials on a variety of contraceptive methods and issues. Using the latest scientific information, the modules are expected to be used as a tool for influencing policymakers, and changing the knowledge and updating the practices of family planning service providers.

Project Description: FHI plans to coordinate, monitor, fund, produce and distribute CTU modules on the following subjects: injectables, LAM, oral contraceptives, IUDs, barrier methods, postpartum contraception, female sterilization, male sterilization, NFP, implants, and policy issues and options. Each module will include narrative, slides, summary fact sheet, pertinent references and reprints of articles.

Technical content of each module will address issues such as method advantages and disadvantages, indications and contraindications, client care issues, care provider requirements, counseling and quality of care issues. CTU modules are written at a level that will appeal to a broad audience. Sets of more technical slides are being produced for medical audiences.

Collaborating Agencies: numerous

FY'94 Planned Activities: To finalize and distribute modules on injectables, LAM, postpartum contraception, and OCs. To commence translation activities (French and Spanish) on all four.

Expected Outputs, FY '94: Four modules in three languages (French, English and Spanish) will be distributed to family planning colleagues nationally and internationally for use at CTUs and other trainings.

Possible Problems, Barriers to Completion: Extended review process that lengthens revision and production time. Inability to agree upon key scientific aspects of slides and texts.

Initiation Date: April 1992
Projected End Date: July 1995

Funding Source: USAID/W
FY '94 Budget: \$364,618
Total Budget: \$1,093,000

202

Project Title: Expert Slide Sets: CTUs

Country(s): Worldwide

Division: Policy and Research Utilization

FCO: 3211

Technical Monitor: Lynn Krueger Adrian

Project Objective: To provide 35mm color slides in English, French and Spanish to leading international experts on various contraceptive technologies and issues.

Project Description: Each slide pack will contain 20-30 slides. Unlike the modules, no narrative or audience handouts will be provided. The slides will be similar, but more technically and scientifically sophisticated than the partner module slides.

Collaborating Agencies: numerous

FY '94 Planned Activities: Preparation of Injectables, Oral Contraceptives, and IUDs sets are underway.

Expected Outputs, FY '94: Production and distribution of slide sets on Injectables, OCs, and IUDs.

Possible Problems, Barriers to Completion: Unavailability of key USAID/W, cooperating agencies, or FHI staff.

Initiation Date: November 1993

Projected End Date: July 1995

Funding Source: USAID/W

FY '94 Budget: \$13,702

Total Budget: \$24,000

Project Title: Regional Experts Meeting: Improving Service Practices Workshop

Country(s): Panama (for Latin America region)
Division: Policy and Research Utilization **FCO:** 3022
Technical Monitor: Belinda Irsula

Project Objectives: 1) To review the latest scientific findings regarding contraceptive technologies; 2) to identify and discuss country-specific service practices; 3) to draft proposed priority country-specific activities aimed at improving access to contraceptive services through the improvement of practices; and 4) to develop a regional core group of experts.

Project Description: FHI, in collaboration with JHPIEGO, AVSC, Pathfinder International, and the Population Council, will conduct a three-day workshop in Panama City, Panama, November 26-27, 1993. Approximately 30 participants from 10 Latin American countries will attend. We expect that participants will become key advocates of improving provider practices in their countries and in the region.

Collaborating Agencies: AVSC, JHPIEGO, IPPF, WHO, The Population Council and Pathfinder International

FY '94 Planned Activities: A 3-day workshop will be planned and conducted in November 1993, followed up by an evaluation.

Expected Outputs, FY'94: Regional core groups of experts on service practices will be identified. Outline of initial country plans to address local service practices will be drafted.

Possible Problems, Barriers to Completion: None

Initiation Date: June 1993
Projected End Date: December 1993

Funding Source: USAID/W
FY'94 Budget: \$97,786
Total Budget: \$111,000

2028

Project Title: Regional Experts Meeting: Improving Service Practices Workshop

Country(s): Philippines (for the Asia region)
Division: Policy and Research Utilization **FCO: 3023**
Technical Monitor: Kyle Spivey

Project Objective: 1) To review the latest scientific findings regarding contraceptive technologies; 2) to identify and discuss county-specific service practices; 3) to draft proposed priority country-specific activities aimed at improving access to contraceptive services through the improvement of practices; and 4) to develop a regional core group of experts.

Project Description: FHI, in collaboration with JHPIEGO, AVSC, Pathfinder International, and the Population Council, will conduct a two-day workshop in Manila, Philippines, November 13-14, 1993. Approximately 30 participants, leading obstetricians, gynecologists, and family planning experts from 10 Asian countries will attend. We expect that participants will become advocates to improve provider practices in their countries and throughout the region. The final session of the workshop will identify a core group of these advocates.

Implementing Agency: Local assistance through Dr. Rebecca Ramos

Collaborating Agencies: AVSC, JHPIEGO, The Population Council, Pathfinder International, WHO

FY'94 Planned Activities: To plan, conduct and evaluate a workshop in November 1993.

Expected Outputs, FY '94: Completion of workshop. Regional core groups of experts will be identified. Outline of initial country plan will be drafted.

Possible Problems, Barriers to Completion: None

Initiation Date: June 1993
Projected End Date: November 1993

Funding Source: USAID/W, with financial assistance from JHPIEGO, The Population Council, AVSC, WHO, Pathfinder International
FY '94 Budget: \$110,074
Total Budget: \$154,000

Project Title: Review of Service Delivery Guidelines and Training Curricula. Development of CTUs

Country: Jamaica
Division: Policy and Research Utilization FCO: 3213
Technical Monitor: Lynn Krueger Adrian

Project Objective: 1) To determine the extent to which training and service delivery guidelines are followed in practice and whether any of the written guidelines perpetuate unnecessary practices that inhibit access to contraceptive use; and 2) to develop a series of CTU workshops to disseminate more current, barrier-free information on contraceptive methods and service delivery systems and practices. CTUs will be based on the information collected during an FHI/Futures Group-supported private physicians survey.

Project Description: FHI, in collaboration with National Family Planning Board, the Ministry of Health, PATH, and other appropriate groups, and with the assistance of a local consultant, will provide technical assistance to evaluate service delivery guidelines training curricula. Several CTU workshops are envisaged to be based on the results of the Physicians' Mapping Survey and the evaluation of service delivery guidelines, being conducted with assistance from SDR.

Implementing Agency: A local training agency or consultant -- to be identified.

Collaborating Agency: The Futures Group

FY'94 Planned Activities: FHI will hire a local consultant and will complete Physicians' Mapping questionnaire development and data collection. Data analysis is underway. A preliminary trip to Jamaica to plan CTU workshops is scheduled for January 1994.

Expected Outputs, FY '94: A series of parish-level information dissemination events linked with findings from FHI/Futures Group research will be conducted.

Possible Problems, Barriers to Completion: None

Initiation Date: March 1993
Projected End Date: July 1995

Funding Source: USAID/W
FY '94 Budget: \$71,640
Total Budget: \$151,000

206

Project Title: Service Guidelines Dissemination Workshops

Country: Cameroon
Division: Policy and Research Utilization FCO: 3215
Technical Monitor: Lynn Krueger Adrian

Project Objective: To improve client access to contraceptive services in Cameroon through the dissemination of newly developed national service guidelines, standards, and protocols.

Project Description: One national and five provincial-level 3-day workshops will be conducted in collaboration with INTRAH and the Ministry of Public Health (MOPH) to disseminate Cameroon's national service guidelines, standards, and protocols. Fifty service providers from each of the five provinces will participate in the 3-day activity. In a parallel activity, FHI is conducting research on provider adherence to the national service guidelines.

Implementing Agencies: MOPH, Eura-Audit
Collaborating Agency: INTRAH

FY'94 Planned Activities: To provide technical assistance to the MOPH and Eura-Audit for the facilitation of five provincial dissemination workshops.

Expected Outputs, FY '94: One national and five provincial workshops will be completed and participants will become familiar with the new national service guidelines and with the importance of improving service practices.

Possible Problems, Barriers to Completion: None

Initiation Date: November 1993
Projected End Date: July 1994

Funding Source: USAID/W
FY '94 Budget: \$132,046
Total Budget: \$132,046

Project Title: FHI Fellow - USAID/W

Country: United States

Division: Policy and Research Utilization

FCO: 3212

Technical Monitor: Christine Vincent

Project Objective: To provide support to USAID/W's Office of Population in the area of improving service practices.

Project Description: FHI has funded an FHI fellow and limited needed activities in USAID/W's Office of Population since 1992, in order to provide support to the Office's efforts in improving service practices. Until October 1993, this project was housed under the CUE Division (FCO 6720).

FY'94 Planned Activities: One fellow will be funded.

Expected Outputs, FY '94: Critical support on improving provider practices provided to USAID/W.

Possible Problems, Barriers to Completion: None

Initiation Date: October 1992

Projected End Date: September 1994

Funding Source: USAID/W

FY '94 Budget: \$44,254

Total Budget: \$102,480

208

Project Title: Consensus Building Activities

Country: Ghana
Division: Policy and Research Utilization FCO: 3216
Technical Monitor: Lynn Krueger Adrian

Project Objective: To improve access to contraceptive services in Ghana through the distribution of up-to-date national service guidelines. Numerous consensus building activities will be jointly conducted with INTRAH during the guidelines development phase; in addition, national and regional dissemination activities will be held to garner support for creating updated national service guidelines.

Project Description: FHI, in collaboration with INTRAH, will provide technical assistance to the government of Ghana to develop national service guidelines for Ghana's family planning program. Orientation workshops, consensus-building activities, dissemination and follow-up workshops will be jointly conducted with INTRAH. As a parallel activity, FHI will be conducting research on service practices to better enable policymakers to develop guidelines.

Implementing Agency: To be determined
Collaborating Agency: INTRAH

FY'94 Planned Activities: Three trips will be held, an initial project plan will be developed and a needs assessment will be proposed.

Expected Outputs, FY '94: Project plan will be developed and needs assessment will be conducted.

Possible Problems, Barriers to Completion: none

Initiation Date: November 1993
Projected End Date: September 1994

Funding Source: USAID/W (with potential for additional funds from Mission)
FY '94 Budget: \$56,696
Total Budget: \$56,696

Project Title: Policy Implementation

Country(s): Nepal
Division: Policy and Research Utilization **FCO:** 3512
Technical Monitor: Shyam Thapa

Project Objective: To assist the Government of Nepal (GON) and its agencies to implement policies that will lead to increased contraceptive prevalence and improved women's reproductive health.

Project Description: At the request of USAID/Kathmandu, FHI's full-time advisor and several part-time staff and consultants work with the Ministry of Health to assist them in carrying out a diverse array of activities critical to the development and implementation of policies regarding Nepal's family planning program. They also provide assistance to other cooperating agencies and NGOs in Nepal. This project supports these efforts through small research and technical assistance activities.

FY'94 Planned Activities: The FHI advisor and staff will: 1) assist local agencies in educating policymakers about the effective implementation of population policies, 2) work with local agencies in reviewing service delivery and training guidelines and in revising them to increase contraceptive access to all appropriate groups of clients, 3) assist local agencies in the design and facilitation of training curricula to implement appropriate current policies and guidelines, 4) collaborate with women's health advocates in developing strategies to increase support for access to a broader range of contraceptive methods, and 5) develop a strategy to address gender-related issues in contraceptive choice.

Expected Outputs, FY'94: The Ministry of Health, National Population Council, USAID/Kathmandu, other local agencies and USAID cooperating agencies will receive regular updates on population policy issues and potential actions on these issues compiled from study results and various relevant sources. One or more studies dealing with policy issues related to experience of contraceptive choice will be designed and initiated. Technical assistance will be provided in the design and implementation of training curricula. Forums will be held to address women's health advocates who will be responsible for developing strategies to increase support for access to a broader range of contraceptive methods. A strategy will be developed and presented to key decision makers for review.

Possible Problems, Barriers to Completion: Availability of Nepal in-country staff to work with FHI staff. Availability of funds to initiate small operations research projects.

Initiation Date: October 1993
Projected End Date: July 1995
Funding Source: USAID/W
FY'94: \$22,414
Total Budget: \$48,000

Project Title: MIS Workshop

Country: Nepal

Division: Policy and Research Utilization

FCO:3725

Technical Monitor: Shyam Thapa/Ami Israel

Project Objective: To provide technical assistance: 1) to review past experiences with the management information system (MIS) under the various vertical programs; 2) to assess MIS needs under the integrated system; and 3) to work toward developing a comprehensive MIS, with identification of training and reorientation needs.

Project Description: In July 1993, the Government of Nepal took a major step in restructuring the Ministry of Health. A prominent feature of the restructuring was to integrate the entire health service delivery system. Up until the reorganization, each major program division had essentially a stand alone MIS. This resulted in inefficiency and duplication of efforts.

At the request of USAID/Kathmandu, FHI will provide technical assistance to the Ministry of Health to support and conduct a workshop on strengthening and improving the MIS for the health service delivery system. This support will help strengthen the family planning service delivery system and, at the same time, it will be an essential step towards integrating the monitoring of various health services subsystems

FY'94 Planned Activities: FHI will provide technical assistance and coordinate a workshop for the Ministry of Health on developing a comprehensive management information system. The workshop will be held in Kathmandu in November 1993.

Expected Outputs, FY'94: These activities will result in a final report from the MIS workshop with recommendations to the Ministry of Health and USAID on next steps for MIS program development.

Possible Problems, Barriers to Completion: Due to the restructuring of the Ministry of Health and the absence of an appointee for the MIS division, it is uncertain when and if the recommendations from the workshop will be implemented.

Initiation Date: November 1993

Project End Date: December 1993

Funding Source: USAID/Kathmandu

FY 94 Budget: \$23,892

Total Budget: \$23,892

4. Field Operations

The Field Operations Division serves as a focal point for FHI's country specific programs and activities, matching country needs with FHI resources. Field Operations keeps current with the needs, abilities and interests of population programs in specific countries.

Currently Field Operations work falls into the following four areas:

- **Development of Regional and Country Strategies**

Field Operations is responsible for ensuring that strategies are developed for regions and countries that are significant to FHI. Strategies include demographic information, descriptions of health and family planning systems, identification of population needs, a description of FHI activities and a definition of FHI's role in the region or country.

- **Liaison for Country Activities**

Field Operations staff serve as the primary contacts within FHI for information on FHI programs, especially for those programs funded by USAID Missions. Mission funded programs are usually an interdivisional effort, which Field Operations staff coordinates. Quarterly feedback is provided to Missions in key countries on all FHI activities.

- **Support to Regional and Country Offices**

Field Operations staff provide backup support to FHI's regional and country offices funded under the Population Cooperative Agreement. At present, FHI is maintaining a regional office for Africa in Kenya and country offices in Nepal and Egypt. Field Operations staff serve as the primary communications point for field staff, provide logistical backup and ensure appropriate approvals are obtained.

- **Identification of New Opportunities**

Field Operations staff seek new opportunities for FHI by emphasizing FHI capabilities in discussions with mission personnel, by leveraging USAID core funds in cooperative funding with other organizations and by obtaining bilateral mission funds through add-ons to cooperative agreements or responses to Requests for Proposals that will complement USAID-funded core activities.

FY '94 Activities

The Field Operations Division will continue to concentrate its work in these four areas during FY '94.

The activities, ongoing and new, which Field Operations will implement during the coming year are listed below:

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■ **Development of Regional and Country Strategies**

Continuing Activities:

- Refinement of Kenya and Haiti Strategies

New Activities:

- Development of regional strategies for Africa, Asia/Near East and Latin America/Caribbean
- Development of country strategies for Senegal, Egypt, Jordan, the Philippines and Mexico

■ **Liaison for Country Activities**

Continuing Activities:

- Coordination of Mission-funded programs in Kenya, Nigeria, Senegal, Mali, Egypt, Nepal and Haiti
- Regular quarterly feedback on FHI activities to Missions in 12 key countries

New Activities:

- Coordination of Mission-funded programs in El Salvador and Jordan

■ **Support to Regional and Country Offices**

Continuing Activities:

- Continue support to Kenya, Egypt and Nepal offices

■ **Identification of New Opportunities**

Continuing Activities:

- Work to expand efforts in Senegal, Egypt, Jordan, the Philippines and Mexico

New Activities:

- Explore opportunities for bilateral funding in Malawi and Mali

Project Title: Reproductive Health Research/Institutional Development Project

Country: Kenya
Division: Field Operations FCO: 7793
Technical Monitor: Melissa Allen/Kathy Jesencky

Project Objective: To strengthen the capacity of the University of Nairobi Ob/Gyn Department to manage a broad-based contraceptive and reproductive health research program; to plan, design, implement and evaluate contraceptive and reproductive health research in support of the Kenyan family planning program; and to develop a network of trained investigators throughout Kenya interested in all phases of family planning research.

Project Description: For the past five years, FHI has provided training and technical assistance to the University of Nairobi Department of Obstetrics and Gynaecology in activities related to reproductive health research, information dissemination and family planning service delivery. Training seminars on research related topics (including clinical trials methodology, data management and analysis, and scientific writing) were conducted to increase the research skills of the Ob/Gyn Department staff; technical assistance was provided in the development, implementation, and analysis of four reproductive health research projects: a Physicians' KAP Survey, studies of Barriers to Contraceptive Use, Acceptability of Three Family Planning Methods, and Causes and Prevention of Maternal Mortality; and computer hardware and software and related training were provided for research and information management.

Implementing Agency: University of Nairobi Ob/Gyn Department

FY'94 Planned Activities: Technical assistance will be provided in the completion of final reports for each of the four research projects. A limited number of activities related to STDs and family planning will be undertaken as set forth in a new scope of work for expenditure of remaining project funds. Construction of additional space for the reproductive health research unit will be contracted.

Expected Outputs, FY '94: A Project Activity Completion Report (PACR) will be prepared. The Ob/Gyn Department building will be expanded to house the Reproductive Health Research Unit.

Possible Problems, Barriers to Completion: None foreseen.

Initiation Date: August 1990
Projected End Date: September 1994

Funding Source: USAID/Nairobi
FY '94 Budget: \$ 216,205
Total Budget: \$1,055,000

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Project Title: Management of the Family Health Services Project of Nigeria

Country(s): Nigeria
Division: Field Operations **FCO:** 7801
Technical Monitor: Susan McIntyre

Project Objective: To support the Nigerian Family Health Services (FHS) Project through the provision of long- and short-term technical assistance, including support to the Project Administrator.

Project Description: The USAID-sponsored Family Health Services Project was begun in 1988 with the purpose of making family planning information and services within Nigeria widely available. The original end-of-project goal was to reach a nationwide contraceptive prevalence of 12 percent, or approximately 2.5 million users. In 1991, following a management review of the FHS Project, it was recommended that the Project Administrator's role be strengthened to improve coordination among the subcontractors. It was decided that one way to strengthen this role was to hire an Administrator through a buy-in to an S&T/POP centrally funded project to provide further backstopping capacity than is possible with a personal services contract.

FHI was selected for this role and, through an add-on to its Cooperative Agreement, both long- and short-term technical assistance are provided to the FHS Project. In this capacity FHI has subcontracted with the International Science and Technology Institute (ISTI) to place Mr. John McWilliam in the role of Project Administrator. In addition FHI has responded to specific requests from the Mission for short-term technical assistance, provided interim support for the FHS Deputy Administrator, and (under FCO 7802) has sought to develop complementary activities.

Collaborating Agency: ISTI

FY'94 Planned Activities: FHI will continue to support the FHS Administrator financially and with the provision of requested and/or timely family planning/contraceptive information. In addition technical assistance in logistics will be provided via an ISTI consultant. Efforts to complement other FHS project efforts through additional FHI-related activities will continue to be explored.

Expected Outputs, FY '94: A written plan for the transition of FHS I to FHS II will be in place. An experienced cadre of Nigerian family planning professionals will be prepared to continue in key leadership roles under FHS II. An article on "lessons learned" in the course of FHS I will be written and submitted to a professional journal by the FHS Administrator, Deputy Administrator and others for the purpose of summarizing experiences gained and sharing with others useful information about the project specifically and process of project development more generally. An improved logistical system for the provision and monitoring of contraceptive supplies for the FHS project will be adopted and in use.

Possible Problems, Barriers to Completion: Civil unrest, which has erupted on an intermittent basis since mid-1993, could curtail the ability of the FHS Administrator and the logistics consultant to work effectively throughout the country. If unrest persists, it could jeopardize the ability of both to remain in-country and the ability of the logistics system to function.

Initiation Date: September 1991
Projected End Date: June 1994

Funding Source: USAID/Lagos
FY '94 Budget: \$399,520 (\$388,095 obligated to ISTI)
Total Budget: \$1,250,000

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Project Title: FHI Complementary Activities in Support of the Family Health Services Project of Nigeria

Country(s): Nigeria
Division: Field Operations FCO: 7802
Technical Monitor: Susan McIntyre

Project Objective: To support the Nigerian Family Health Services (FHS) Project through "complementary FHI projects", developed in consultation with USAID/Nigeria. The original illustrative list of potential projects included study tours, training, research on reproductive health and contraceptive technology updates.

Project Description: The USAID-sponsored Family Health Services (FHS) Project was begun in 1988 with the purpose of making family planning information and services within Nigeria widely available. (See FCO 7801 for additional background.) Since September 1991 FHI has been involved in the provision of both long- and short-term technical assistance. Complementary activities which were to be funded under the same add-on that provided funds for this technical assistance, have thus far been limited to the participation of an FHI staff member in the long-range planning meeting for FHS held in Lagos in January 1993 and an international expert at a contraceptive technology update meeting held by the Association of General and Private Medical Practitioners (AGPMPN) in Ilorin, Nigeria in May 1993. Additional activities which FHI has sought to develop included an assessment of costing issues related to the family planning program as a whole, costing studies relating to Norplant and planning and participation in the Annual Meeting of the AGPMPN to include a Contraceptive Technology Update.

Collaborating Agency: FHS

FY'94 Planned Activities: Collaboration with the Association of General and Private Medical Practitioners of Nigeria in planning and organizing a contraceptive technology meeting will be pursued provided local costs can be covered by the FHS project itself. Available funding will allow for one additional activity: assistance with either a magazine on up-to-date contraceptive technology produced with the AGPMPN or preliminary costing work relating to the provision of Norplant relative to other contraceptive methods within Nigeria.

Expected Outputs, FY '94: The Annual Meeting of the AGPMPN will be held in March 1994 with a focus on family planning and contraceptive technology. Anticipated attendance is approximately 3000 private and general practitioners from throughout Nigeria. FHI will provide an internationally known expert on contraceptive technology. Available funding will limit remaining activities to either assisting in the preparation, writing and production of approximately 8000 copies of an edition of the magazine "The Nigerian Family Practice" highlighting family planning topics including summations of recent research results pertaining to the safety and efficacy of current contraceptive methods; or a technical assistance visit by two FHI staff to develop a study outline and identify local researchers for a study of the cost of providing Norplant relative to other family planning methods used for similar period of time.

Possible Problems, Barriers to Completion: All activities above still require the approval of USAID/Nigeria. Travel will be restricted if civil unrest continues, making technical assistance trips or visits by guest speakers impossible.

Initiation Date: September 1991

Projected End Date: June 1994

Funding Source: USAID/Lagos

FY '94 Budget: \$49,439

Total Budget: \$50,000

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Project Title: Norplant Introduction in Senegal

Country: Senegal
Division: Field Operations **FCO:** 7755/7005
Technical Monitor: Ami Israel

Project Objective: To provide technical assistance to the Senegal National Family Planning Program in introducing Norplant as another contraceptive choice in Senegal.

Project Description: FHI is providing technical assistance to the Government of Senegal, Ministry of Health to facilitate the introduction of Norplant as an accepted method of contraception in the national family planning program. This began in 1986 as a pre-introductory clinical trial of Norplant for 50 women. Based on positive response, it was later expanded. At total of 333 women were enrolled through June, 1991.

In 1991, FHI and JHPIEGO developed a joint strategy for making the transition from research to routine service delivery of Norplant. Under the strategy, the "lead agencies" formed a Norplant Coordinating Committee, comprised of senior officials from the Ministry of Public Health and Social Action (MPA/SA), staff of Le Dantec and representatives of USAID's and UNFPA's family planning programs. FHI and JHPIEGO guided the Coordinating Committee in developing protocols for Norplant services, in selecting five clinics in Dakar to deliver services, in identifying physicians and midwives for JHPIEGO's medical training and midwives and social workers for AVSC's counseling training, and in convening clinic based "information days" sponsored by FHI.

Implementing Agency: University of Dakar, Aristide Le Dantec Hospital

Collaborating Agencies: JHPIEGO, AVSC

FY'94 Planned Activities: FHI will: 1) complete data analysis for the Client Perspective Study; 2) convene a dissemination workshop for policymakers and program managers to present the results of the Client Perspective Study; 3) design and implement a follow up component to Client Perspective Study dissemination workshop targeting each of the five pilot clinics in addressing specific problems in service delivery; 4) support three regional Norplant "information days" for clinicians and media representatives from the 10 regions in Senegal; 5) support the Norplant Coordinating Committee in planning the expansion of Norplant services beginning with one to three regions, with a phase-in plan for all 10 regions; 6) assure that Norplant sets and related supplies are available at the Norplant clinics; 7) explore opportunity of conducting a Return to Fertility Study at the clinical trial site; 8) collaborate with other USAID cooperating agencies (JHPIEGO, AVSC, the Population Council) in providing technical assistance to all aspects of Norplant introduction in Senegal.

Expected Outputs: These activities will result in: 1) a report from Client Perspective Study; 2) evaluation reports from host country supervision monitoring visits illustrating improvements in Norplant services at the pilot clinics; 3) continued adequate Norplant supplies and systems for supplies distribution at the pilot clinics and potential regional clinics; 4) decision to (or not to) pursue the Return to Fertility Study; 5) a workplan

produced by policymakers, program managers and CAs for the planning and execution of the expansion of Norplant services into regional areas.

Possible Problems, Barriers to Completion: Due to restructuring of the National Family Planning Program and the politics between the key players delays in activities may occur.

Initiation Date: August 1990
Project End Date: September 1995

Funding Source: USAID/Dakar, USAID/W
FY94 Budget: \$117,280
Total Budget: \$446,000

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Project Title: Technical Assistance to the Mali Association for the Promotion and Protection of the Family

Country(s): Mali
Division: Field Operations FCO: 7581
Technical Monitor: Beverly Tucker

Project Objective: To strengthen the institutional capacity of the Mali Association for the Promotion and Protection of the Family (AMPPF) to conduct family planning research in order to use the results to improve local service provision.

Project Description: Since 1983, FHI has assisted the AMPPF in its institutional development in order to increase the organization's effectiveness. FHI will continue supporting the AMPPF as they work to improve local service delivery. The current subagreement, which runs through 31 December 1993, provides funds for the establishment of a computerized client information service, evaluations of two IEC campaigns in rural Mali, improvement of the AMPPF library, and the printing of the AMPPF bulletin.

Implementing Agency: AMPPF

FY'94 Planned Activities: During this 3-month period, the client information service will be used to provide service-delivery data. A fifth bulletin, this one on male sterility, will be prepared and distributed. The books, journals and reports in the AMPPF library will be sorted and classified. Clarification of future USAID/Bamako funding for FHI-AMPPF activities will be obtained.

Expected Outputs, FY '94: The AMPPF will classify and store its books, journals, and reports in its library. The client information system will be used on a regular basis. A bulletin on male sterility will be distributed.

Possible Problems, Barriers to Completion: None.

Initiation Date: November 1991
Projected End Date: December 1993

Funding Source: USAID/W
FY '94 Budget: \$21,928
Total Budget: \$196,000

**Project Title: Technical Assistance to the Joint USAID/GOE
National Population Council Institutional
Development Project**

Country: Egypt
Division: Field Operations FCO: 7788
Technical Monitor: Melissa Allen

Project Objective: To strengthen the institutional capability of the National Population Council (NPC) and its implementing agencies to plan and coordinate research and other activities which support the delivery of improved and expanded family planning services in Egypt.

Project Description: The NPC takes a lead role in updating service providers and policymakers in Egypt on both contraceptive technology and related reproductive health issues and in setting research priorities. With an add-on to its Cooperative Agreement, FHI has provided technical assistance to the NPC on two initiatives. The first required establishing a Research Management Unit (RMU) at the NPC to set national research priorities, to coordinate family planning research supported by the Egyptian government, to ensure the quality of the research and to provide funding for studies on a competitive basis. The second initiative was to introduce the concept of operations research (OR) to family planning organizations in Egypt and to assist them in study design, protocol development, implementation, data management and analysis and reporting. Through a subcontract with E. Petrich and Associates (EP&A), technical assistance is also provided to the Central Office of the NPC and twenty Governorate offices to implement management information systems, program planning and evaluation.

Collaborating Agency: E. Petrich and Associates

FY'94 Planned Activities: An assessment of the maximum service delivery capacity of both physical and human resources within various public and private sector family planning clinics will be conducted. This assessment will establish standards for case-load capacity for physicians and nurses at the service delivery points and thereby determine clinical training needs. Technical assistance in the preparation of final reports and papers for publication for the biomedical and programmatic research projects that have been or will be completed during the last few months of the project will be provided.

Expected Outputs, FY '94: A PACR will be written in February 1994. A monograph based on research findings from the completed research projects to be distributed at the International Population Conference to be held in Cairo in 1994 will be prepared. A paper entitled "The Impact of Nurse Training on Family Planning Knowledge, Attitudes and Practice Among MOH Clinic Clients in Egypt" prepared by Egyptian collaborators and FHI staff will be finalized and submitted for publication.

Possible Problems, Barriers to Completion: None foreseen.

Initiation Date: August 1990
Projected End Date: March 1994
Funding Source: USAID/Cairo
FY '94 Budget: \$ 400,473
Total Budget: \$3,649,167

222

Project Title: Support to the Government of Nepal

Country: Nepal
Division: Field Operations
Technical Monitor: Ami Israel

FCO: 7724

Project Objective: To strengthen the institutional capacity of the Government of Nepal to develop and implement policies and strategies to increase the availability of and access to quality family planning and child survival services.

Project Description: FHI has been providing technical support to the Government of Nepal in family planning and the population sector for over a decade. FHI support began in 1981 with a month-long research methodology workshop for the National Planning Commission (NPC), Ministry of Health (MOH), Family Planning Association of Nepal (FPAN), Center for Development Administration, and Tribhuvan University. During the period of 1985-1990, FHI supported pre-introductory clinical trials of the Norplant implant contraceptive. These trials paved the way for the inclusion of this new contraceptive option in Nepal's national family program. FHI, at the request of GON and with support of the USAID Mission, has attached a Technical Advisor to the Family Health Division (FHD) of the MOH and the Population Division of the NPC. Most recently, with funding obtained from the Asia Bureau, FHI has contracted a policy and management specialist to work part-time with the Family Health Division. This is assisting FHD in assessment of program performance, utilization of data for policy and program development, and investigation of implementation issues and problems, and is providing research and training opportunities to local population and health professionals.

Collaborating Agencies: The Research Triangle Institute (RTI) and The Futures Group

FY 94 Planned Activities: FHI will: 1) develop plans for a study tour program for selected host country nationals; 2) assist the RTI and The Futures Group in the preparation and presentation of the RAPID-type model to the parliamentarians in Nepal; 3) plan and convene two in-country workshops on providing training opportunities in conceptualization of research issues, use of software programs, data analysis, and scientific writing skills; 4) continue providing technical support to the Family Health Division, Ministry of Health and Population Division, National Planning Commission; 5) continue to assist in the development of the Nepal Population and Health Data Bank; 6) continue to conduct the analysis of district level data on utilization of family planning and MCH services; 7) collect, compile and edit papers on preventive health care issues; 8) provide assistance to health care professionals to participate in short and long-term training programs.

Expected Outputs FY 94: These activities will result in: 1) a final report from the MIS workshop with recommendations to the Ministry of Health and USAID on next steps; 2) decision to (or not to) pursue plans for a study tour program for selected host country nationals; 3) a final report on the presentation of the RAPID-type model to the parliamentarians in Nepal; 4) final report from the two workshops with recommendations on evaluation of training and follow up; 5) quarterly updates on progress of providing technical support to the FHD, MOH, NPC; 6) quarterly updates on the progress of population and health data bank; 7) mid-project update on analysis of district level data on utilization of family planning and MCH services; 8) dissemination of papers to appropriate

parties in Nepal and U.S.; and 9) attendance of 3-5 health care professionals at short- and long-term training programs outside of Nepal.

Possible Problems, Barriers to Completion: Due to the restructuring of the National Family Planning Program and the politics between the key players, delays in activities may occur. Availability of funding is also a potential issue. USAID/Asia Bureau is expected to support all costs for above activities, current monies may not be sufficient at this time and will need to be augmented before the fiscal year is complete.

Initiation Date: September 1991
Project End Date: September 1996

Funding Source: USAID/Kathmandu
FY 94 Budget: \$259,974
Total Budget: \$385,000

224

Project Title: Technical Assistance to the Family Planning Association of Haiti (PROFAMIL) in Norplant Logistics.

Country(s): Haiti
Division: Field Operations FCO: 7705
Technical Monitor: Beverly Tucker

Project Objective: To improve PROFAMIL's inventory and tracking system for supplies as well as the client tracking system for Norplant users.

Project Description: Based on the success of pre-introductory clinical trials of Norplant contraceptive implants and the subsequent introduction of Norplant service provision in selected clinics, FHI is collaborating with several Haitian organizations to expand the provision of Norplant services in Haiti.

Under this FCO, FHI is providing technical assistance to PROFAMIL to improve their logistics system for tracking supplies as well as clients.

Implementing Agency: PROFAMIL

Collaborating Agency: IPPF Port-au-Prince Field Office (PAPFO)

FY'94 Planned Activities: Pending resolution of the current political crisis, discussions will continue with PROFAMIL to finalize the scope of work and budget for the Norplant project in which FHI will provide technical assistance in the design of Norplant inventory and tracking systems. A series of meetings with PAPFO, PROFAMIL and INHSAC will be held to plan a national Norplant information day and the Norplant expansion in Haiti.

Expected Outputs, FY '94: A Norplant inventory and tracking system will be implemented. A national Norplant information day will be celebrated.

Possible Problems, Barriers to Completion: Currently, all activities in Haiti have been postponed until the political crisis is resolved.

Initiation Date: July 1993
Projected End Date: September 1995

Funding Source: USAID/Port-au-Prince
FY '94 Budget: \$29,071
Total Budget: \$62,000

225

Project Title: Norplant Introduction in El Salvador

Country(s): El Salvador

Division: Field Operations

FCO: 7704

Technical Monitor: Laura Bani Doerfer

Project Objective: To provide technical support to the Ministry of Health, Social Security Institute (ISSS), Asociación Demográfica Salvadoreña (ADS) and ANTEL (health care agency serving communication workers) to ensure the coordinated introduction of Norplant as an alternative contraceptive choice in El Salvador.

Project Description: This project is designed to assist El Salvador to integrate the delivery of Norplant into its existing family planning programs. A unified information system for the inclusion of Norplant services into each institution's family planning recording system will be developed. Training of providers, dissemination of information about Norplant, development of method-specific IEC materials, and evaluation of service delivery systems and of the overall impact of Norplant introduction on incremental costs and contraceptive use in the four institutions are the major elements of the project.

Implementing Agencies: Ministry of Health, ISSS, ADS, ANTEL

Collaborating Agency: JHPIEGO

FY'94 Planned Activities: After approval and support from the Mission is obtained, technical assistance for the new MIS and training of providers on the new system will begin. Norplant IEC materials will be developed for acceptors and the general family planning brochure for new users will be revised to include information on Norplant.

Expected Outputs, FY '94: An established unified data management system and program guidelines.

Possible Problems, Barriers to Completion: Approval and support from the USAID/San Salvador Mission is needed. The PIO/T has not been submitted by the Mission to USAID/W, given other mission priorities.

Initiation Date: June 1994

Projected End Date: August 1995

Funding Source: USAID/San Salvador

FY '94 Budget: \$ 11,752

Total Budget: \$116,000

Project Title: Technical Assistance in Developing Strategies for Introducing Birth Spacing Methods

Country: Jordan
Division: Field Operations FCO: 7009
Technical Monitor: Sandor Balogh

Project Objective: To provide technical assistance in the development and implementation of projects for introducing new methods of birth spacing, particularly DMPA, Norplant and postpartum IUDs, into the Jordanian family planning program.

Project Description: Recently in Jordan there has been increasing recognition of the importance of slowing population growth and improving reproductive health through the promotion of effective breastfeeding practices and acceptance of modern contraceptive technologies to achieve adequate birth spacing intervals. One component of this overall strategy is to expand the existing method mix and to increase accessibility to contraceptive services by introducing safe, effective family planning methods such as DMPA, Norplant and postpartum IUDs. Under this project, FHI will provide technical assistance to the Ministry of Health, Royal Medical Services, University of Jordan and the private sector to help design, implement and evaluate introduction projects that will effectively integrate these new methods into existing programs. USAID/Amman will provide funding and local logistical support for in-country costs associated with the introduction effort.

FY 94 Planned Activities: FHI will work with Jordanian counterparts to identify program needs, including provider training, information and education, client counseling and screening, and appropriate channels for service provision associated with birth spacing methods new to Jordan's program. Specifically, FHI will develop, in collaboration with Jordanian representatives from the various health sectors, one or more project proposals that outline a plan for adding DMPA, Norplant, and postpartum IUDs to the range of methods available to couples.

Expected Outputs, FY 94: Approval and funding will be obtained for at least one introduction project; appropriate training will be provided, and initiation of services will begin in at least one site, initially probably at the university.

Possible Problems, Barriers to Completion: Availability of funding; USAID/Amman funding is expected to support all local costs of the introduction projects. In the past, funding has been restricted due to delays in Jordan receiving U.S. foreign assistance. Political instability in the region is always a consideration.

Initiation Date: October 1993
Projected End Date: December 1994

Funding Source: USAID/W
FY 94 Budget: \$65,161
Total Budget: \$65,161

C. MATERNAL AND NEONATAL HEALTH CENTER

The Purpose

The Maternal and Neonatal Health Center (MNHC) is an interdisciplinary unit established at FHI in 1992 and is an outgrowth of the organization's 20 years of experience in the field of maternal and neonatal health. The Center applies FHI's broad base of resources to intervention-oriented issues in maternity care research and service delivery. The goal of the MNHC is to reduce maternal mortality and morbidity by:

- developing concepts and strategies to improve maternal and neonatal care at all health system levels;
- assisting governments and other health organizations to assess their maternal health needs, plan for solutions, and translate their plans into action;
- designing, implementing, and evaluating innovative interventions;
- disseminating information on maternal health to clinicians, consumers, policymakers, and the scientific community.

The Structure

A small core of experienced maternal and neonatal health professionals provides overall direction and coordination of Center activities. Staffing and technical assistance for each MNHC project are drawn from FHI's pool of specialists in the areas of health economics, demography, management, evaluation, statistics, training, medicine, education, computers and information science.

FY'94: Activities Associated with the Cooperative Agreement

Although not part of FHI's Contraceptive Technology and Family Planning Research Cooperative Agreement, the MNHC coordinates activities with those carried out under the Cooperative Agreement. In FY'94, through an OYB transfer to the Cooperative Agreement, the MNHC will conduct research on the health impacts of TBA training on mothers and children in Ghana at the request of USAID/Accra. The study is described on the following page.

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Project Title: Study of the Health Impacts of TBA Training

Country(s): Ghana
Division: Maternal and Neonatal Health Center FCO: 9870
Technical Monitor: Jason B. Smith

Project Objective: To determine the health impacts on mothers and infants resulting from training traditional birth attendants (TBAs).

Project Description: This study is funded through an OYB transfer from USAID/Accra. Over the years, Ghana has made considerable investments in TBA training programs in an attempt to reduce high levels of maternal and neonatal morbidity and mortality. The National TBA Training Program is widespread and functioning well in much of the country. A process evaluation of the program was conducted a few years ago and the results were favorable overall. With this background it is possible to attempt to answer two questions: 1) does TBA training reduce maternal and neonatal death and disability? and 2) what factors enhance or inhibit the impact of TBA training?

The answers to these questions will help the Government of Ghana to allocate resources and organize their maternity care services. Also, many other countries are investing health resources in TBA training and would benefit from the results of the study.

The study will be conducted in one region in Ghana and will consist of four parts: a household enumeration necessary for constructing a sampling frame, qualitative research on TBAs, qualitative research on health facilities, and a household survey.

Implementing Agency: To be determined; negotiations are currently underway with the Department of Community Health at the University of Science and Technology in Kumasi (DCH-US&T/Kumasi).

FY'94 Planned Activities: The MNHC will finalize a subagreement with an implementing agency, design study protocol, design and pretest questionnaire instruments, and conduct the household enumeration and the qualitative research with TBAs.

Expected Outputs, FY'94: Completed household enumeration; qualitative research report on TBAs, which will be useful in informing the questionnaire design; and completed survey instruments.

Possible Problems, Barriers to Completion: To date, DCH-US&T/Kumasi has not been timely in its responsiveness to this project. Communication difficulties play a role in this. Beginning new negotiations with another implementing agency would cause delay. The study faces a variety of implementation barriers both political and logistic, particularly transportation. Rainy seasons will effect the windows of time available for survey data collection. There is a shortage of qualified data collection personnel.

Initiation date: August 1993
Projected End Date: April 1996

Funding Source: USAID/Accra
FY'94 Budget: \$126,584
Total Budget: \$250,000

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Agenda Item 6 (a)

Barrier Methods and Spermicides

- 1) Introduction and FHI history
- 2) Male condoms
- 3) New product development
- 4) Spermicides and microbicides

Introduction and FHI History

FHI History in Barrier Methods

Since the mid-1970s Family Health International has investigated a host of barrier contraceptive products. Our work has included product development as well as studies of safety, acceptability and effectiveness. Some of this work has been important in broadening the number of barrier options available on the market. Specifically, data from FHI trials of the Today™ contraceptive sponge and the Reality® female condom were used to support successful manufacturer applications for marketing approval to the U.S. Food and Drug Administration. Other new products have proved to be less successful and have fallen by the wayside. Still other studies have looked at existing products, for which we collected impartial, site-specific data on contraceptive effectiveness and acceptability.

To compile what we and others have learned about these products in a single source useful to service providers, policymakers, USAID Mission staff and others, FHI is writing a monograph on barrier methods that will be ready for the Cairo Population Conference in September. The monograph will include sections on these topics, and should be a clear and easy-to-use guide to the science of barrier methods for the non-scientist.

Barrier methods continue to be one of FHI's priority areas of research. We will soon study the contraceptive effectiveness of VCF®, the nonoxynol-9 film, and we will do further work with the Reality® female condom. As they are ready, we will test the effectiveness of plastic condoms. And we will collaborate with other organizations in the development of new microbicides for STD prevention.

We have broken up the TAC session on barrier methods into three parts, each of which will be followed by a discussion. The first session covers development of male plastic condoms, latex condom testing, and latex condom breakage.

The second session will highlight methodological issues in product development and clinical testing. The regulatory environment for barrier methods is changing, as was seen in the April meeting in Bethesda sponsored by the NIH, FDA and CDC. FHI must adapt our methods to suit these changes.

The third session will be devoted to vaginal products that are spermicidal and/or microbicial. This is an exciting and high-profile area to work in right now, with a tremendous amount of research on and advocacy for female-controlled prophylactic methods.

Male Condoms

Materials Technology Program Update

The Materials Technology Division's goal is to increase the variety, choices and quality of contraceptives available to the public. Division activities have two areas of focus; quality assurance testing of contraceptive devices, and development of new contraceptive devices, both with their defined working groups. Quality assurance testing is conducted by the presently titled Product Quality and Compliance (PQC) group, and development of new contraceptive devices is carried out by the Product and Process Development (PPD) group.

Production Quality and Compliance (PQC)

Until 1992, the quality assurance program consisted primarily of projects to evaluate latex condoms. Since then, the program has been expanded to reflect an increasing emphasis on other contraceptive products, including OCs, injectables, suppositories and IUDs. In response to USAID's requests, a major initiative was undertaken in the past year to broaden the scope and capabilities of the QA program. A new facility was designed and occupied, increasing laboratory area more than two-fold. In addition to the condom testing equipment already used, state of the art equipment was also acquired to support the expanded role of testing pharmaceutical contraceptives. This equipment includes a dissolution tester, which determines the dissolution rate of oral contraceptive or other pills, and a high performance liquid chromatograph (HPLC) for quantitative analysis of contraceptive composition, and assessing product homogeneity. Spectrometry analysis can be performed using ultraviolet/visible (UV/VIS) and Fourier Transform Infrared (FTIR) spectrometers, allowing for the identification of molecular "fingerprints" of contraceptives and other substances. New environmental chambers permit the determination of the stability of both devices and pharmaceuticals.

In addition to new test equipment, the capabilities of PQC have been expanded via improved data acquisition, particularly through an upgrade of the tensile tester. A new staff position has been established, Program Compliance Manager, to permit more thorough manufacturer audits and generally support the broader product line now being monitored. The direct assignment of a Biostatistician and the addition of a third Associate Director with primary technical management and science review responsibility in PQC also strengthens PQC's capacity to support USAID's Commodity and Program Support Division program. These and other staff assignments will facilitate more complete data analysis and in-depth program reviews, as well as improve information dissemination.

The condom production surveillance program has intensified during the past year. The single supplier of USAID condoms has experienced scale-up difficulties which has necessitated doubling the number of site audits and product lots tested.

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Field evaluations have also dramatically increased, with over thirty days of site visits during the last six months.

Product and Process Development (PPD)

The primary effort of the PPD group has been the development of two marketable, patentable, cost-competitive plastic condoms. One is a roll-on condom with employs a knitted spandex band for retention on the penis, and the other a baggy slip-on design which uses a double aperture for retention. These condoms will overcome significant shortcomings of latex condoms by offering longer storage potential and compatibility with oil based lubricants. It is also believed that plastic condoms allow greater thermotactile sensitivity than latex condoms, thereby reducing a barrier to use, but will have comparable efficacy in preventing pregnancy and STDs.

Major strides have been accomplished during the year to finalize these products. A second slip-on condom cut/weld and roll station was designed and is under construction. An automated, multi-station fabrication machine which will perform the functions of stress-softening, thermal treatment, leak detection and sorting, as well as condom cutting and welding is in the final shakedown stage. With it's completion, FHI will have a complete pilot scale manufacturing line for both condoms. In addition, stability incubators and tensile testing equipment has also been installed to allow for in process testing and stability studies.

FHI has accomplished significant progress in patenting this technology. Notices of Allowance, indicating that a patent will be issued, were received for the design of the roll-on knitted ring condom in February, 1994, and for the design of the slip-on twin aperture condom in May, 1994. Two Notices of Allowance were received on the stress-softening process for making the plastic film softer and thinner, one in December, 1993 and the second in April, 1994.

The pursuit of regulatory approval for these projects has been pursued during the past year. Toxicology and biocompatibility testing was completed on both the finished product and candidate films with acceptable results. A donning study for the slip-on condom contributed to final design and film selection decisions. In depth discussions with the FDA on approval requirements highlighted the need for a six-month contraceptive efficacy study which will be conducted by the Clinical Trials Division.

In addition to plastic condom development, other projects were undertaken which will be given increased attention in the future. These include the development of a non-surgical (transcervical) method of sterilization using iodine or some other chemical agent, development of spermicides and lubricants which are compatible with polyurethane, and spermicides which offer improved efficacy with reduced potential for irritation.

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CONDOM BREAKAGE IN HUMAN USE

Carol L. Joanis
Contraceptive Use and Epidemiology
Family Health International

Since the advent of AIDS, greater interest has been shown in the use effectiveness of condoms. To ensure provision of quality products, manufacturers are required to tests condoms to the standards prescribed by the American Society for Testing Materials (ASTM) or the International Standards Organization (ISO). Condom quality, as measured by the required laboratory tests, has little meaning to the average consumer. What is meaningful, however, is how well condoms perform in actual use.

What is an average/expected breakage rate for latex condoms? This question has several answers and depends on factors such as partner type, age of the condom, age of the user, educational level of the user, user experience with condoms, and storage conditions. It can be expected that an intact latex condom less than two years old (from date of manufacturer) will break at a rate of two to five percent during heterosexual vaginal intercourse. This is the range of breakage experienced by most married or cohabiting couples studied. Lower rates of breakage (1% or less) have been reported among brothel prostitutes in the U.S. The highest rates of breakage (greater than 5 percent) have been seen among lovers and casual sexual partners.

These figures by partner type are not absolute; variance does occur. What is consistent from study to study is that partners who live together and people with more than a high school education (U.S. only) break condoms at half the rate of those who do not cohabituate or those with less education. Further, race, ethnicity or cultural background have no bearing on condom breakage within any of the partner type or education categories.

Age of the condom, however, is critical to condom performance. Ideally, a condom that is four months old (from date of manufacture) is at its peak strength, assuming that it has been stored under optimal conditions. This strength is maintained for a period of about two years. After that time the condom, begins to break with greater frequency during intercourse, often at rates in excess of 10 percent. A condom that is over five years old should probably be discarded unless it is the only available method of protection. As with partner type these figures are not absolute. Improper storage (excessive heat, exposure to sunlight, etc.) can alter these figures. FHI is conducting a five year study to determine the effects of different storage conditions on the condom quality timetable.

Condom breakage is a rare event with condoms less than two years old. All condom breakage within any given study occurs with about 5 percent or less of enrolled participants. We refer to these individuals as "condom breakers". In general, these "breakers" are inexperienced with use of condoms, have less education, misuse the devices and have more lengthy or intense sexual acts.

While we have gained much knowledge about how condoms perform in human use, research needs to be continued to better understand (1) the relationship between laboratory testing and condom breakage in human use; (2) whether existing laboratory tests are valid predictors of breakage in use and, (3) the sexual behaviors and individual differences that impact consistent and correct use of the devices.

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Barrier Session Questions (Howard Price)

The objective of FHI's condom product quality and compliance program is to provide to USAID the assurance that it is providing reliable condoms, both when purchased from the manufacturer and after several years of storage under possibly adverse conditions. To this end, FHI puts proportional samples of condoms through a battery of six tests to measure their physical strength and compares test results to specified standard values as a reflection of quality.

However, the question has arisen in past years of whether laboratory test results actually do predict breakage during sexual intercourse. To answer this question, FHI conducted a study in 1991 which correlated the results of certain physical tests and reported condom breakage during intercourse.

The study's null hypothesis was that the condom quality index (CQI), a computation involving the number of bursts and the air volume at which they burst, had no correlation with in-use breakage. However, study results indicated a definite correlation between CQI and breakage, with a square of the correlation coefficient (R^2) of .75. Secondary analysis showed other physical tests including ultimate elongation and percentage of reject (the number of condoms that burst before reaching a standard volume) to have comparable correlations, with respective R^2 values of .75 and .70. Condom age proved to be the best correlator, with an R^2 of .92.

The above study highlighted the fact that much more data is needed to enlighten us on the relationship of testing results and breakage in use. There is, first of all, no fundamental understanding of condom composition, and its effect on breakage. Are there variable chemical changes that occur during the manufacturing process that effect quality? Are there physical and chemical properties which determine performance? What physical and chemical changes occur during storage? What are the physical and chemical properties which most determine the resistance to breakage during intercourse? How should the specifications and quality testing protocols be changed to better measure the condom properties which contribute to breakage resistance?

We also have an incomplete understanding of condom use behavior. What causes condoms to break? Are specific physical or chemical stresses producing breakage? What portion of broken condoms have serious manufacturing defects and would have failed airburst testing?

In designing the follow-up study to address these questions we submit the following questions for your consideration.

1. The original study showed that some demographic factors affected breakage. For example, couples in which one person

had no previous condom experience had nearly twice the breakage rate of couples with two experienced partners. In the committee's opinion, should study subjects be a selected population (i.e. potential high breakage, experienced users, etc.) or non-selected subjects?

2. Should additional questions regarding specific sexual practices and anatomy be asked if they have potential for elucidating the nature of breakage stresses?
3. What differing condom characteristics, such as style, age, and manufacturer should be represented in the study?
4. Should condoms that have known quality test values (poor, medium, good) be selected from field lots or custom manufactured, or should regular (non-selected) production samples be used?
5. The original study included airburst volume, airburst pressure, tensile break/strength and elongation tests. Should other tests, including elemental analysis, oxidation, modulus, work to rupture, microscopic surface homogeneity, thickness variance, package integrity, or lubricant quantity/type be included be used to better describe the condoms?

New Product Development

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BARRIER METHODS AND SPERMICIDES: New Product Development Session

Regulatory Framework for Approval of New Products

Contraceptive barriers and spermicides fall into two categories of medical products regulated by the US Food and Drug Administration. Barriers are medical devices and spermicides are drugs. The route of approval of medical devices is currently through either the Premarket Notification Application process or the Premarket Approval process. The Premarket Notification process, also called the 510k process, is used when the new medical device can be shown to be substantially equivalent to a currently marketed device, called the predicate device. If a new medical device is not substantially equivalent to a currently marketed device, then it must be reviewed and approved for marketing by FDA through the Premarket Approval (PMA) process. If any clinical trials are to be conducted with the new medical device, this must be done under an Investigational Device Exemption (IDE).

The route of approval for drugs is usually through the New Drug Application (NDA) process. Any clinical trials to be conducted with a new drug are done under an Investigational New Drug Application (IND). Spermicides are drugs, but fall into a special category of products that are subject to the specifications for formulation, testing, and labeling contained in a monograph. Thus, currently marketed spermicides have not gone through the NDA process, but FDA is now reviewing the need for this activity.

With the increased concern about transmission of sexually transmitted diseases, including HIV, there will be greater scrutiny by FDA before approval of any barrier, spermicide, or combination thereof which claims to prevent sexually transmitted disease in addition to preventing pregnancy.

Measurement of Efficacy

The evaluation of new barrier methods includes the assessment of several indicators of effectiveness. These include post-coital test results, condom breakage and slippage rates and pregnancy rates. Currently, slippage and breakage data are collected as secondary indicators of efficacy in pregnancy studies. With convincing clinical data on the relationship between pregnancy and condom failure the requirement for pregnancy data may be dropped. Should FHI prioritize collecting data which examines this relationship?

Three types of cumulative pregnancy rates are measured. The typical use rate is the accidental pregnancy rate among women who consider the method to be their primary method of contraception, regardless of whether they are using the method according to instructions during every act of intercourse. These rates are usually considered the primary measure of effectiveness in pregnancy studies. The consistent use rate is the accidental pregnancy rate among women who are using the product during each act of intercourse, regardless of whether they are using it correctly. The perfect use rate is the accidental pregnancy rate among women who are using the product according to instructions during every act of intercourse. Should FHI incorporate methodologic objectives into clinical studies which might demonstrate how more valid data on consistency and correctness of use can be collected?

Clinical studies need statistically justifiable sample sizes appropriately linked to the study objectives. Pregnancy studies usually have two efficacy objectives. The first is to provide a reasonably precise estimate of the typical use pregnancy rate for a new method. The second is to demonstrate the typical use pregnancy rate for a new method is not substantially worse than the rate for a similar, marketed product.

When there are concerns about the potential for heterogeneity of results across subgroups, the statistician's solution is to plan for sufficient sample size to meet study objectives within each of the important subgroups. However, the time required to recruit adequate numbers of subjects for barrier studies is quite lengthy and a prolonged recruitment period may delay a useful product from reaching the market. Should we do further research to investigate potential subgroup differences for marketed products and should we invest in larger studies to learn more about subgroup differences for new products during development?

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Latex vs. Roll-on Plastic Condom: Proposed Study Design

Gaston Farr, Associate Director, Clinical Trials Division

This talk will provide a brief summary of the design of Family Health International's proposed study comparing a marketed latex condom with our Roll-on plastic condom. The objective of the study is to demonstrate that the contraceptive effectiveness of FHI's Roll-on condom is substantially equivalent to a marketed latex condom. The primary outcome variable is accidental pregnancy. The trial will be a prospective, parallel group, randomized study done in 6 to 8 centers. The scheduled follow-up period is 28 weeks.

The size of the study population will be based on an assumption of a 12-month expected pregnancy rate for typical use of latex condoms of 12-16 per 100 women, or an expected 6-month rate of 7-9 per 100 women. The enrolled study population will be at least 326 couples per group. If the 6-month pregnancy rate in the control group (latex condoms) is equal to 8 per 100 women, the planned sample size of 326 couples per group is considered sufficient to detect an absolute difference in pregnancy rates of 7 per 100 women, i.e. 15 per 100 women for the Roll-on condom. This size study will have 90% power for a one-sided test, assuming an attrition rate of 30%, and a significance level of 0.10. This design has been reviewed by the FDA.

A major issue for this study is how to recruit couples rapidly. Given FHI's experience with recruitment of participants for previous barrier method studies, it is possible that it could take as long as two years to recruit the number of couples needed. FHI is considering a small operational research study of various approaches for recruitment strategies to improve this process. Another recruitment issue is the proportion of couples with recent condom experience. In order to be able to pool data from the 6 or 8 centers, it is important to have similar proportions of experienced users at different centers.

A number of instructions are included with standard latex condoms that may not apply to the Roll-on condom. FHI is considering a simplified set of instructions. This may be an important issue for this protocol, because the instructions used during this trial may be the ones the FDA would require when the Roll-on condom is marketed. There are two standard instructions used with latex condoms that may not be needed with the Roll-on condom: 1) there is no tip in the Roll-on condom, so the usual latex instruction to press the air out of the tip is not appropriate, and 2) there is no need to instruct uncircumcised men to pull back their foreskins before donning the Roll-on condom, because it is loose fitting.

FHI would appreciate any comments on our proposed design, and would especially be interested in your suggestions regarding: 1) recruitment strategies and 2) condom instructions.

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Spermicides and Microbicides

Progress Report on Barrier Use and STDs

FHI has done a great deal of work to measure the contraceptive effectiveness and the acceptability of vaginal methods. In the Contraception and STD Unit of the Contraceptive Use and Epidemiology Division, we have several active or planned studies to look at the associations between use of various barrier methods and the risk of STDs.

1. Under way in the Dominican Republic is a study to measure the relative effectiveness of spermicidally lubricated *versus* plain lubricated latex condoms. Since the cost of spermicidal condoms is greater than that of plain condoms, we would like to know whether that higher cost is justified by better protection against cervical gonorrhea and chlamydial infection.
2. Another study is following couples at high risk of HIV infection in Zambia who are given latex condoms, N-9 film and female condoms. This study is not designed to measure the prophylactic effectiveness of the barrier products, but focuses instead on behavioral issues. Its objectives are to measure the consistency of use of the three barrier methods; evaluate the acceptability of the female condom among these high-risk couples; and identify determinants of long-term use of the three products.
3. We plan to study the prophylactic effect of the female condom in one or more sites. These randomized studies will compare infection rates in a group assigned to use male or female condoms compared with infection rates in a group assigned to use male condoms only. This design will allow us to measure the epidemiologic association between female condom use and cervical infection, as well as evaluate the impact on male condom use of female condom promotion.
4. All those interested in HIV prevention agree that women at risk of infection desperately need female-controlled methods that prevent sexual transmission of the virus. We have conducted two studies that found that nonoxynol-9 reduces the risk of HIV infection, but the studies had important design limitations. Another study done in Kenya found that the N-9 sponge did not reduce the risk of HIV, so HIV programs remain in the dark as to whether they should recommend use of N-9 products when condoms are not used.

We plan to conduct a study of the relationship between use of N-9 film and the risk of contracting HIV infection. Ron Roddy has had approved a randomized controlled trial of N-9 film use by sex workers. Latex condoms will be given to all participants and condom use will be accounted for in the analysis. Unfortunately, the study has not yet received funding from the NIH, although we expect to be funded soon. In addition to measuring the effect of N-9 use, we will also evaluate the frequency of genital irritation and its impact on HIV infection.

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N-9 and Iodine Vaginal Products: Recent developments

Dr. David C. Sokal, Associate Medical Director
Clinical Trials Division

I. Introduction

This talk will provide a brief update on some two areas relating to the development of vaginal microbicides. The talk will briefly discuss the speed of dissolution and the persistence of different spermicidal preparations, and will present some provocative data on a unique advantage of Betadine as a possible vaginal microbicide.

II. Dissolution of Vaginal Contraceptive Film (VCF) and Vaginal Foaming Tablets

There is presently no standard method to measure the rapidity of dissolution of vaginal spermicides or microbicides. We have begun work on such a method. For this pilot protocol, we will compare different methods corresponding to different levels of fluid or moisture. We have developed methods for testing of vaginal preparations based on minor modifications of standard methods used for pills. Of related interest, a recently approved spermicide called Advantage 24 can reportedly be inserted up to 24 hours before sexual intercourse.

III. The in vitro Effect of Low Concentrations of Povidone Iodine on Bovine Papilloma Virus

In collaboration with Paul Hermonat PhD, a virologist at the Univ. of Arkansas for Medical Sciences, we tested the effectiveness of Betadine against papilloma virus. Approximately 90% inhibition of papillomavirus growth was demonstrated with a 15 minute exposure to 0.1% betadine and 99% inhibition with exposure to 0.3% betadine. Complete inhibition was shown at levels of 0.6% and above.

The concentrations of Betadine which were effective in this study are much lower than the 10% concentration used in the suppository and gel formulations which are available OTC. Betadine is also spermicidal and effective against HIV in-vitro, but it has a number of limitations.

Questions for the TAC:

1) What importance would you give to following up our preliminary work on the dissolution speed of vaginal compounds?

2) Given the provocative data we have generated on the sensitivity of papillomavirus to Betadine, what should we do next?

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Agenda Item 8

Date/Site of 1995 Meeting

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1995

JANUARY							IMPORTANT DATES							JULY								
S	M	T	W	T	F	S								S	M	T	W	T	F	S		
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15	16	17	18	19	20	21	16 Martin Luther King, Jr. Day	16	17	18	19	20	21	22	16	17	18	19	20	21	22	
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25	26	27	28	29	30	25 Christmas Day	31															

1995
Annual TAC
Meeting

Please consider a set of the following dates for the 1995 annual meeting to be held at FHI:

Wednesday/Thursday, June 28/29

Wednesday/Thursday, July 12/13

Wednesday/Thursday, July 19/20

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