

PD-ABE 045

76901

DIRECTIONS

FYs 1990/1991



FAMILY HEALTH INTERNATIONAL • Durham, NC 27713 USA

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INTRODUCTION

The rapid fall of fertility observed in many countries and data from the Demographic and Health Surveys document a strong demand for family planning services. Based on research conducted by staff of Family Health International (FHI), it is both necessary and achievable to work towards a doubling of the number of contraceptive users in Third World countries (excluding China) in the 1990s. The forcefulness and realism with which family planning resources are used in this critical decade will help to determine whether the world reaches a stable population of close to 10 billion or nearer to 15 billion. This, in turn, will have a profound impact on the rate of environmental degradation due to human activity in the 21st century. At a health level, if we fail to make family planning universally available as quickly as possible, then there may be more induced abortions and more maternal deaths in the 1990s than in any other decade in human history.

The challenge to respond quickly and drive programs forward rapidly is, if possible, even more evident in the case of the spread of AIDS than in family planning. Efforts to slow AIDS will have the biggest payoff if applied early in the epidemic.

FHI sees its work as responding to the vast and urgent challenge to expand family planning and AIDS prevention services. A major part of our work is increasing the availability and use of safe and effective contraceptives and preventing sexually transmitted diseases, especially HIV infection. We have a strong commitment to reducing reproductive health problems, including maternal morbidity and mortality and reproductive cancers. In carrying out our programs, we give priority to strengthening and transferring the skills and capabilities that will enable colleagues in the developing world to address these problems in their own countries.

Our work is funded, primarily, by the U.S. Agency for International Development (A.I.D.). A Cooperative Agreement with A.I.D.'s Office of

Population supports a wide range of research and technical assistance to improve family planning options. A second Cooperative Agreement with A.I.D.'s Office of Health funds activities to prevent and slow the spread of AIDS. Our funding from A.I.D. is supplemented with support from a number of foundations, the National Institutes of Health (NIH), the World Health Organization (WHO), as well as with funds generated by Clinical Research International (CRI), a separate, for-profit company established by FHI in 1986.

FHI carries out its programs with a multidisciplinary staff of professionals who work in close collaboration with colleagues in more than 50 countries. Our staff are organized into six program divisions that correspond to the areas of technical emphasis and methodological approaches used. However, a high degree of interdivisional collaboration and coordination through working committees, task forces, and joint projects serves to bring a wide range of skills and expertise from all divisions to the implementation of specific strategies.

The great majority of the work that needs to be done to increase the use of family planning in the next decade will involve current methods of contraception made available through well understood channels of distribution. Even small improvements in the efficacy of widely used methods will have a significant numerical impact. For example, the Program Evaluation Division (PE) intends to accelerate its important work on the use compliance of oral contraceptives. We have already demonstrated that many providers of contraception are ignorant of key facts in pill use and that users make frequent mistakes. We also know that pregnancy rates among pill users in many countries are many times higher than those that are theoretically possible. PE's action oriented research should be able to improve this situation. The proximate variables controlling fertility also require continued attention and the PE Division will give priority to testing the "Bellagio" guidelines on breastfeeding as a contraceptive.

All reasonable channels of contraceptive distribution--especially condom distribution--will have to be enlarged. FHI will continue to give attention

to voluntary sterilization, intrauterine devices and the interaction between these technologies and the infrastructure necessary for their distribution. Increased emphasis will be given to increasing postpartum contraception. FHI has formalized the important area of contraceptive introduction as a priority program within the Field Development and Training Division (FDT), which also has responsibility for FHI's institutional strengthening and information dissemination programs.

The work that the Clinical Trials Division (CT) is doing on new methods of contraception, particularly sustained release of systemic active contraceptive steroids, will produce methods with lower failure rates than those currently available. In turn, this will have an important effect on the number of unintended pregnancies and be one further step towards reducing the many millions of induced abortions occurring around in the world. In 1990, we expect to see the start up of the NET-90 injectable program which was interrupted in 1989 due to problems of formulation.

Numerically, FHI's most important contribution to new methods of contraception could result from the current efforts to develop plastic condoms. Enormous quantities of condoms will be required in the 1990s, both to meet the need for family planning and to control the spread of sexually transmitted diseases, including AIDS. With major support from A.I.D. and some use of corporate resources, FHI is making an important investment in the development and testing in human use of plastic condoms. This is an area of such importance that FHI has created a new Materials Technology Division (MT). FHI's strategy is to evaluate a variety of designs which are compatible with the materials chosen and the limitations of manufacturing techniques, and then to test these for acceptability with panels of volunteers in various parts of the world. FHI's goal is not to replace latex condoms with plastic ones, but to offer one or more additional choices which will lead to an increased prevalence of use of barrier methods of contraception at this critical time. Parallel with the work on plastic condoms, an important endeavor is under way to correlate the quality assurance tests that are performed on latex condoms with breakage during actual use. This key piece of research has not previously been attempted.

In the last analysis, contraceptive use is always a personal decision by an individual. All decision-making requires consideration of advantages and disadvantages, and family planning choices are no exception. Women and men who use contraception, and their health care advisers, need information to help them choose which contraceptive method is best for them. In addition to selecting a method which suits their contraceptive needs and plans, women (and couples) require information on noncontraceptive effects that may influence their decisions. The whole of FHI contributes to this process, but the Reproductive Epidemiology and Sexually Transmitted Diseases Division (RESTD) has a particular responsibility in this area.

The AIDSTECH Division has now developed more than sixty projects in over forty countries and the Cooperative Agreement with the Office of Health at A.I.D. has been supplemented with funds from a number of bilateral agreements through USAID missions. FHI is using corporate resources to explore the challenge of dealing with HIV transmission in countries, such as India, where AIDSTECH is not able to work. FHI has also broken new ground by establishing a joint initiative with the International Planned Parenthood Federation, financed by the United Kingdom Ministry of Overseas Development, targeted at work nongovernmental organizations can do in the field of AIDS prevention.

All FHI's activities in AIDS continue to emphasize the importance of slowing HIV transmission among groups who practice high risk sexual behaviors, although AIDSTECH also has extensive programs dealing with transmission through the blood supply. AIDSTECH continues its important program of information dissemination to decision makers and technical personnel in a variety of countries.

The RESTD, CT, and PE Divisions all have programs of work relating to AIDS prevention. In particular, FHI continues to pursue interactions between spermicides and sexually transmitted diseases in HIV prevention and important clinical studies are being implemented on the possible relationship between HIV acquisition and transmission and the methods of contraception.

FHI's work to estimate the costs of family planning in the 1990s has already contributed to new thinking and planning among international agencies and the donor community. This work will be deepened and expanded with funding from a variety of sources.

In all its work, FHI continues to be committed to international assistance as a partnership. We are fortunate to enjoy the help and collaboration of an ever-increasing network of colleagues around the world. We are privileged to work with institutions such as the Family Health Research Centers and we hope we can share our skills and experience as well as the excitement of learning from others--which is the ultimate reward of working internationally.

The goal of Directions is to categorize FHI's main areas of activity for the coming year. It is my hope that it will be useful to the FHI staff, to our network of colleagues around the world, to FHI's Board of Directors and the advisory committees on whose wisdom and leadership we depend. We are vividly aware of the critical nature of the work we attempt to do and we promise to be responsive to any criticisms or suggestions that may come out of reading Directions.

A handwritten signature in black ink, appearing to read "Malcolm Potts", written over a horizontal line.

Malcolm Potts, President FHI

AIDSTECH DIVISION

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AIDSTECH DIVISION

The AIDSTECH Division, funded through a Cooperative Agreement with A.I.D.'s Office of Health, is a partner with other A.I.D. programs and the WHO Global Programme on AIDS (GPA) in a worldwide strategy to strengthen the capacity of developing countries to confront the AIDS crisis. The goal of AIDSTECH is to prevent HIV infection and control the spread of AIDS by providing technical assistance, funding, training, research support, and information to developing countries to enable the implementation of their programs.

AIDSTECH works with national AIDS committees and with USAID Missions to identify the needs of host countries (in accordance with GPA-approved national AIDS control plans, where they exist). Support for AIDS activities is country-specific and depends upon local factors such as the extent and nature of host country requests for assistance, the nature and capacity of available infrastructures, the segments of the population at highest risk, the primary modes of transmission of HIV, and the prevalence and incidence of HIV infection. Priority is given to utilizing the existing infrastructures in health, nutrition, and family planning programs, especially those supported by USAID Missions.

The emphasis of the AIDSTECH program is on prevention, with three major program components:

- o prevention of sexual transmission through AIDS education, STD control and condom distribution,
- o prevention of blood transmission through technical assistance and training for blood screening programs, and
- o development of cost-effective and sustainable AIDS prevention programs.

AIDSTECH provides limited funding, as well as technical assistance and training, to establish and strengthen programs in these areas. Research and evaluation in program operations, blood screening technologies, health care

financing and epidemiology provide the basis for program development and sustainability. Regional strategies have been prepared for Africa, Latin America/Caribbean and Asia/Near East.

PREVENTION OF SEXUAL TRANSMISSION

The primary mode of transmission of HIV infection is through sexual contact, and AIDSTECH's first priority is to slow and prevent sexual transmission of the virus that causes AIDS. The strategy for accomplishing this includes:

- o identifying groups whose behaviors place them at high-risk for sexual transmission,
- o developing AIDS education programs targeted to those groups and their sexual partners,
- o promoting condom use and assuring accessibility of condoms through institutionalized distribution networks, and
- o improving the surveillance and control of other sexually transmitted diseases (STDs), especially those that are cofactors for HIV transmission.

In most countries, intervention programs with high-risk behavior groups begin as small pilot projects, many of them involving an operations research or evaluation component to give insights into the most effective program options to reduce high-risk behaviors and promote protective behaviors, such as consistent use of condoms. As experience is gained in working with high-risk groups, AIDSTECH assists local programs to plan and implement expanded interventions to reach an epidemiologically significant target population. Consistent access to affordable condoms is a key component of such prevention programs, and AIDSTECH encourages the development of social marketing programs to meet this need.

AIDSTECH's program to prevent sexual transmission also includes improving methods of STD surveillance and integrating components of the AIDS control programs into the primary health care system through clinics that provide STD treatment. The use of HIV surveillance to evaluate the impact of

intervention programs is not always feasible because of the large numbers of individuals who must be screened, especially in low prevalence areas, and associated difficulties with confidentiality and inadequate counseling resources for those who test positive. AIDSTECH, therefore, uses surveillance of other STDs as a tool to monitor and evaluate the effectiveness of interventions. There is also strong evidence that STDs, especially genital ulcer disease, are an independent risk factor for HIV transmission. With joint funding by GPA, AIDSTECH is developing a multicountry study to assess the impact of genital ulcer disease control programs on HIV transmission.

PREVENTION OF BLOOD TRANSMISSION

The demand for technical assistance to prevent HIV transmission through transfused blood continues to be high, and is AIDSTECH's second program priority. AIDSTECH'S strategy is to give assistance in:

- o strengthening national blood screening programs,
- o establishing cost-effective and efficient blood transfusion systems,
- o improving blood transfusion practices and reducing the number of inappropriate blood transfusions,
- o identifying appropriate methods for screening blood through evaluation of new technologies,
- o improving the competencies of laboratory technicians, and
- o establishing measures for effective supervision and quality control of laboratories.

Assistance to countries to develop programs to assure blood safety includes needs assessments, program planning, identification of equipment and supplies required, training of laboratory staff, and establishment of supervision and quality control systems. Measures, in addition to screening, are needed to assure efficient and sustainable blood safety programs. Such measures include reducing the number of blood transfusions

that are unnecessary or inappropriate and discouraging individuals who are, themselves, at high-risk of HIV infection from donating blood. AIDSTECH is also carrying out research on cost-reducing techniques, such as pooling several blood samples for screening.

Many developing country hospitals, especially those not located in major urban areas, do not have sufficient demand for blood screening to justify the expensive equipment and training needed to use ELISA and Western blot tests, but do need quick, simple, accurate and less expensive tests to screen blood, often on an emergency basis. AIDSTECH's research program has evaluated the use of new rapid screening assays under field conditions in Ghana, Kenya, Senegal and Zaire. Based on the results of these studies, many countries have already adopted rapid tests for screening and confirmation at substantial cost savings for their programs.

COST-EFFECTIVE AND SUSTAINABLE PROGRAMS

AIDSTECH is emphasizing AIDS prevention programs that are cost-effective and sustainable and is measuring the economic impact of AIDS. AIDSTECH's strategy is to give assistance in:

- o determining recurrent costs for AIDS intervention programs and planning for program sustainability,
- o comparing the cost-effectiveness of two or more intervention programs,
- o assessing the cost-effectiveness of different components within an intervention program, and
- o designing cost recovery programs for interventions.

As the AIDS epidemic continues to grow, the financial burden on already overextended health budgets in developing countries will become even greater as they attempt to mount and sustain effective prevention programs, as well as to provide care for individuals with AIDS. The AIDSTECH finance program recognizes that unique solutions that fit a particular country's resources and that are compatible with its public health policies and cultural

practices must be devised. Assistance to strengthen administrative infrastructures and improve program management includes financial planning, accounting, establishing management information systems, and developing cost recovery systems, where feasible.

Prevention and treatment programs must be as cost-effective as possible and AIDSTECH is developing simple cost-monitoring tools to enable program managers to track the costs of various components of interventions. Data generated by these systems will be essential in determining the usefulness and affordability of various intervention strategies and will provide the basis for planning for program sustainability.

RESEARCH

AIDSTECH works in close collaboration with our colleagues around the world to carry out programs in operations research, basic and applied behavioral research, epidemiological research, health care finance research and laboratory research.

- o A Postgraduate Research Fellows Program provides post-graduate training for United States researchers in developing countries while enhancing the developing countries' expertise in the field of behavioral research. The Fellows work with local country counterparts on research projects. Support is available for two fellows per year.
- o AIDSTECH, in collaboration with A.I.D. and several National Institutes of Health (NIH), is establishing a program that will:
 - support basic research that will provide information about high-risk behaviors and behavior changes related to HIV transmission, and
 - strengthen developing country capabilities to carry out behavioral research related to HIV transmission and prevention.

The program will provide grants to U.S. behavioral researchers to work in collaboration with developing country colleague in such areas as (1) reducing gaps in understanding the extent and nature of high-risk behaviors; (2) determining appropriate strategies to modify such behaviors; (3) identifying barriers and enhancers to behavior change; and (4) determining how to sustain behavior changes.

- o The operations research component focuses on answering key intervention program questions such as the short- and long-term impact of paying peer educators, providing free condoms versus charging for condoms, evaluating different condom distribution strategies and evaluating the impact of intervention programs.
- o The epidemiology research component focuses on evaluating the efficacy of spermicides and STD control in preventing HIV transmission.
- o The health care finance research component includes testing methodologies for measuring recurrent costs.
- o The laboratory research component includes evaluation of new screening technologies and effectiveness of blood pooling.

OTHER PROGRAMS

While AIDSTECH's approach is to concentrate its efforts in a few key countries of each region in order to have a meaningful impact on the epidemic in those countries, a variety of other programs and activities help to extend the limited resources available through AIDSTECH to as wide an audience in as many countries as possible.

AIDSTECH has developed a Small Grants Program to enable private voluntary organizations (PVOs) working in developing countries to apply for project funding. As resources permit, the small grants are funded to a maximum of \$50,000 each after approval by the relevant USAID Mission and the host country National AIDS Committee and review by AIDSTECH, AIDSCOM, and A.I.D./Washington.

In keeping with its mandate to inform USAID missions, national AIDS committees and technical experts about recent developments in AIDS, the AIDSTECH Division works with the Field Development and Training Division's information dissemination program to mail more than 850 information packages worldwide on a bimonthly basis, and contributes to the publication of AIDS information through the quarterly newsletter, network.

AIDSTECH supports participants from developing world countries to attend the annual International Conference on AIDS and selected regional AIDS conferences.

Training is one of the approaches AIDSTECH uses to strengthen local programs in AIDS prevention. AIDSTECH has adopted a "Train the Trainers" approach, training those in supervisory positions to initiate in-service training of those they supervise. Training is competency-based, assisting trainers to acquire, enhance, or maintain skills rather than knowledge transfer. Training activities encompass clinical and laboratory skills, program management, and information, education, and communications.

CLINICAL TRIALS DIVISION

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CLINICAL TRIALS DIVISION

The goal of the Clinical Trials (CT) Division is the enhancement of the quality of family planning programs by expanding the number of safe and effective contraceptive options.

To address this goal, the Division uses clinical trials methodology to carry out two major research approaches.

- o The CT Division focuses on the development and evaluation of new contraceptive products with the goal of obtaining FDA and other regulatory agency approval, product introduction and large scale use worldwide.
- o The CT Division conducts programmatic studies on approved contraceptives to give family planning providers clinical experience and information about the efficacy, safety and acceptability of these methods in different cultural and social situations.

DEVELOPMENT AND EVALUATION OF NEW CONTRACEPTIVES

In response to the need to increase the contraceptive options available to couples worldwide, the Clinical Trials Division has concentrated its development and evaluation activities on long-acting steroidal contraceptive methods as well as female and male sterilization procedures. Also, in recognition of the importance of spermicides and barrier methods for contraception and prevention of sexually transmitted diseases, the Division is testing a variety of new products.

Long-acting Steroids

The first priority of the CT Division is to develop one or more effective, long-acting methods of contraception that do not require daily decision making for continued use, and that are easily reversible. The products the

Division is currently studying are NET (norethindrone) implants and NET-90 injectables. CT is also sponsoring multicenter studies of the NORPLANT^R implant developed by the Population Council.

- o **NET-90 Injectables:** FHI is studying a biodegradable injectable formulation of the progestin, norethindrone (NET), encapsulated in a polymer matrix and formed into micronized spheres. The injection is intended to last 90 days and deliver good efficacy with less than half the equivalent steroid of other available injectable contraceptives. Phase III clinical trials of the NET-90 injectables were initiated in October 1987 and all sites were fully operational by mid-1988; however, in the Spring of 1989, the trials were canceled because serum concentrations of norethindrone during Phase III trials were lower than the NET levels considered necessary to inhibit ovulation in the majority of women. The manufacturer, Stolle Research and Development Corporation, has developed a new formulation of NET-90 microspheres to improve on the release level of the original batches. It is anticipated that a new Phase I pharmacokinetic study will start in the Spring of 1990, leading to expanded Phase III trials of this product in early 1991.

- o **NET Implants (Annuele^R):** FHI has been studying a 12-18 month biodegradable implant, composed of norethindrone (NET) and cholesterol, with the brand name Annuele^R, produced by Endocon, Inc. The implants can be removed at any time, if necessary, and are inexpensive to manufacture. The Phase I clinical trials of three dosage levels of the product, initiated in March 1987 and conducted among 35 women at the CONRAD program, is nearing completion. The results to date show that the serum NET levels of one of the three implants manufactured under automatic conditions approximates the NET levels of the original hand-made implants used in an earlier Phase II study. However, experience with other long-acting norethindrone contraceptives has shown that higher NET serum levels are necessary to obtain adequate contraceptive effectiveness. Consequently, the manufacturer, Endocon, has been reformulating the implants in order to obtain higher serum NET levels that will last for a longer period of time.

Endocon has prepared implants that contain a higher ratio of NET to cholesterol than those previously used. Implants with increased NET content are expected to release the norethindrone faster and produce higher serum NET levels. Serum levels can also be raised by increasing the surface area or the number of implants inserted. Following in vitro testing of new formulations, several formulations will be selected for an 18-month, Phase I study scheduled to start by mid-1990.

- o **NORPLANT^R:** FHI-sponsored multicenter clinical trials of NORPLANT^R, the contraceptive implant developed by the Population Council, are continuing at 43 sites in 12 countries. FHI has prepared country-specific reports intended to provide local policymakers and family

planning experts with information on the clinical use and acceptability of NORPLANT^R in their own countries for the purpose of considering regulatory approval. Data have been collected on over 8,000 insertions and all acceptors are being followed up every six months until removal of the implants or until the 5-year use effectiveness period is reached. Due to the high acceptability of NORPLANT^R and increased demand for the method, FHI has expanded the trials in selected centers, while at the same time helping to build the infrastructure for wide scale distribution when local regulatory approval is obtained. As a direct result of FHI's efforts, NORPLANT^R subdermal implants have now been approved for programmatic use in Bangladesh, Haiti, Nepal and Sri Lanka.

FHI also is using funds from the Andrew W. Mellon Foundation to collaborate with the Population Council and the World Health Organization in a postmarketing surveillance (PMS) study of NORPLANT^R, which began in 1989. The study will include 7,500 NORPLANT^R users and an equal number of comparison subjects in 6-10 countries. FHI is funding the projects in Bangladesh and Sri Lanka. With support from USAID/CAIRO, FHI is also providing technical support to the Egyptian Fertility Care Society to conduct a 2,000-subject cohort study that will be incorporated into the larger PMS study.

Surgical and Nonsurgical Sterilization

The Division also gives high priority to evaluating new methods of female and male sterilization that are appropriate for the developing world. Surgical sterilization procedures currently under study include the Filshie Clip and no-scalpel surgical vasectomy. CT continues research in the difficult, but potentially important, area of nonsurgical female sterilization. The goal is to develop a simple, inexpensive, noninvasive method associated with minimum morbidity that medical or paramedical personnel can safely offer in large-scale programs. CT is investigating the use of quinacrine hydrochloride as well as iodine for nonsurgical female sterilization.

- o **Filshie Clip:** The efficacy and safety of the Filshie Clip for female sterilization was evaluated in noncomparative trials in Britain, Canada

and Mexico. Comparative trials of the Filshie Clip's performance in relation to other methods of occlusion, the Wolf Clip, Falope^R ring and Pomeroy method, were conducted in Asia, Latin America and Africa. The Filshie Clip was also compared to bipolar electrocoagulation procedures in Europe, Korea and Taiwan. These comparative trials are the basis for FHI's application to the USFDA for a Premarketing Approval (PMA). The Division is in the process of preparing the application and submission is planned for mid-1991.

Related studies to detect any carcinogenic effects associated with the Filshie Clip or to the Falope^R Ring have been completed in two rodent species. Microscopic histological examination of rodent tissues by two pathologists continued throughout 1989 and is being finalized in 1990.

- o **No-scapel surgical vasectomy:** The no-scapel (puncture and ligation) method of male sterilization, developed in China, has been evaluated in comparative trials with the standard incision and ligation technique of vas occlusion. Complication rates, acceptability and efficacy are being compared. Future studies are planned to compare cautery and ligation and to assess efficacy with the use of fascial interposition.
- o **Long-term safety of quinacrine:** FHI, with Mellon Foundation support, is sponsoring a long-term follow-up study of Chilean women who have been sterilized using transcervical administrations of quinacrine hydrochloride to determine long-term safety.
- o **Iodine for Nonsurgical Female Sterilization (NFS):** The FDA has granted FHI an IND to test an iodine formulation delivered to the Fallopian tubes via the FEMCEPT device, a balloon-tipped cannula designed to deliver a measured amount of the iodine mixture to each tube by extruding the mixture into the apex of the fundus. A 30-case Phase I study of iodine administered 24 hours before hysterectomy will be initiated in the US in 1990 to determine the safety of the procedure.

Spermicidal and Barrier Contraception

The increasing concern about AIDS and other sexually transmitted diseases (STDs) has resulted in additional research on barrier and spermicidal contraceptives. Nonoxynol-9, the active ingredient in most spermicidal products, has been shown to kill in vitro the various pathogens causing STDs, including the AIDS virus (HIV). In vitro tests also have demonstrated the impermeability of latex condoms to bacteria and viruses. Clinical data

have shown that condoms or spermicides provide significant protection against the traditional STDs. Thus, while barrier and spermicidal contraceptives remain an important component of contraceptive options, the role they play in reducing the spread of STDs has given them increased importance. The activities of the CT Division in this area fall into the following categories:

- o **Development of new spermicidal formulations:** The CT Division, with funding from the National Institute of Child Health and Human Development and A.I.D., has been studying D-propranolol, a membrane stabilizing agent, that has been shown, both in vitro and in vivo to be a potent spermicide. A recent study has also demonstrated that D-propranolol is bactericidal in vitro. In mid-1987, an IND was submitted to the FDA. Formulation of a suitable delivery vehicle for D-propranolol promises to be a fairly expensive and involved process and has been delayed because of problems in developing a stable formulation. This year, CT plans to conduct a comparative Phase I postcoital evaluation of the spermicidal properties of vaginal creams containing either D-propranolol or nonoxynol-9 to determine if D-propranolol has any advantage over N-9 in spermicidal potency or duration of action.
- o **Evaluation of new female barrier devices:** An Investigational Device Exemption (IDE) has been obtained to evaluate a new vaginal barrier device, Lea's Kap. A recent Phase I postcoital evaluation of Lea's Kap demonstrated its effectiveness in keeping sperm out of the cervix. Two tolerance studies will be initiated in 1990, partially funded by the Mellon Foundation. A comparative postcoital study of Lea's Kap and the Prentif cervical cap also will be initiated in late spring 1990.

The FDA has granted an IDE for study of the Reality Vaginal Pouch. A 350-case Phase II efficacy trial on this polyurethane female condom will be initiated at six sites in the United States, one site in Mexico, and one site in Dominican Republic by spring 1990. The project is a combined effort of CONRAD and FHI.

EVALUATION OF THE EFFICACY, SAFETY AND ACCEPTABILITY OF ESTABLISHED CONTRACEPTIVES

In recent years, the CT Division research effort on established contraceptives has focused on the evaluation of oral contraceptives and intrauterine devices. It also has been assisting in the programmatic study of barrier contraceptives.

Oral Contraceptives

The CT Division has coordinated and sponsored clinical trials to determine the efficacy, safety, continuation rates and reasons for discontinuation of different oral contraceptive (OC) formulations in developing countries. Clinical trials have focused on a wide range of combined oral contraceptives (COC) and progestogen-only oral contraceptives (POC). Data analysis will be completed by the Fall of 1990.

FHI's COC research program has consisted of four strategies:

- o Two strategies were designed to determine the impact of switching from a standard estrogen-dose COC to a low-estrogen dose COC on the experience of side effects and on continuation rates.
- o A series of trials addressed concerns about the effect of progestogen on lipid metabolism. This strategy compared women who took Loestrin, a COC with a lower dose of progestogen, with Lo-Femenal. Data analysis will be completed and reports based on data from the five participating centers prepared this year.
- o The triphasic COC, Triquilar, has been compared to a low dose COC to determine the appropriateness of these newly marketed COCs for developing country programs.

FHI has completed two major research strategies to address the use of progestogen-only oral contraceptives (POC) in lactating women.

- o The first strategy, a non-comparative clinical trial, had as its objective the wider distribution of POCs in areas where such pills were not being provided for breastfeeding women. Initial analysis has confirmed a high efficacy of POCs for lactating women, as well as showing low discontinuation rates.
- o The second strategy, comparing POCs with non-hormonal methods, helped assess the effect of the mini-pill on the breastfed infant and was carried out in three sites. Initial analysis indicates that there is similar, or less, reported complications or complaints in the POC user group than the non-hormonal group. Also, there were no significant differences on health indicators for infants of mothers receiving POCs and users of non-hormonal contraception (e.g. IUDs).

When to initiate progestogen-only contraception in lactating women remains a most important clinical and programmatic concern. The Division will initiate a clinical trial in the Fall of 1990 to address this issue.

Intrauterine Devices

The CT Division has recently completed a 10,000 case multicenter study comparing the Copper T 380A (TCu 380A) IUD with the IUD most commonly used in the country where the trial was conducted. The primary aim of this activity was the development of a worldwide TCu 380A database that will provide A.I.D. and family planning programs in developing countries with information on the safety and efficacy of this device. Data analysis and information dissemination activities will be completed in 1990.

- o Studies of the infection rates associated with the insertion of IUDs with or without strings were completed. Analysis indicates no significant differences between the two types of IUDs in terms of infection rates.
- o CT has collaborated with Nigerian investigators to evaluate the effect of prophylactic antibiotics administered one hour before IUD insertion on the incidence of pelvic inflammatory disease (PID) among a population of IUD users. Final analysis of data is under way.
- o In a small pilot study, women having a TCu 200 IUD inserted with the crossarm trimmed to a width determined by measurement of the fundus were compared with women using a standard TCu 200 IUD. The study is designed to determine if a carefully fitted T would be associated with fewer side effects or fewer removals and expulsion than with a standard T IUD. The study will be completed in late Spring 1990.
- o A study to evaluate the safety and expulsion rates associated with IUD insertion at the time of Caesarean section was recently completed. Data are currently being analyzed and preliminary results suggest that this procedure is safe and acceptable.

A high degree of interest in programmatic postpartum IUD insertion continues in family planning programs, Ministries of Health and USAID Missions in the

developing world. Immediate postpartum IUD insertion offers a number of advantages to women:

- o it is safe and convenient,
- o women are more motivated to accept contraception,
- o IUD use does not affect lactation, and
- o contraception is made available to women who may not be able to return to the clinic for an IUD at some later date.

CT plans to initiate noncomparative studies evaluating the safety, efficacy and acceptability of immediate postpartum insertion of the TCU 380A IUD in 1990. These clinical trials will be conducted in countries which express an interest in offering this contraceptive option to its clients. These trials will be conducted in conjunction with full-scale training and introductory programs developed by the FDT Division.

Barrier Contraception

The CT Division is supporting programmatic research on barrier contraceptives.

- o FHI is providing technical support to the National Research Institute for Fertility Control in Pakistan to conduct a comparative study of spermicides. An efficacy, safety, and acceptability trial of NeoSampoon and the foaming vaginal tablets containing nonoxynol-9 supplied by A.I.D. was initiated in September 1989 at ten centers.

SECONDARY ANALYSIS OF EXISTING DATA BASES

Through extensive clinical trials, FHI has accumulated large data sets for several contraceptive areas including IUDs, oral contraceptives, female sterilization and NORPLANT^R. These data sets provide the basis for the extensive secondary analyses that are conducted by the Division. They help FHI address practical issues and identify solutions to the problems faced by family planning providers, as well as serve to identify guidelines and future research strategies.

Using the existing data bases, the CT Division has been examining issues related to postpartum contraception: for example, the effectiveness and safety of the TCU 380A IUD inserted postpartum, as well as the optimal timing for postpartum sterilization.

Also, CT has been analyzing the effects of different contraceptive methods on lactating women and the relation of pre-existing health conditions and the choice of contraceptive method. Similar program oriented analyses will continue in 1990.

FHI has data on more than 14,000 cases of female sterilization spanning more than a decade. CT is examining practical issues that will orient future work in female sterilization. For example, planned analyses will determine the advisability of double clipping the Fallopian tube when bleeding complications and occlusion difficulties are encountered, as well as the possible different effects of the application of a tubal occlusion technique on different locations of the Fallopian tubes.

FIELD DEVELOPMENT AND TRAINING DIVISION

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FIELD DEVELOPMENT AND TRAINING DIVISION

The goal of the Field Development and Training Division (FDT) is strong Third World in-country capacity to plan, implement, and disseminate policy and program relevant research in the areas of family planning and reproductive health. The objectives that support this goal are:

- o to introduce existing and new contraceptive technologies to developing countries,
- o to strengthen reproductive health research organizations in developing countries,
- o to provide training and technical assistance in research methods and program management,
- o to disseminate research findings and reproductive health information effectively, and
- o to provide field support to the other FHI divisions as needed.

During the coming year, FDT will expand the contraceptive introduction and information dissemination programs, while maintaining the current level of effort in institutional development and training. Over the next two years we will implement our contraceptive introduction strategy in five to ten countries, beginning with an initiative on postpartum contraception. We will build on our past experience in information dissemination to develop curricula to train journalists in health reporting and to strengthen mid-level researchers' scientific writing skills, and we will conduct national and regional workshops on these topics.

FDT will focus its efforts in a few key countries in each region, selecting countries where FHI has program activities that require involvement by FDT staff and where we can make a significant impact on contraceptive use and reproductive health.

In 1989, FDT added a new associate director responsible for developing and implementing a strategy to help countries accelerate the introduction of new methods of family planning. The primary goal of the contraceptive introduction program is to facilitate the introduction of methods through the most appropriate service delivery systems. Program activities include:

- o developing national strategies in collaboration with local leaders involving government, NGO and private channels of distribution,
- o estimating costs and staffing needs,
- o facilitating government approval and product registration,
- o establishing policies on local production,
- o developing information and education materials,
- o sponsoring national and regional seminars,
- o strengthening provider training,
- o helping to establish commodities supply channels and effective, service delivery systems,
- o estimating the potential for cost recovery,
- o establishing user registries and surveillance programs, and
- o identifying programmatic and policy research needs.

The contraceptive introduction program draws upon both in-house and outside resources to implement its activities. Collaborative relationships with host country agencies, ministries of health, other international family planning organizations and private sector channels will support local capabilities to plan, implement, and sustain introduction projects. By projecting the costs of alternative strategies, FHI will help to develop and refine plans for the most cost-effective introduction through both government and private sector organizations. The contraceptive introduction program will work closely with FHI's Clinical Trials and Program Evaluation Divisions to formulate an overall strategy for selected products and to coordinate specific program activities.

During the current year, the major initiative of the contraceptive introduction program is to promote postpartum contraception and to encourage service providers to prescribe a wider range of methods during the postpartum period. FDT will work with other FHI divisions and other collaborating agencies to sponsor an international conference and several smaller regional meetings where family planning providers and policymakers will discuss and share information about the appropriateness of different family planning methods for postpartum women.

FDT is also helping to establish or strengthen existing regional and national programs, such as the Mexican Social Security System (IMSS), that emphasize postpartum contraception. FDT's contraceptive introduction program will utilize IMSS and other similar organizations as regional training facilities where clinicians from other countries can be trained in various postpartum technologies. In January 1990, for example, FDT funded a study tour of Turkish physicians to learn about IMSS's successful postpartum IUD program.

Over the next 1-2 years, the introduction program will also focus on the TCu 380A IUD and NORPLANT^R. Plans will be developed to introduce other new methods including the Filshie clip, NET-90 injectables, Annuelle biodegradable implants and plastic condoms as they become available through the work of other FHI divisions. New contraceptive developed by other organizations will also be considered for programmatic introduction.

INSTITUTIONAL DEVELOPMENT

All of FHI's divisions foster the development of strong research capacity through technical assistance and close collaboration with developing country researchers. The FDT program focuses on development of institutions in selected countries that share a common interest in family planning services, research, training and information dissemination. FDT's institutional strengthening approach is comprehensive and integrated. Our strategy

involves long-term assistance and collaboration, including core support, training and technical assistance, transfer of technology, and project funding. The selected institutions include non-government organization (NGOs), university departments, and government agencies. FDT is currently collaborating with ten such institutions, which we call Family Health Research Centers (FHRCs):

Indonesian Fertility Research Coordinating Board (BKS PENFIN)
Thailand Fertility Research Association (TFRA)
Bangladesh Fertility Research Programme (BFRP)
Egyptian Fertility Care Society (EFCS)
Family Planning Association of Sri Lanka (FPA/SL)
University of Nairobi, Department of Obstetrics and Gynecology
(UON/Kenya)
Malian Association for Family Planning (AMPPF)
National Center for Family Health of Niger (CNSF)
The Mexican Interuniversity Group for Epidemiologic Research in
Reproductive Health (GIMIESAR)
National Population Council of Egypt (NPC/Egypt)

The nature and structure of the FHRCs vary widely, but all of them operate at a national level and have the capability to influence national family planning policy and program decisions. FHI support is geared to the unique circumstances and needs of each program. Core support to cover some or all general operating costs, such as salaries, rent, and communications, may be granted for a finite period of time to provide a period of financial stability during which the organization can develop its technical and managerial capacity. As FHRCs gain research and management capabilities and experience, they are increasingly able to attract specific study and project contracts and grants from various sources. At this point, FHI core support may be phased out, although FHI funding for specific research and development activities may continue.

FDT supports the development of FHRCs through a broad range of training and technical assistance involving hands-on experience in addressing programmatic needs in the country. To date, training and technical assistance has focused on:

Clinical trials and other research methods
Data analysis

- Computer skills
- Information dissemination/research utilization
- Program planning and budgeting
- Financial management and accounting
- Fund raising

Program assessments are conducted periodically to measure progress and reassess program directions. Bilateral funding, through "add-ons" from the USAID Missions to FHI's Cooperative Agreement, is becoming an increasingly significant source of support for institutional development, reflecting the high priority attached to it by the Missions.

FDT also provides support to several national and regional scientific organizations in Latin America that play a leading role in reproductive health research and the dissemination of research findings in the region. FDT provides partial funding for these organizations' scientific meetings to help them promote the sharing of research and the development of appropriate health and family planning policies in the region.

FDT will continue its program of institutional strengthening in the current year, addressing the specific needs of each FHRC and, as resources allow, exploring options to develop additional FHRCs, especially in sub-Saharan Africa where contraceptive needs are great and the threat of AIDS is increasingly severe.

TRAINING

FHI fosters the strengthening of research skills of collaborating investigators, research staff, and program managers through formal and informal training, including workshops, seminars, individual training, technical assistance, and fellowships.

FDT has placed emphasis on conducting workshops in clinical trials, data analysis, and epidemiologic methods in order to transfer skills in FHI's areas of primary expertise. These workshops serve the complementary

objectives of strengthening local capacity as well as maintaining FHI's network of collaborating investigators. FDT has developed a standardized clinical trials research curriculum using a modular self-instructional format and participatory training approach. The curriculum is available in English, Spanish, French, and Portuguese. A related curriculum for more advanced training in clinical trials data analysis has been developed and field tested; it will be finalized in the next year. A training package on epidemiologic research methods has been produced in Spanish. The epidemiology curriculum is being refined and expanded in collaboration with the World Health Organization (WHO) and the Centers for Disease Control (CDC); it is anticipated that an epidemiologic research methods manual in English, French, and Spanish will be published and tested in several country workshops in 1990 or 1991.

FDT also sponsors and organizes workshops to meet local needs, train investigators and strengthen research centers in other areas of research design, analysis, management, and dissemination. Workshops are scheduled on the following topics in 1990 and 1991:

- Clinical trials methods
- Epidemiologic research methods
- Rapid survey methodology
- Qualitative research methods
- Computer training
- Data analysis
- Contraceptive technology updates
- Research utilization
- Scientific writing
- Family planning issues and health reporting skills for journalists

FDT sponsors investigators and program managers to attend conferences and external training programs considered important to their professional development and the success of their programs.

Specialized individual support also is offered through site visits by FHI staff and visits to FHI by collaborating researchers. In addition, the Sharon Camp Fellowship Program, which was inaugurated in 1984, provides

opportunities for one to two senior researchers per year to spend six to 12 months at FHI working on a reproductive health project of their choice.

INFORMATION DISSEMINATION

FDT's information dissemination program is designed to bridge the gap between the technical world of medical research and the information needs of health care personnel, policymakers, and consumers in developing countries. Although the specific problems in the use of research vary from region to region, the need for increased and improved research utilization exists throughout the developing world. Too often, important research findings receive only an initial announcement of study results, with no follow-up for program or policy implementation.

The single most important communications need in the 1990s may well be the need to ensure that existing contraceptive methods--especially oral contraceptives--are better understood by policymakers and potential users. FHI will continue to fulfill its obligation to A.I.D. and our international network of colleagues to provide objective data to assist in the interpretation of new findings, particularly adverse ones.

As part of this work, FDT provides international wire services and magazines with interpretive articles on contraception and reproductive health tailored to individual country needs, often using research data from the target country or region. USAID missions, collaborating investigators and the media are provided background information on controversial family health issues as they arise to enable our colleagues to communicate accurate information to the health community and the public.

FDT's information dissemination programs are aimed at the groups with which we work most closely--our network of collaborating investigators, family planning and health personnel, and sister research organizations.

FDT's information dissemination program includes:

- o regular publications, both scientific and non-technical,
- o "translations" of technical material into lay language, which are disseminated through the media in developing countries,
- o training of journalists on family planning issues and journalism skills to overcome obstacles to more accurate reporting on family planning,
- o transfer of database technologies and technical assistance in setting up family health libraries, and
- o training of researchers in scientific paper writing.

One important information dissemination tool is FHI's newsletter, network. The English version of network, now sent to 4,600 readers, covers a wide variety of reproductive and related health issues. Semiannual editions of network in Spanish and French reach an additional 6,000 readers.

FDT also sponsors the dissemination of research results and research ideas through the support of annual national meetings of investigators. In 1990, FDT will develop plans for consensus-building seminars to ensure that research is utilized in the development of family planning policy and improved service provision.

Little research has been done on the effectiveness of information dissemination programs. FDT will review, synthesize, and document the approaches to, and evaluations of, information dissemination systems which have been used by health organizations.

PROGRAM DEVELOPMENT AND SUPPORT

FDT supports the work of other FHI Divisions through collaboration on project development and implementation. FDT program officers are responsible for the coordination of FHI activities in specific countries.

In this capacity, FDT staff normally take the lead in the following activities:

- o liaison with USAID missions, government officials, and potential investigators,
- o the development of country or regional strategies where appropriate, and
- o the identification of local program needs and opportunities.

In addition, FDT program staff may assist other FHI divisions on specific projects by working with them on the development of project proposals, protocols, and subagreements with collaborating agencies, and the initiation, implementation, and monitoring of FHI studies and other projects.

MATERIALS TECHNOLOGY DIVISION

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MATERIALS TECHNOLOGY DIVISION

The Materials Technology Division was formed in late 1989 to provide better coordination and management of FHI's condom development and testing programs as a reflection of the level of priority given to this work by A.I.D. and FHI. The activities of the Division are grouped into two broad areas--development of a polyurethane condom and quality surveillance of latex condoms supplied by A.I.D. The Materials Technology Division is also responsible for coordinating related research on condoms, such as consumer preference studies and clinical trials, conducted by other FHI Divisions.

The expertise of the Materials Technology Division staff is wide-ranging and encompasses industrial experience in polymer science, product development, quality assurance and physical testing of medical products. This expertise permits the Division to focus on two major goals:

- o develop a new polyurethane condom that will have a better shelf life and be less subject to breakage than currently available products, and
- o conduct quality surveillance of latex condoms supplied by A.I.D. to developing world family planning programs and evaluate existing methods for assessing quality.

DESIGN AND DEVELOPMENT OF A POLYURETHANE CONDOM

FHI is embarked on an extensive research program to develop a condom that can be made inexpensively from thermoplastic elastomers by automated processes common to the plastics industry. A wide range of materials have been examined and novel designs constructed and tested to determine user convenience and satisfaction with the new products. Based on studies with volunteer users, FHI now has a patent pending on a design that was rated highly for convenience and acceptability. The Division is planning the following activities in the next twelve months:

- o Define manufacturing requirements, improve aesthetics, and seek ways to reduce costs while retaining the superior mechanical properties of the

selected thermoplastic film. If design changes result, their acceptability will be tested by panels of volunteer users.

- o Submit a 510(k) application to the United States Food and Drug Administration for approval to market the new device by July 1990.
- o Construct condom production equipment to be used for process and further product development and subsequently for large volume production. Several novel packaging ideas are being explored preparatory to machine construction. Installation of the equipment in a facility near FHI is planned for late spring and will be fully operational within three months.
- o Explore the possibility of improvements in the design and development of second generation products.

QUALITY SURVEILLANCE OF LATEX CONDOMS

The Materials Technology Division assesses the quality of latex condom stocks that A.I.D. maintains overseas and examines the physical stability of condoms stored under a variety of conditions. A high priority research activity for the Division is, through its clinical research component, to correlate the results of physical laboratory tests with breakage rates in human use. There are four basic programmatic areas:

- o field evaluations,
- o physical test development and accelerated artificial aging of condoms,
- o prospective aging of condoms (aging of condoms under field conditions), and
- o human use trials.

Field Evaluations

Distribution systems and storage facilities differ from country to country. Condoms collected from distribution systems in Mexico, Bangladesh, Nepal, Jamaica, and Egypt have undergone a range of laboratory tests. The majority of defective lots were discovered in remote areas beyond the regional warehouse level and in local pharmacies and clinics. When defective lots are identified,

the Material Technology staff notify the USAID Mission and country program requiring the proper disposal of the condoms. The Division will continue field evaluations by surveying condom stocks in approximately six different countries each year.

Developing Quality Assurance Tests and Accelerated Aging

FHI will continue to seek more reliable and convenient physical tests that are inexpensive, yet predictive of condom quality.

- o Modification of the water burst test and development of a tear test are under investigation. The performance of naturally aged, artificially aged, and new condoms in these new tests will be compared to their performance in the standard tensile, air burst, and water burst tests.
- o Laboratory methods and accelerated condom aging for research purposes are being developed. The effects of ultraviolet light, gamma radiation, elevated temperatures and ozone on the integrity of latex are being evaluated. The effects of lubricants, spermicides, and packaging will also be studied. A successful artificial aging method will make it easier to correlate the results of laboratory tests with breakage rates during human use.

Aging of Condoms Under Field Conditions

To determine the effects of climate and storage conditions on the quality of condoms, FHI is developing a prospective study on the aging of condoms. In a selected country, new condoms will be placed in a variety of specific climatic and storage conditions for up to five years. Samples will be lubricated with silicone, silicone containing nonoxynol-9 or water-based nonoxynol-9, and packaged in either plastic or foil. Samples will be withdrawn every six months and laboratory test data developed to determine the rate of deterioration.

Human Use Trials

Sites have been selected and a protocol developed to conduct human use trials to determine the predictive value of laboratory testing of condoms. Only volunteers using some other form of contraception and not exposed to STDs will test condoms retrieved from overseas warehouses. Data will be gathered on which condoms break during vaginal intercourse and when and where the breaks occur. These data will be correlated with mechanical test data from the same condom lots.

Based on the finding from the initial study, the protocol will be adjusted and the condom lots will be better defined. It is planned that the number of study sites and the total number of subjects will increase rapidly so that subtle differences in condom quality will be detected and the relative ability of the various laboratory testing procedures to predict failure in use will be established.

PROGRAM EVALUATION DIVISION

PROGRAM EVALUATION DIVISION

While new and improved methods of family planning are important to increase the options that individuals around the world have to achieve the number and spacing of children they desire, an equally important aspect is the way in which those methods are made available. The goal of the Program Evaluation Division (PE) is to improve, through research, the delivery of family planning services and the use of methods by consumers. PE staff employ a wide range of applied quantitative and qualitative research methodologies, but with a focus on population-based studies that complements the clinic- and technology-based research of other FHI divisions. As with other FHI divisions, PE emphasizes collaboration with and technical assistance to researchers in developing countries to improve local skills and capabilities for evaluative and programmatic research.

Research is conducted by the PE Division in five major areas of emphasis:

- o acceptability of contraceptive methods,
- o evaluation of family planning programs,
- o quality of care,
- o breastfeeding as a contraceptive, and
- o AIDS and family planning.

Most of PE's research is practical in orientation and directed toward enhancing contraceptive use. To assure that findings are disseminated widely, PE uses a variety of mechanisms, including scientific publications, conferences, workshops, and the popular media, as well as through individual presentations to policy makers and programs managers.

ACCEPTABILITY OF CONTRACEPTIVE METHODS

Contraceptive acceptability studies provide information on potential demand for a particular product, including who is interested in using the product and why. Findings of acceptability research can lead to increased acceptance, satisfaction and continuation of use of a family planning method. During the past few years, NORPLANT^R has been the major focus of acceptability studies, as this new technology has been introduced into family planning programs in several countries. Consumer and provider surveys have helped to identify sociocultural and service delivery obstacles that may impede NORPLANT^R acceptance and to reveal factors that make this new method an attractive contraceptive option.

The spread of the AIDS epidemic has led to increased concern about the acceptability of barrier contraceptives, especially condoms, that are being promoted as the primary method to prevent the sexual transmission of HIV. The current emphasis of PE's acceptability work, therefore, is on condoms, both male and female. A wide variety of latex male condoms are provided through A.I.D.'s commodity distribution program and PE has a number of completed and ongoing studies to guide A.I.D.'s procurement program. Issues for multicenter consumer preference studies include condoms lubricated with the spermicide, nonoxynol-9, stronger (thicker) condoms, colored versus non-colored condoms, and condoms of different sizes for particular populations, as well as packaging (plastic versus foil).

The female condom presents an important new choice for women, both for pregnancy and STD prevention. While efficacy studies of the female condom are being undertaken by the Clinical Trials Division, PE is carrying out acceptability studies of this new method. Thailand was the site for the first study, conducted during the past year, but requests from many countries have been received, and several additional acceptability studies are under development.

Acceptability studies conducted by the PE Division are also playing a key role in guiding the staff of the Materials Technology Division in the design and development of the polyurethane condom. Initial studies were conducted among FHI staff, but consumer preference studies are now under way in several centers.

During the coming years, PE's acceptability work will focus increasingly on other new methods being developed by FHI, with priority on the NET 90-day injectables and the NET implants.

FAMILY PLANNING SERVICES EVALUATION

Most developing countries have a substantial unmet demand for family planning services. Programmatic and evaluative studies carried out by the PE Division help to define the most appropriate and acceptable ways of delivering family planning services.

Studies to evaluate the performance of contraceptive social marketing programs (SMPs) include assessments of the degree to which SMP methods are substituted for those provided through other channels, market segmentation, price elasticity, the impact of introducing new brands, and contraceptive continuation, as well as the methodological issues involved in measuring impact of programs on fertility. During the coming year, PE will carry out an evaluation of the condom social marketing program in India.

In countries where family planning programs are a fairly recent development, many obstacles still prevent individuals from obtaining contraceptives. In these situations, improving the delivery of available methods is often more important than introducing new methods. Examples of PE research to reduce service delivery obstacles include an investigation of the impact of requiring expensive laboratory tests prior to provision of systemic (OCs and injectables) contraceptives in Senegal, and studies of providers' attitudes and their influence on the provision of services.

New family planning programs are often plagued with high rates of discontinuation. PE studies in several countries in sub-Saharan Africa are addressing this problem.

QUALITY OF FAMILY PLANNING SERVICES

Many developing countries have well-established family planning programs and relatively high levels of contraceptive prevalence. Research issues in such programs focus on improving the quality of services and the ways in which contraceptives are used. The PE Division has two major research components that address quality of care issues:

- o contraceptive compliance and use-effectiveness, and
- o informed choice.

User-dependent methods, such as oral contraceptives, often have disappointingly low use-effectiveness among the general population. Improvements in the use of OCs could result in millions of fewer unintended pregnancies. The PE Division has pioneered research on user compliance with OCs in non-clinical settings. Recently completed studies in Colombia and Egypt have shown not only the serious problems that women have in taking OCs correctly, but also revealed the limited knowledge of service providers regarding the correct use of pills. Continued work in this area will constitute a major effort of the PE Division in the coming years. PE will work with Demographic Health Surveys in a number of countries to collect and analyze data on OC compliance. Work is also under way with ORTHO Pharmaceuticals and APREX Corporation to test compliance using a computerized device inserted into the pill pack that provides precise information on the time when each pill is removed from the pack. Other research initiatives in the coming year include the development of a case-control study to determine the impact of poor compliance on unintended pregnancy, and to evaluate the degree to which improvements in compliance

will result in fewer accidental pregnancies. The impact of interventions with both consumers and providers to improve compliance will be evaluated.

FHI strongly supports A.I.D.'s policy of informed choice for voluntary family planning as a critical aspect of improving the quality of care in family planning services. The PE Division, with funding from A.I.D.'s Bureau for Program and Policy Coordination, is carrying out research to promote and implement informed choice in selected countries. Activities already completed include an extensive review of the literature on informed choice and diagnostic studies in two countries (Nepal and the Dominican Republic) where there is predominant use of one method of family planning (sterilization). During the current year, PE staff will prepare a policy paper on the importance of informed choice in family planning programs, and will support projects to develop and evaluate materials on informed choice for use in family planning programs, both at the clinic and provider level and from the user perspective.

BREASTFEEDING AS A CONTRACEPTIVE

PE's work in breastfeeding focuses on increasing our knowledge of the contraceptive effects of breastfeeding in order to inform women about how long they are protected by breastfeeding, when to start other contraceptive methods and which methods to use.

A multicenter study is under way, in collaboration with Georgetown University, to evaluate the effectiveness of concurrent breastfeeding and use of natural family planning (NFP). This study is an inquiry into the basic nature of the recovery of fertility in lactating women, as well as an assessment of the degree of protection that is provided by NFP during this important period in the reproductive cycle.

PE is exploring opportunities to evaluate the impact of breastfeeding promotion programs, particularly in countries where the prevalence and duration of breastfeeding are declining.

Following on earlier studies that investigated barriers to breastfeeding promotion in hospitals, several countries have begun hospital breastfeeding promotion programs. PE is developing studies to evaluate the cost implications of rooming-in as well as the impact of these programs on breastfeeding patterns.

Growing out of FHI's extensive work on lactational amenorrhea as a method of contraception, an international Consensus Conference on Breastfeeding as a Contraceptive was convened in Bellagio, Italy, in 1988. PE is developing a series of studies to evaluate the "Bellagio Consensus", which considers full or nearly full breastfeeding without resumption of menses to be 98 per cent effective during the first six months postpartum. The current studies will apply the same rigorous efficacy evaluation as has been applied to other contraceptives.

AIDS AND FAMILY PLANNING

Consistent with the need for effective public education programs to prevent the spread of HIV infection, PE has begun supporting projects on AIDS and family planning. This work includes the acceptability of male and female condoms described earlier, as well as efforts to evaluate the impact of AIDS on family planning programs and procedures, and the contribution of family planning programs to AIDS prevention.

In settings where family planning clients are at high risk of HIV infection, service providers need to take this risk into account in recommending contraceptives. The PE Division is planning studies to evaluate different approaches to risk screening for use in such settings.

AIDS prevention programs, including those run by family planning programs, must be evaluated carefully to determine their impact and cost-effectiveness. The PE Division has been involved in several pilot interventions to educate and provide condoms and spermicides to high-risk individuals, and collaborates closely with the AIDSTECH Division to develop approaches to evaluation of AIDS intervention programs.

**REPRODUCTIVE EPIDEMIOLOGY AND SEXUALLY
TRANSMITTED DISEASES DIVISION**

**REPRODUCTIVE EPIDEMIOLOGY AND SEXUALLY
TRANSMITTED DISEASES DIVISION**

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

It is the goal of the Reproductive Epidemiology and Sexually Transmitted Diseases Division (RESTD) to provide much-needed information on the benefits (disease prevention) and risks (disease promotion) of family planning methods. During the coming year, the Division will continue to emphasize the study of STDs, including AIDS. We seek to determine the extent of protection that barrier contraception provides against STDs and whether hormonal contraception increases susceptibility to HIV infection. Other areas of reproductive health that are of high priority include reproductive cancers, contraception for women with special needs, and morbidity associated with pregnancy and childbirth.

The Division concentrates its activities in the following programmatic areas:

- o AIDS,
- o other sexually transmitted diseases,
- o contraception and the risk of disease,
- o contraception for women with special needs, and
- o maternal health

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AIDS

Around the world, HIV is most commonly transmitted by means of sexual contact. Laboratory and epidemiologic evidence suggests that contraceptive use can alter the risk of transmission of the virus in much the same way that other STD organisms are affected. One much-quoted but still unconfirmed study found that oral contraceptive use increased the risk of HIV infection several-fold, while other studies have not detected this effect. Condoms are presumed to reduce the risk of HIV infection, but the magnitude of that reduction has not been determined. More research is needed to characterize the risks and benefits of contraceptive use, taking into account disease prophylaxis and pregnancy prevention. The Division's AIDS research program includes:

- o In Zambia, the Division is following HIV-discordant couples to determine whether barrier contraception can prevent HIV transmission. Couples making regular clinic visits to the University Teaching Hospital in Lusaka have been counseled on the use of spermicides and condoms. They maintain a pictorial coital log between visits and return for quarterly testing of the seronegative partner.
- o In Kenya, RESTD has begun a pilot case-control study to determine the association between recent contraceptive use and new HIV infection. Based in the family planning clinic of Kenyatta National Hospital in Nairobi, a cohort of seronegative women attending the clinic is being identified and will be followed for one year. When a seroconversion occurs, three controls will be selected from women scheduled to return to the clinic in the same period. This will permit us to ascertain the risk of incident HIV infection associated with oral contraceptive use among family planning clinic attenders.
- o Data on the protection against HIV infection offered by spermicides is sparse, and no consensus exists on whether to recommend spermicides to women at risk of HIV. To address this issue, the Division is conducting a prospective study of the effect of spermicides (and condoms) on the incidence of HIV infection in Cameroon.
- o Several studies have found that genital ulcers increase the risk of HIV infection. Many hypothesize that reducing the prevalence of genital ulcer disease would slow the spread of HIV infection. In some areas in Africa, the most common cause of genital ulcers is chancroid, which is often associated with prostitute contact. RESTD will conduct a chancroid intervention and evaluation project at three or four African sites, with funding from FHI/AIDSTECH and the World Health Organization.

The project will locate special nurses, outreach workers and clinics in the test neighborhoods to detect and cure chancroid infections. Control neighborhoods will receive a condom promotion program. The evaluation will consist of comparisons of chancroid rates in the test and control districts. Also, HIV prevalence rates will be compared in men with and without genital ulcers, and in men who come to the polyclinics for non-STD complaints.

- o The Division is planning to conduct a study to assess the effect of frequent use of nonoxynol-9 (N-9) on the vaginal mucosa. One of the greatest assets of spermicides is its safety, although nonoxynol-9 is occasionally irritating to mucus membranes and other tissues. There is concern that frequent use of N-9, by women with multiple sexual partners for instance, might be sufficiently irritating to foster acquisition of HIV. To address this issue, RESTD will conduct a study of irritation caused by an N-9 contraceptive suppository among women who are not at risk for pregnancy and who will be assigned randomly to use a vaginal lubricant suppository (placebo) or a 150 mg N-9 suppository.

OTHER SEXUALLY TRANSMITTED DISEASES

STDs have long been a major public health problem around the world and a leading cause of infertility and adult and infant morbidity. Modern contraceptive methods affect the risk of STDs. Oral contraceptives appear to increase the risk of lower genital tract infection with chlamydia, yet they may reduce the likelihood that such infection will ascend into the Fallopian tubes. IUDs increase the risk that vaginal and cervical infections reach the upper reproductive tract. Mechanical (condoms) and chemical (spermicidal) barrier methods inhibit the organisms responsible for most STDs. To refine measurement of the relationships between contraceptive use and STDs, several projects are currently under way or are planned for this year.

- o A clinical trial will begin in 1990 to test the effect of using Vaginal Contraceptive Film (VCF), an unobtrusive and inexpensive spermicidal product, on the incidence of gonorrhea and chlamydia in high-risk women in Bangkok, Thailand. The women will also be provided with condoms.
- o Cervical cancer is the most common cancer among women in developing countries. Not only does cervical cancer exhibit the epidemiologic characteristics of an STD, but certain types of human papillomavirus (HPV, the cause of genital warts) may cause or promote the disease. A

case-control study of hormonal contraceptive use and cervical cancer has been completed in Jamaica and data analysis is underway. The Division is now developing a study in Kenya to evaluate the effect of high parity on cervical cancer.

CONTRACEPTION AND THE RISK OF DISEASE

The Division has pioneered the development of a life-table model that takes into account the risks and benefits of oral contraceptive (OC) use on specific diseases and estimates the net effect of OC use on life expectancy. A streamlined analysis system that enhances the existing model is being developed. It will allow users to evaluate simultaneously the risks and beneficial effects of OCs on various causes of death. Work is in progress to incorporate, into the risk/benefit analyses, information on low-dose OCs in order to estimate the effect of their use on deaths caused or averted for each of nine broad categories of disease.

The Division plans to expand risk/benefit analyses to include developing countries. Based on local patterns of disease and OC use, we will be able to provide estimates of the number of deaths caused or averted by oral contraceptives in different countries.

We continue to use this analytic technique to evaluate the effects of newly reported associations between OC use and specific diseases. FHI is disseminating up-to-date perspectives on the Pill to users and health care providers. Projects include:

- o FHI has developed a corporate strategy for public service and information dissemination on breast cancer. The long-term aim is to provide women and their health care providers, as well as health planners in the U.S. and abroad, with information that will allow them to take this disease into account when making reproductive choices. Breast cancer is the first or second most common cancer in women worldwide and is increasing rapidly in countries undergoing economic development. Breast cancer incidence is related to diet, hormone profile, and reproductive patterns, including age at menarche, timing of childbirth and duration of breastfeeding. In addition, there are continuing unanswered questions about the long-term safety of oral

contraception in relation to breast cancer. The Division will monitor developments in this area and assist in disseminating information to colleagues in the developing world, as well as A.I.D.

- o RESTD has developed a case-control study of the association between breastfeeding and the risk of breast cancer. This is only the second study designed specifically to examine breastfeeding as a risk factor for breast cancer and will explore the issue more thoroughly than previous studies. A pilot study will start in Hong Kong.
- o Data analysis is underway on a cross-sectional study of osteoporosis and oral contraceptive use among North Carolina women aged 40-54. The study was conducted to test the hypothesis that oral contraceptives retard the osteoporotic process.
- o The Division will continue to keep abreast of new findings on the associations between contraceptive use and occurrence of other diseases, and will undertake studies as needed and where feasible.

CONTRACEPTION FOR WOMEN WITH SPECIAL NEEDS

In spite of advances in contraceptive safety, there remain certain groups for whom choice of an appropriate method is difficult. These groups include older women, teenagers and women with diabetes, heart disease, sickle cell disease and a variety of other diseases. Although contraindications to certain methods of contraception may be more common in these groups, so are the contraindications to pregnancy, making it imperative to find safe and effective family planning. The following projects are planned or active:

- o Premenopausal women are at risk of pregnancy, yet a large proportion do not use any method of family planning. Although there is a great deal of controversy about the advisability, and even the extent, of oral contraceptive use by older women, many doctors believe that their use is justified by generally healthy older women under a physician's care. Indeed, the U.S. Food and Drug Administration recently approved the removal of the upper age restriction for healthy, non-smoking women. We will seek to conduct a clinical trial of bone loss and oral contraceptive use by older women with no other contraindications to OC use.
- o Many doctors consider oral contraceptives to be contraindicated in women with sickle cell disease. These women are in special need of suitable contraception, since in countries where sickle cell disease is prevalent, childbirth is more than usually hazardous and few methods of

family planning are accessible. Several small studies suggest that hormonal methods may well be safe for women with sickle cell disease, and may even reduce the number of sickling crises. A placebo controlled cross-over clinical trial of the use of a low-dose oral contraceptive by women with sickle cell disease is underway in Jamaica. A study of NORPLANT^R use by women with sickle cell disease in Nigeria is being carried out with funding from the Rockefeller Foundation.

- o A study of the acceptability of three spermicidal products among young men and women attending an STD clinic in Lusaka, Zambia has just begun. The results will be useful for risk reduction strategies developed by the Zambia National STD Control Programme.

MATERNAL HEALTH

More than half a million women around the world die annually as a result of pregnancy and childbearing, 99% of which occurs in developing countries. FHI conducted the first large-scale efforts to obtain data on causes of death to women in a traditional society with the Reproductive Age Mortality Survey (RAMOS) studies. They were designed to determine the proportion of deaths to women of reproductive age due to pregnancy, childbirth, abortion and contraception. In Bali, Indonesia and Menoufia, Egypt, maternal mortality accounted for one quarter of all deaths to women of reproductive age. Maternal mortality was the leading cause of death to women of reproductive age in Bali, and the second leading cause in Menoufia. The risks of childbearing greatly outweighed any risks related to family planning; only 2% of reproductive deaths could be ascribed to contraception.

- o The burden of maternal morbidity is also great; it has been estimated that there are 15 serious morbidities for each death. With support from the Ford Foundation and A.I.D., RESTD will initiate a study to measure the prevalence of maternal morbidity in selected countries, determine the causes, and identify solutions that are feasible, effective and culturally acceptable. Standardized survey instruments will be developed in consultation with local clinicians and medical anthropologists, following focus group discussions with local women.