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PROGRESS REPORT

COOPERATIVE AGREEMENT NO. A.I.D./DPE-3050-A-00-8059-00

JULY 17, 1988 - FEBRUARY 28, 1989

THE POPULATION COUNCIL
ONE DAG HAMMARSKJOLD PLAZA
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POPULATION COUNCIL PROGRESS REPORT
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I. INTRODUCTION AND SUMMARY

INTRODUCTION AND SUMMARY

This is the first progress report on activities supported under Cooperative Agreement No.AID/DPE-3050-A-00-8059-00. The agreement provides support for a program in family planning services for the period July 17, 1988 through August 25, 1993. Programmatic areas supported under the agreement are contraceptive development, contraceptive introduction and management, and family planning program research, support and technical assistance. This report includes narrative progress reports and financial information for each in-house activity and subcontract supported under the agreement during the period July 17, 1988 through February 28, 1989. The progress reports and the summary of activities are presented by programmatic areas.

Contraceptive Development

Support was continued for contraceptive development projects involving subdermal implants, contraceptive rings, levonorgestrel releasing IUD's, LHRH analogs and high potency androgens, inhibin, gonadotropin surge inhibiting factor, and a New Drug Application (NDA) for NORPLANT^R. Other projects being supported are: an androgen binding protein kit, barrier methods, studies on the androgen CDB-1781, non-surgical male sterilization, and LHRH analog toxicology.

This work was carried out in-house and under subcontracts to other institutions. Comparative studies on NORPLANT^R and NORPLANT^R-2 continued at the Professional Staff Association of LAC/USC Medical Center (USA). The Professional Staff Association of the LAC/USA Medical Center continued studies on the use of contraceptive rings. Comparative studies on use-effectiveness and safety of levonorgestrel and TCu 380Ag IUDs also continued at this medical center.

A major advancement was accomplished in the development of NORPLANT^R implants with the submission of an NDA to the U.S. FDA in August, 1988. NORPLANT^R-2 has been reformulated to replace the elastomer that is no longer available. The new elastomer has the additional advantage that it can be manufactured by coextrusion. This could greatly reduce the manufacturing costs over the present method. Reformulation of contraceptive rings has also been accomplished. Efforts to complete the tasks

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necessary for submission of an NDA for the levonorgestrel releasing IUD have continued. Toxicology issues were addressed by a team of experts in preparation for the filing with regulatory authorities in Finland and the U.S. FDA in the near future. Progress has been made in the development of a single implant system that would ensure the delivery of LHRH analogs and other peptides for up to one year. Alpha- and β-B subunits of inhibin were successfully cloned. It was shown that the amino acid sequence of the β-A subunit was almost identical to human and porcine β-A subunits, and that isolated β-A subunit cDNA contained the complete sequence for the mature peptide. The efforts to prepare reagents for a rat androgen binding protein assay kit were nearly completed and the reagents are expected to be ready for shipment in the near future. The studies on the metabolism of the high potency androgens testosterone-trans-n-butyl-cyclohexane carboxylic acid identified several metabolites in monkey liver homogenates. For this purpose a highly sensitive and specific procedure for detecting compounds containing a carboxylic was established. This fluorometric technique may be useful also for quantitating other similar compounds.

Contraceptive Introduction

Current activities focus on two highly effective, long-acting, reversible contraceptives: NORPLANT[R] Contraceptive Subdermal Implants and the Copper T 380A Intrauterine device.

The Council seeks to prepare program managers and providers in developing the skills and information needed to satisfy users' needs as they relate to these new contraceptive methods. This program emphasizes collaboration, among the various divisions of the Council with other public sector agencies and with commercial organizations.

NORPLANT[R] is manufactured and distributed by Leiras Pharmaceuticals, an international company based in Turku, Finland. Regulatory approval for marketing or programmatic use has been gained in twelve countries. Filings have been made to regulatory authorities in several additional countries. A New Drug Application to the United States Food and Drug Administration (USFDA) was submitted in October, 1988. Pre-introduction trials have been conducted or are ongoing in 44 countries. Over 300,000 women have now used NORPLANT[R] in clinical studies, pre-introduction trials or as a distributed product.

Over the last two years, emphasis has shifted from initial training of providers in insertion and removal techniques and evaluation of effectiveness and safety in different settings, to study of user-and-programmatic needs for wide-spread use. Prototype training and informational materials for program managers, clinicians, counselors and users have been written, and a training curriculum is now being tested in selected countries. This package of materials will be produced and available for adaptation to specific country needs in 1989.

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In preparation for USFDA approval and wide availability through international procurement and distribution channels, the Council and its current collaborators are now developing joint activities with agencies involved in training, logistics, and service delivery management. In the next year, a priority will be to provide technical assistance in incorporation of the method into ongoing family planning programs in countries that already have an initial experience with the method. Securing regional and local financial resources will be critical to this endeavor. Another priority is to assist several new countries in Africa wishing to introduce the method. Introduction in Africa will require particular care because infrastructure for family planning service delivery is less well developed in that region.

The Copper T 380A is broadly available. USFDA approval was gained in 1984. Marketing in the United States began in 1988. In addition to private sector distribution throughout the world, the Copper T 380A is provided through the major public sector procurement and distribution channels that supply family planning programs in developing countries, including the United Nations Fund for Population Activities (UNFPA) and the International Planned Parenthood Federation (IPPF). More than eight million Copper T 380A IUDs from a number of Council-licensed manufacturers have been distributed in over 70 countries.

The Council and Program for Appropriate Technology in Health (PATH) previously collaborated to prepare prototype materials for clinicians and field workers. These materials have been updated. Additionally, PATH has developed guidelines for informed choice, a wall chart describing the method, and a flyer for policy makers. A package of these and other materials will soon be available for adaptation to regional or country needs. Furthermore, Family Health International (FHI) conducted pre-introduction trials of the device in several countries, affording leading clinicians the opportunity to compare the Copper T 380A with IUDs commonly used in family planning programs. Over the past two years PATH and the Council have provided technical assistance to programs in Bangladesh, Brazil, Colombia, and Egypt to develop country-specific and culturally-appropriate informational materials for decision makers, clinicians, field workers and new and potential acceptors. Each of these countries now has staff trained in how to prepare materials, and they also have sets of locally produced materials. In each instance, the previously-developed prototype materials were utilized, but adapted to local culture and medical practices.

We are currently developing an overall strategy to improve the quality of IUD provision, especially that of the Copper T 380A, to better serve womens' health needs.

In this program, we will stress a regional perspective because, although we believe that the Copper T 380A is an appropriate contraceptive option for women in most settings, special considerations must be taken in developing strategies to prepare service delivery systems that have specialized needs for safe and efficient inclusion of the new method.

Family Planning Program Research and Technical Assistance

The only activities begun during the reporting period were the continuation of ongoing work in Bangladesh, and a project in Peru to assess the impact on breastfeeding patterns of intensive training in lactation management.

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In Bangladesh, the Council continued its long-term collaboration with the ICDDR on the MCH-FP Extension Project. The major efforts of the Extension Project are now directed toward expanding efforts to disseminate important Project findings to policymakers. A series of briefing papers which summarize key Project findings have been developed and distributed, and Extension Project staff are providing direct technical assistance to the Ministry of Health and Family Planning in implementing key findings of the Project throughout the Government program.

In Peru, a project to develop and evaluate a set of public hospital-based interventions, including education of professionals in lactation management, designed to increase the duration of exclusive breastfeeding is being conducted at three public hospitals in Lima, Peru, through the Department of Pediatrics of Cayetano Heredia University. Health care professionals from Peru were trained in lactation management at the Wellstart/San Diego Lactation Program.

PROGRESS REPORTS ON IN-HOUSE ACTIVITIES, AWARDS, AND SUBCONTRACTS ACTIVE DURING REPORTING PERIOD

1. CONTRACEPTIVE DEVELOPMENT PROGRAM

No. AID/DPE-3050-A-00-8059-00

POPULATION COUNCIL IN-HOUSE PROJECT

CONTRACEPTIVE DEVELOPMENT PROGRAM - 1988/1989

Period: July 17, 1988 to February 28, 1989 Amount: $ 1,315,287

Approved by A.I.D.: February 28, 1989 Status: Expired

Purpose: To support contraceptive development activities pertaining to subdermal implants, the contraceptive vaginal ring, the levonorgestrel IUD, LHRH analogs and high potency androgen, inhibin, gonadotropin surge inhibiting factor, New Drug Application preparations, barrier methods, simple male sterilization, androgen binding protein kit, high potency androgen metabolism, and LHRH analog toxicity.

Subproject: Subdermal Implants ($200,247)

The preparation of a New Drug Application (NDA) for NORPLANT^R to permit consideration by the U.S. Food and Drug Administration has been completed and the NDA was submitted in August 1988. Phase III clinical studies comparing NORPLANT^R and NORLANT^R-2 are in their fifth year in the United States. These studies are necessary to provide U.S. data on the contraceptive effectiveness of these implant systems for the period of their expected life of five years. The weight of women in these trials has emerged as a correlate of effectiveness, with heavier women having significantly higher pregnancy rates than lighter women. The rates in large women are still low. Parallel studies comparing levonorgestrel levels in blood of women using the two dosage forms have also shown the effect of weight in that heavier women have lower plasma levels of levonorgestrel. Recent analysis revealed marked differences in the performance among heavier women according to the type of tubing used in the manufacture of NORPLANT^R. All women independent of weight who used softer tubing (with less inert filler) showed very low pregnancy rates through five years. Thus, trials with softer tubing will be extended from 5 to 6 years for all women.

Following the withdrawal of a component of NORPLANT^R-2 (Medical Grade Elastomer 382) by its manufacturer, attention was concentrated on reformulation of this implant. Substitutes for the elastomer have been identified. A major advantage of one of the elastomers is that it can be extruded with levonorgestrel, so that the cost of manufacturing could be greatly reduced over the present method.

Exploratory studies continued on implant forms that might provide protection with a single implant. Of the two steroids that have been under investigation, ST 1435 has been selected for futher development.

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Clinical trials in small numbers of women showed that ovulation was suppressed.

Subcontract:
CB88.21A/ICCR Professional Staff Association of the LAC/USC Medical Center ($61,708)

Subproject: Contraceptive Ring ($367,153)

Research efforts continued on progesterone rings for use in lactating women and on rings releasing norethindrone acetate or ST 1435 with or without ethynylestradiol. *In vitro* and *in vivo* tests showed that the reformulated rings had release rates that were virtually identical to those of the rings made with the discontinued elastomer. Studies are under way to identify the optimal dose of ethynylestradiol and the treatment regimen with the least side effects.

Subcontract:
CB88.22A/ICCR Professional Staff Association of the LAC/USC Medical Center ($108,439)

Subproject: Levonorgestrel Releasing IUD ($64,591)

The phase III clinical comparison of the levonorgestrel IUD and the Copper T Model TCu 380Ag is now in its sixth year. Both methods are highly effective. Measurements of levonorgestrel remaining in the device after six years of use indicate effectiveness for at least seven years. The analysis of data through six years indicates that the levonorgestrel-releasing device is perhaps the most effective long-acting reversible method devised. However, the elastomer that is no longer available for the production of NORPLANT®-2 is also a component of this IUD, which necessitates modification of the manufacture of the levonorgestrel IUD. Toxicology issues of this device were discussed by a team of experts in preparation for filing with regulatory authorities in Finland and for reports to the FDA.

Subcontract:
CB88.20A/ICCR Professional Staff Association of LAC/USC Medical Center ($40,472)

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Subproject : LHRH Analogs and High Potency Androgen ($147,235)

Phase I studies with the antagonistic and agonistic analogs of LHRH, LHRH-34 and LHRH-13 were continued in men. Effectiveness of the antagonist decreased with time in some subjects suggesting the possibility of antibody formation, which is being evaluated. Efforts to develop a gel-like delivery system were continued. Preliminary results suggest that it may be possible to obtain a system that would ensure that LHRH analogs and other peptides could be delivered from a single implant for up to one year.

Subproject: Inhibin ($91,422)

Following insertion of the double stranded ovine inhibin cDNA, into the host EcoRI site of the bacteriophage vector lambda gt10, the ram testicular cDNA library was screened for cDNAs cloning inhibin α, β-A and β-B subunits. Several positive clones for the α and β-A subunits were identified. The amino acid sequence of mature ram testicular β-A subunits was almost identical to that of human or porcine ovary. Since the β-A subunit cDNA contained the complete sequence for the mature peptide, this cDNA clone will be used for the expression of the ram testicular β-A subunit. Both human α and β-A subunits of inhibin have been expressed in a bacterial system.

Subproject: Gonadotropin Surge Inhibiting Factor (GnSIF) ($52,014)

A strategy for the isolation of GnSIF from porcine follicular fluid (pFF) and its separation from inhibin has been developed over the past three years. During the last year, efforts have been concentrated on adapting the purification method to a preparative level. GnSIF was isolated and purified from 10 liters of pFF by ammonium sulfate precipitation, Heparin-Sepharose chromatography, Affi-Gel Blue agarose chromatography, Concanavalin-A Sepharose chromatography, and anion exchange HPLC. The final product was sent to Dr. Gary Hodgen's laboratory for bioassays of GnSIF and inhibin in order to confirm separation of GnSIF from inhibin. Work is ongoing to further purify GnSIF to a degree suitable for physical chemical characterization and amino terminal sequence analysis.

Subproject: Androgen Binding Protein (ABP) Kit ($45,964)

Efforts to prepare reagents for a rat ABP assay kit continued. High titer polyclonal antisera were obtained and monoclonal antibodies suitable for assay requirements were tested.

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Several candidates were identified, and are undergoing the final testing for stability to purification, storage, and labeling with radioactive iodine. These final tests should be completed within one month and the reagents will then be ready for shipment.

Subproject: Barrier Methods ($16,578)

Three major leads were pursued: a) incorporation of sodium tetradecyl sulfate (STS) into a polymer that could be used in a diaphragm, b) development of a spermicide releasing fiber that could be incorporated into a diaphragm or cervical cap and c) evaluation of short-acting beta blockers as potential spermicides. STS is a surface active agent that has anti-acrosin activity. Initial studies were begun to incorporate the compound into a polymer formulation to be molded into a form that will serve as a vaginal barrier from which STS would defuse over a period of at least 24 hours. A study on the effects of STS on the AIDS virus, clamydia, and other sexually transmitted diseases, as well as its action on human sperm, has been initiated in Finland and at the Population Council.

A reference laboratory for HIV, anti-herpes, anti-clamydia and anti-viral agents in Finland has expanded to also test spermicidal agents. Studies on the release of nonoxynol-9 from coaxial fibers have been continued. The two most active beta blockers were sent to Finland to test whether they are active against the AIDS virus, clamydia, and other sexually transmitted diseases. Studies on their stability in vaginal fluid are ongoing.

Subproject: Non-Surgical Sterilization ($106,000)

The study was designed to test the efficacy of a percutaneous method for performing vasectomy. The method utilizes a device (Vasocclude) designed to puncture the scrotal skin, encircle the vas deferens and apply a series of non-crushing, locking metal clips on each vas. Arrangements have been made with a manufacturer to produce the Vasocclude and animal studies have been initiated in dogs. Semen analysis will be performed before vasectomy and weekly following vasectomy until azoospermia has been achieved. Vasa histology will be examined for presence of blow-outs or granulomas.

Subproject: Toxicity of LHRH analog ($97,310)

A ninety-day toxicology study of LHRH-34 in rats and rabbits has been completed and a final report has been submitted.

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Subproject: High Potency Androgen Metabolism ($118,541)

This project was aimed at evaluating the metabolism of the androgen CDB-1781 and its side chain ester moiety: trans-n-butyl-cyclohexane carboxylic acid (CDB-2725), monkey liver homogenates hydrolyzed CDB-1781 to testosterone and CDB-2725. The latter is further metabolized. In order to identify the various metabolites, a sensitive and specific procedure for detecting CDB-2725 and its metabolites *in vitro* has been developed by derivatising the compounds into highly fluorescent pyrenyl ester. This extremely sensitive technique may be useful also for quantitation of other compounds containing a carboxylic group.

Subproject: New Drug Application Preparation for Submission to FDA ($8,232)

The efforts to submit an NDA for NORPLANT^{R}-2 have been discontinued due to the unavailability of a critical component of NORPLANT^{R}-2 implants which percipitated the need for reformulation. Instead, major emphasis had been put on rapid submission of an NDA for NORPLANT^{R} implants. The NDA was submitted to the FDA in August 1988.

POPULATION COUNCIL SUBCONTRACT NO. CB88.21A/ICCR

To: Professional Staff Association of LAC/USC Medical Center
Los Angeles, California, U.S.A.

Period: August 1, 1988 to June 30, 1989

Amount: $ 61,708

Approved by A.I.D.: October 15, 1988

Status: Current

Purpose: To support the project entitled, "Comparative Use-Effectiveness of NORPLANT[R] and NORPLANT[R]-2 Contraceptive Subdermal Implants."

This comparative study began in August 1982, enrolling a total of 583 women to use one of the two implants. As of April 1989, there were still 62 women known to be using implants and 38 women (only 6.5 percent) are considered lost to follow-up. This study is one of the pivotal studies in the Population Council's submission to the FDA for approval of NORPLANT[R] capsules for commercial distribution by the FDA in May, 1989.

POPULATION COUNCIL SUBCONTRACT NO. CB88.20A/ICCR

To: Professional Staff Association of LAC/USC Medical Center
Los Angeles, California, U.S.A.

Period: August 1, 1988 to June 30, 1989

Amount: $ 40,472

Approved by A.I.D.: October 15, 1988

Status: Current

Purpose: To support the project entitled, "Comparative Use-Effectiveness and Safety of Levonorgestrel and TCu 380Ag IUDs."

This study initiated in January 1984, recruited 253 women for a period of five years. Performance to date has been excellent with respect both to continuation and pregnancy rates. Two users of the Copper IUD, and one user of the LNg have become pregnant accidentally: fifty women are considered still active, and another fifty-two are considered lost to follow-up as of April 1989. The study has been extended to seven years for the levonorgestrel releasing devices, and to ten years for the Copper T 380.

POPULATION COUNCIL SUBCONTRACT NO. CB88.22A/ICCR

To: Professional Staff Association of LAC/USC Medical Center
Los Angeles, California, U.S.A.

Period: August 1, 1988 to June 30, 1989

Amount: $ 108,439

Approved by A.I.D.: October 15, 1988

Status: Current

Purpose: To support the project entitled, "Evaluation of Candidate Vaginal Ring Formulations."

In an earlier study, several women experienced nausea during the first day of ring usage, presumably due to the initial high release of EE. It has been suggested that lowering the dose of EE by removal of the ring for a finite time period during the first morning of insertion might avoid the nausea.

NETA-AA rings were prepared releasing an average of 600 micrograms of NETA and an average of either 20 or 30 micrograms of EE. Two groups each comprising 30 subjects were enrolled for each of these two rings. In each of these two groups of 30 subjects, 15 are using the ring on the usual schedule of 3 weeks in and one week out. However, during the first cycle only, the other 15 subjects in each of the two groups are inserting the ring for eight hours, removing it for eight hours, and then reinserting it. After this procedure, they are then following the regular schedule for the remainder of the study. Blood analysis will be performed for NETA, EE, estradiol, and progesterone levels. We expect the study to conclude by September 1. At that time, it is expected that the optimum EE dosage can be selected, and that further studies will be planned.

2. CONTRACEPTIVE INTRODUCTION

- PRE-INTRODUCTION EVALUATION OF NORPLANT[R] CONTRACEPTIVE SUBDERMAL IMPLANTS

- INTRODUCTION OF THE COPPER-T 380A INTRAUTERINE DEVICE

POPULATION COUNCIL IN-HOUSE PROJECT

PRE-INTRODUCTION EVALUATION OF NORPLANT[R]

CONTRACEPTIVE SUBDERMAL IMPLANTS

Period: January 1, 1989 to December 31, 1990

Amount: $ 132,560

Approved by A.I.D.: Pending

Status: Current

Purpose: To facilitate the widespread availability and use of NORPLANT[R] contraceptive subdermal implants in family planning programs throughout the world.

The activities under this in-house project for the period January 1, 1989 - February 28, 1989 were included in the report of activities for the in-house project "Pre-Introduction Evaluation of NORPLANT[R] Contraceptive Subdermal Implants" under Cooperative Agreement No. AID/DPE-3005-A-00-3003-00. A copy of that report follows.

POPULATION COUNCIL IN-HOUSE PROJECT

PRE-INTRODUCTION EVALUATION OF NORPLANT[R] CONTRACEPTIVE SUBDERMAL IMPLANTS

Period: April 1, 1987 to March 31, 1988
Extended to December 31, 1989 (a)

Amount: $ 983,983
$ 164,480 (a)

Approved by AID: October 30, 1987
July 11, 1988 (a)

Status: Current

Purpose: To facilitate the widespread availability and use of NORPLANT[R] Contraceptive Subdermal Implants in family planning programs throughout the world.

The Council's contraceptive introduction program aims to facilitate wide availability and appropriate use of the contraceptive technologies developed by the Center for Biomedical Research, consistent with the goals of the Council's User Perspective and Quality of Care in Family Planning programs. The Council seeks to prepare program managers and providers in developing the skills and information needed to satisfy users' needs as they relate to such new contraceptive methods.

The NORPLANT® introduction program emphasizes collaboration among the various divisions of the Council, with other public sector agencies and with commercial organizations. A critical activity has been to coordinate activities of a team of collaborators from Family Health International (FHI), the Program for Appropriate Technology in Health (PATH), the Association for Voluntary Surgical Contraception (AVSC), World Health Organization (WHO), Leiras Pharmaceuticals and institutions in many developing countries.

Training of health care providers in countries wishing to introduce NORPLANT® is the highest priority of the program. Clinical or pre-introduction trials, in which leading clinicians receive the initial training and "first hand" experience in their own settings, are complete or ongoing in 44 countries. The preintroduction trial experience is being monitored in a joint database project by the Council and FHI. An evaluation of acceptor status and significant events (pregnancies and discontinuations) in preintroduction trials in 28 countries involving nearly 49,000 women was an important component of the New Drug Application to the United States Food and Drug Administration.

The development of prototype training and informational materials for managers, providers and users nears completion. A training curriculum, developed by an interagency group, is now being tested in selected countries. The first test was conducted by PATH and AVSC in Nigeria. A guide for Counselors was completed in English. Spanish and French versions will soon be available. A book, providing managerial guidelines for introducing NORPLANT® into family planning programs, was developed in collaboration with WHO.

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Research into the experiences and attitudes of NORPLANT® users, completed or ongoing in several countries, has provided important feedback to informational and training materials and in guidance for family planning management. The next phase of the user-oriented research program will address case studies of women who discontinue use of the method and clinic management practices that impact (either positively or negatively) on user satisfaction.

Introduction in Africa requires particular care because infrastructure for family planning service delivery is less well developed in that region. The preintroduction trials are near completion in Kenya, Nigeria and Zambia, and technical assistance is being provided to develop in-country training programs to prepare for wide distribution. A physician has been hired to backstop these activities and to support introduction programs in new countries.

Regulatory approval for commercial distribution or programmatic use of NORPLANT® has been gained in 12 countries. Submissions have been made in several countries and a number of approvals are expected in the next year. USFDA approval is expected in late 1989 or early 1990. In preparation for FDA approval and wide availability, through international procurement and distribution channels, the Council and its collaborators are now developing joint activities with agencies involved in training, logistics and service delivery management.

POPULATION COUNCIL AWARD NO. I89.02A

To: Instituto Chileno de Medicina Reproductiva (ICMER)
Santiago, Chile

Period: January 1, 1989 to December 31, 1989

Amount: $ 10,534

Approved by A.I.D.: January 25, 1989

Status: Current

Purpose: To continue the pre-introduction evaluation of NORPLANT[R] contraceptive subdermal implants in Chile.

The pre-introductory evaluation of NORPLANT® is continuing. Insertions are being done at the six participating clinics and follow-up of previous acceptors is continuing. More physicians are currently being trained.

POPULATION COUNCIL AWARD NO. I89.01A

To: Kenyatta National Hospital,
University of Nairobi

Period: January 1, 1989 to December 31, 1990

Amount: $ 53,770

Approved by A.I.D.: March 21, 1989

Status: Current

Purpose: To extend the pre-introduction evaluation of NORPLANT[R] contraceptive subdermal implants in Kenya from a rural environment to an urban environment based at Kenyatta National Hospital.

Due to administrative problems, the start-up of this project was delayed as the principal investigator was out of the country at various points and was, therefore, unable to sign the terms of award. The first payment was not issued until May, 1989. The project is now underway at Kenyatta National Hospital.

POPULATION COUNCIL IN-HOUSE PROJECT

INTRODUCTION OF THE COPPER T380A INTRAUTERINE DEVICE

Period: January 1, 1989 to April 30, 1989

Amount: $ 67,440

Approved by A.I.D.: Pending

Status: Current

Purpose: To facilitate better utilization of Copper T 380A IUD in family planning programs.

The activities under this in-house project for the period January 1, 1989 - February 28, 1989 were included in the report of activities for the in-house project "Introduction of the Copper T 380A Intrauterine Device" under Cooperative Agreement No. AID/DPE-3005-A-00-3003-00. A copy of that report follows.

POPULATION COUNCIL IN-HOUSE PROJECT

INTRODUCTION OF THE COPPER-T 380A INTRAUTERINE DEVICE

Period:	April 1, 1987 to March 31, 1988 Extended to December 31, 1989 (a)	Amount:	$ 328,694 $ 235,520 (a)
Approved by AID:	October 30, 1987 July 11, 1988 (a)	Status:	Current

Purpose: To facilitate the better utilization of Copper T380A in family planning programs.

The overall goal of this program is to improve the quality of IUD provision, especially that of the Copper T 380A, to better serve women's health needs. In general, we seek to: (1) improve client information about the Copper T 380A and provide it in the context of broad choice; (2) improve the possibility of continued satisfied use by improving the responsiveness of the service delivery environment in family planning programs offering this device.

The Copper T 380A is now broadly available. Marketing in the United States began in 1988. In addition to private sector distribution throughout the world, the Copper T 380A is provided through the major public sector procurement and distribution channels that supply family planning programs in developing countries. More than eight million Copper T 380A IUDs from a number of Council-licensed manufacturers have been distributed in over 20 countries.

As colleagues from other population organizations travel and work abroad, they report that there is a dearth of information in most developing countries on the Copper T 380A that is appropriate for various levels of clinic staff, including paraprofessionals, and for clients. The Council and PATH previously collaborated to prepare prototype materials for fieldworkers and clinicians. These materials have been updated. Additionally, PATH has developed guidelines for informed choice; a wall chart describing the method and a flyer for policymakers. A package of these and other materials will soon be available for adaptation to regional or country needs.

Future activities will be directed to dissemination of program standards, training guidelines, informational materials and guidance to family planning programs through a series of meetings with agencies involved in training, logistics and service delivery. Subsequently we plan to organize regional meetings that will focus on specific programmatic needs of different areas.

See Population Council Award No. I88.20A. Purpose: To provide continued support to the project entitled "Activities to Enhance the Introduction of the Copper T 380A IUD" begun under Population Council Award No. I86.36A.

3. FAMILY PLANNING PROGRAM RESEARCH AND TECHNICAL ASSISTANCE

POPULATION COUNCIL AWARD NO. I88.60A

To: Universidad Peruana Cayetano Heredia
Lima, Peru

Period: August 26, 1988 to January 25, 1990 Amount: $ 46,370

Approved by A.I.D.: November 22, 1989 Status: Current

Purpose: To support a project entitled, "A controlled trial to extend the duration of exclusive breastfeeding in low-income mothers in Lima, Peru."

The purpose of the current study is to demonstrate the effect of a hospital - based intervention of modifying infant feeding practices in the first three months of life with special emphasis on successful establishment of lactation and delayed introduction of waters, teas and formulas. The planned intervention consists of multidisciplinary training of hsopital personnel who work with mothers before, during and after delivery, and production of educational materials of health care providers and for mothers. Training is to be carried out in two public hospitals in Lima. A third study hospital will not receive the intervention, serving as a control. The project is being conducted through the Department a Pediatrics of Cayetano Heredia University (UPCH)

The project comprises three stages:
1) baseline data collection,
2) development and implementation of the intervention,
3) evaluation.

This report covers the first six months period of the project during which time Stage 1 was completed, and Stage 2 was initiated.

Stage 1 activities completed during this period were:

- A rapid ethnographic assessment of early infant feeding practices and attitudes among 80 mothers living in communities served by the three study hospitals,

- A self-administered survey of 323 health care providers (physicians, residents, nurses, midwives, and auxiliary nurses) working in obstetric and pediatric (especially neonatal and outpatient peds) services in the three hospital,

- An interview survey of 308 postpartum mothers delivering in the three

hospitals.

Stage 2 activities initiated during the reporting period include:

- Recruitment and contracting of a local production firm (Asociacion Peru Mujer) by the Academy for Educational Development (AED) Consultant - Ms. Peggy Koniz-Booher,

- Development and testing of teaching cards for mothers on breastfeeding and appropriate supplementation,

- Design of an educational poster for distribution to postpartum mothers,

- Translation and adaption of a guide for health personnel on clinical management of lactation (based on the Population Council- produced pamphlet, Breastfeeding: A Nurses' Guide)

- Selection and training of a multidisciplinary team of trainers UPCH at Wellstart/San Diego Lactation Program,

- Initial development of an educational program for hospital personnel in clinical management of lactation.

During January 16 through February 1, 1989 the UPCH multidisciplinary team attended the Wellstart/San Diego Lactation Program. The outcome was extremely well received by the Peruvian participants who returned to Lima highly motivated and prepared to develop and implement the project training intervention.

The Peru Wellstart trained team began work on planning and developing the hospital training program using audio-visual and other training materials obtained in San Diego in addition to developing supplementary training materials. Meetings were held by project collaborations with Department Heads of Pediatrics, Neonatology, Obstetrics and Gynecology, Nursing and Midwifery at the two interventions hospitals to obtain their collaboration and coordinate training activities for hospital personnel. The UPCH Department of Pediatrics agreed to sponsor the training program will be conducted at Cayetano Heredia Hospital on April 17-21 and [illegible]-27, 1989 (see poster attached) and at Dos de Mayo Hospital in May. These dates represent a delay in original project scheduling, principally due to the continued delay in the mials of important back-up literature mailed to Peru by Wellstart.

A subaward was granted to Wellstart (I88.46A) for education of professionals in lactation management. The training of the Peruvian health professional was completed under the subaward. Technical assistance from Wellstart for In-Country Staff Education is to follow. After this, the set of hospital based interventions will be evaluated.

The project activities have been completed on or ahead of schedule with minor problems encountered in the areas of development and execution.

POPULATION COUNCIL IN-HOUSE PROJECT

COUNCIL-ADMINISTERED COMPONENT OF EXTENSION PROJECT, ICDDR, BANGLADESH

Period: January 1, 1989 to September 30, 1989

Amount: $ 227,188

Approved by A.I.D.: April 9, 1989

Status: Current

Purpose: To continue the Population Council's work at ICDDR,B funded through USAID/Dhaka buy-ins to Cooperative Agreement No. DPE-3005-A-00-3003-00.

The activities under this in-house project for the period January 1, 1989 - February 28, 1989 wre included in the report of activities for the in-house project "Council-Administered Component of Extension Project, ICDDR,Bangladesh" under Cooperative Agreement AID/DPE-3005-A-00-3003-00. A copy of that report follows.

POPULATION COUNCIL IN-HOUSE PROJECT

COUNCIL-ADMINISTERED COMPONENT OF THE EXTENSION PROJECT, ICDDR, BANGLADESH

Period: July 1, 1987 to June 30, 1988
Extended to December 31, 1988 (a)
Extended to September 30, 1989 (b)

Amount: $ 346,175
$ 19,885 (a)

Approved by AID: October 30, 1987
July 12, 1988 (a)
Pending (b)

Status: Current

Purpose: In support of the project entitled "Council Administered Component of the Extension Project, ICDDR, Bangladesh."

Established in 1982, the MCH-FP Extension Project has the primary objective of contributing toward improvements in the health and family planning service program in Bangladesh, through a combination of applied research in the Matlab and Extension areas, and pilot testing of selected interventions in its field sites in Abhoynagar and Sirajgonj. An overview of Project activities during the reporting period include:

Research on the Matlab Program:

A central research focus of the Project during the past year has been upon a fuller understanding of the impact of the family planning and MCH services introduced in Matlab upon maternal and child health. A collaborative study with the CMD examined the issue of maternal mortality levels in Matlab, and specifically the impact of the family planning program upon it. The study found that while the family planning program had a significant effect upon deaths through a reduction in the number of pregnancies among women who did become pregnant, the risks of death from childbearing were not significantly lower in the treatment than comparison areas. The study concluded that while family planning programs may thus contribute significantly to reductions in the number of women dying due to childbearing, there at the same time exists a need to expand the range of maternity services offered, if the risks associated with childbearing are to be significantly reduced.

A separate study examined the relationship between birth intervals upon child survival, the former representing a primary mechanism through which family planning programs could contribute to improved child health. The study found that short previous birth intervals

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(less than 24 months) were associated with significantly higher risks of neonatal mortality, and that short subsequent intervals were linked to higher risks of death during ages one to four years. Thus, while risks associated with short intervals appear to be pronounced, due to extended breastfeeding and result postpartum infecundity in rural Bangladesh, short birth intervals remain relatively infrequent, so the potential for family planning programs to improve child survival may be more modest. Current work is focusing on the impact of tetanus and measles immunization programs in Matlab upon reductions in levels of childhood mortality levels, and on the effects of family formation patterns upon maternal mortality levels, and on the effects of family formation patterns upon maternal mortality.

Operations Research in the Project Areas

In contrast to pilot programs such as Matlab, the Extension Project tests the effectiveness of interventions within the context of the Government program. Through pilot testing interventions under the same resource and management constraints which are common to the Government program, the Project obtains a more realistic idea of feasible improvements which can be made in the service delivery program. Through a process of pilot testing interventions based largely upon the experience of the Matlab program, four broad areas of intervention have been identified which contribute significantly to improved delivery of the family planning and MCH services in the Government program:

1) Improved staffing ratios of female fieldworkers: Improvements in the staffing ratios of female community health workers have been shown to make a significant contribution to improved delivery of health and family planning services within the Government program.

2) Strengthened field management: The Project has demonstrated that a package of management improvements - most notably, the introduction of a fieldworker recordkeeping system, the establishment of regular meetings at the upazila and union levels, and a de-emphasis of contraceptive targets can contribute significantly toward improved program performance.

3) Broadened contraceptive choice: For family planning to succeed in rural Bangladesh, couples must be offered the broadest choice of contraceptive methods, to the extent possible through outreach services at the doorstep. The delivery of injectable contraception by female fieldworkers and the emphasis upon all contraceptive methods according to the needs of the individual couple are two interventions which have contributed to improved family planning performance in the Project areas.

4) Decentralized paramedical services: The accessibility of MCH and clinical contraceptive services have been improved through interventions to decentralize services as close to the community as possible, through the establishment of community-donated union clinics and of satellite clinics within the union.

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Current efforts in the Extension Project are directed toward expanding efforts to disseminate important Project findings to policy makers. One component of this dissemination effort has been the establishment of a series of briefing papers which summarize key Project findings; currently, over 800 individuals both within Bangladesh as well as nationally receive these briefing papers. Based upon its experience, the Extension Porject has also begun providing direct technical assistance to the Ministry of Health and Family Planning in the areas of recruitment and training of female fieldworkers and introduction of a fieldworker recordkeeping system nationally. With the filling of several key longstanding vacancies on the Project, it is anticipated that dissemination and technical assistance efforts by the Project will greatly expand during the coming period.

Data Collection

One by-product of the Extension Project has been the development of two highly innovative systems of data collection for demographic and health service research and evaluation. The Sample Registration System (SRS) is a computerized surveillance system which provides rapid feedback on the impact of the Project upon service operations and demographic rates. Independent teams of interviewers visit a representative sample of households (approximately 11,000 as of the end of 1988) every three months to collect data on vital events, use of contraception, and household visits by Government health and family planning workers during the intervening period. The SRS offers considerable advantages over other surveillance systems in terms of:

low cost: relatively inexpensive, since it has been adapted to microcomputers.

rapid turnover time: data are edited and available within a month following the completion of a round. Demographic rates obtained from the SRS for calendar year 1988 are already available.

flexibility: the SRS has ben flexibility to incorporate additional special surveys during the course of routine data collection on short notice. A notable example of this was the rapid assessment of the impact of the flood carried out by the Project beginning in October of 1988 in the Sirajgonj field site.

A second surveillance system which has been developing microcomputer-based recordkeeping system for health and family planning service delivery and evaluative research. In this system, unlike the SRS, data collection and service delivery are carried out by female Community Health Workers (CHWs). In this system, which is currently being introduced in Matlab, all data collection and management is carried out on a microcomputer based in the field. Service data (contraceptive use, immunization status, pregnancy status) are collected and computerized on a monthly basis, and service statistics are routinely generated. In addition, lists of

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the target population for specific program interventions (e.g., pregnant women) can be readily obtained. This second data system is appropriate for programs which wish to integrate data collection with service delivery activities.

It is anticipated that both of these systems will have wide applicability to health and family planning service delivery and research programs both within Bangladesh as well as in other developing countries. Already, efforts are underway to introduce the SRS in Indonesia and Mexico, aided by current or former Project staff.

POPULATION COUNCIL AWARD NO. I89.07A

To: University of Michigan
Ann Arbor, Michigan

Period: January 1, 1989 to September 30, 1989

Amount: $ 93,645

Approved by A.I.D.: April 2, 1989

Status: Current

Purpose: To support the assignment of Professor Rushikesh Maru as the operations research scientist to the International Center for Diarrhoeal Disease Research, Bangladesh (ICDDR/B) under the MCH-FP Extension Project, and of his relocation from the University of Michigan to Dhaka.

This award provides a mechanism for strengthening the research and management staff of the MCH/FP Extension Project at the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) through the assignment of Dr. Rushikesh Maru as the Operations Research Scientist at the Centre.

The responsibility of the Operations Research Scientist is to carry out operations research on various aspects of the national Maternal and Child Health - Family Planning (MCH-FP) program in Bangladesh, within the framework of the MCH-FP Extension Project of ICDDR,B. This will involve design, execution, and evaluation of pertinent interventions in the filed; testing new strategies in service delivery; conducting related research with emphasis upon qualitative studies; and supervision of scientific staff. In addition, he is to assume a primary role in the areas of liaison and dissemination of Project findings with donors and government officials, with the objective of improving Government of Bangladesh policies. The Operations Research Scientist will take on an increasingly prominent role in the areas of management and direction of the Extension Project.

At the request of the ICDDR,B, the Population Council assisted in the identification of Dr. Maru as the Operations Research Scientist and arranged for his secondment from the University of Michigan. Dr. Maru visited Bangladesh during the period February 3 - March 5, 1989 to begin work on his assignment. He will relocate to Bangladesh with his family in late spring 1989 and will remain there for a two year assignment.

V. FINANCIAL INFORMATION:

SUMMARY STATEMENTS OF EXPENDITURES

JULY 17, 1988 - MARCH 31, 1989

Fiscal Report
#1

The Population Council
Cooperative Agreement No. AID/DPE-3050-A-00-8059-0
All Project Summary
P.C. Account # 1-8-62-7523-0010
Statement of Expenditures
For the Period July 17, 1988 through December 31, 1988

	Budget	Cummulative	Current Period
Center For Biomed. Rsch	$1,924,635.81	$983,300.41	$983,300.41
International Programs	61,578.37	19,824.00	19,824.00
Total All Divisions	$1,986,214.18	$1,003,124.41	$1,003,124.41

The Population Council
Cooperative Agreement No. AID/DPE-3050-A-00-8059-0
All Project Summary

Fiscal Report #2

Statement of Expenditures
For the Period July 17, 1988 through December 31, 1988

	Budget	Cummulative	Current Period
Center For Biomed. Rsch	$1,924,635.81	$1,281,830.47	$298,530.06
International Programs	61,578.37	38,448.34	18,624.34
Total All Divisions	$1,986,214.18	$1,320,278.81	$317,154.40