

PD-AAJ-127

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PROJECT STATEMENT

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Date: September 24, 1980

ISN-28117

A. PROJECT SUMMARY

1. Statistical

Project Title: Program for Applied Research on Fertility Regulation PARFR

New or Extension: Extension

Contractor and Address: Department of Obstetrics and Gynecology  
Northwestern University Medical School  
Chicago, Illinois

Principal Investigator: John J. Sciarra, M.D., Ph.D.

Duration: 14 years, 5 year extension requested

Total Estimated Cost: \$27,378,000

Amount Requested for RAC Approval: \$17,793,000

Funding by Fiscal Years:

FY 72 - \$3,350,000	TQ - \$ 250,000	FY 81 - \$2,839,000
FY 73 -	FY 77 - \$1,175,000	FY 82 - \$3,185,000
FY 74 -	FY 78 - \$ 900,000	FY 83 - \$3,614,000
FY 75 -	FY 79 - \$1,500,000	FY 84 - \$3,954,000
FY 76 - \$ 500,000	FY 80 - \$1,910,000	FY 85 - \$4,201,000

Project Manager: James D. Shelton, DS/POP/R

## 2. Narrative

The Program for Applied Research on Fertility Regulation (PARFR) is an ongoing research and development program directed toward actively pursuing promising leads of goal-directed research to develop new or improved means of fertility control suitable for use in less developed countries. PARFR was initiated in 1972 to serve as a flexible administrative mechanism to provide scientific, technical and financial assistance to United States and Foreign institutions for applied research projects with the goal of developing safe, effective and acceptable methods of fertility regulation. The program has been responsible for the development of a significant number of promising new or improved fertility regulation methodologies for both men and women. These include new barrier methods of vaginal contraception; long-acting injectable steroidal preparations; non-surgical methods of permanent contraception for both the male and female; potentially reversible sterilization methods for the female and male; improved methods of intrauterine contraception; and other methods that are in early stages of research and development. The Program has reached the point where several of these new methods of fertility regulation are available for testing in humans; these methods are being given increased Program emphasis by support of Phase I and collaborative Phase II clinical trials in developing countries and in the United States.

Northwestern University will continue to serve as the coordinating institution for PARFR. A strengthened administrative/technical/scientific unit backed-up by a Scientific Advisory Committee composed of experts actively engaged in reproductive research will continue to solicit, screen, fund, monitor, and develop sharply focused fertility research projects with the goal of shortening the required time between the evolution of a new idea in fertility control and its useful application in the field. In the next period of years, the major portion of work will be devoted to determining, through adequate testing, which methods of fertility regulation developed by PARFR are safe, efficacious and acceptable, and which could result in their ultimate availability to developing countries.

## B. EXPANDED NARRATIVE STATEMENT

### 1. Background and Introduction

There is a widespread, erroneous belief that the population problem is now less serious than it was. This belief has been encouraged by articles in both the lay and population press which purport to show that the large number of births occurring in the decade of the 60's did not occur in the decade of the 70's. While it is true that population growth in the past decade did not increase as rapidly as demographic projections made in the early 60's, the rate of increase was and still is sufficiently high to double the world's population to 8 billion by the middle of the next century. In the developing countries of the world, some progress has been made in the reduction of unwanted fertility by the provision of family planning information and services. Complacency with these early results, however, has led to a decrease in efforts and funding by governments and other public and private agencies. Unfortunately, the current situation of continually expanding population growth is even more critical in 1980 than it was in 1970. The huge number of newborns during the past 20 years are now entering their reproductive years and during the next ten years, this bulge of reproductive-age women and men will continue to increase. Estimates of the total number of women at risk of pregnancy has risen from about 500 million in 1971 to over 600 million in 1979. Generally, only about 20 percent of these women use some form of fertility control.

There are many constraints, real and imagined, that prevent effective population program. These constraints have been examined in a multitude of studies, and are well-known. Among these constraints, and the one that this proposal seeks to overcome, are the inadequacies and non-acceptability of presently available methods of fertility regulation. While it is true that developed societies using whatever methods are available have been able to reduce significantly their rates of population growth, the social, economic, religious and health conditions that exist in most developing countries have prevented an effective transfer of this experience. However, a number of developing countries have been able to reduce significantly their rates of population growth using presently available methods. One specific example is the People's Republic of China. In addition to excellent accessibility to a wide range of fertility control methods, the Chinese effort has been aided by a highly conducive political and social climate and (importantly) a rigorous support for research and development of new and improved methods of fertility regulation. Nevertheless, the Chinese situation must be considered unique, and the development of new and improved methods of fertility control will continue to be an essential asset to family planning programs generally.

The existing methods of fertility regulation have inherent limitations with respect to side-effects and long-term safety concerns, acceptability, reliance on medical delivery systems, actual use-efficacy, long-term usage and costs. These limitations have severely curtailed the widespread availability and use of presently existing methods. Yet population studies have demonstrated that improvements in contraceptive technology can lead to improved availability, acceptability and use of a method. It is also true

that extensive differences in cultural, religious and personal attitudes, health status, and socio-economic situations absolutely necessitates a wide range of fertility control methods which can be used by both men and women. These methods must be personally and culturally acceptable, convenient to use, safe, inexpensive, easy to distribute and store, and must accommodate a variety of changing life situations in the same couple as they progress through their reproductive years.

The profound and beneficial impact of contraceptive technological advances on the success of family planning programs had led AID, over the past ten years, to initiate and support a variety of research programs to improve fertility regulation technology. The Program for Applied Research on Fertility Regulation (PARFR) was established, in 1972, at the University of Minnesota, with the financial and technical assistance of AID. In 1975, PARFR moved to its present location at the Chicago campus of Northwestern University. The organization was established to provide assistance to AID for the solicitation, screening, funding, and monitoring of promising applied research projects in the field of fertility regulation, and particularly in the development of new contraceptives. Since 1972, a significant number (approximately 150) of innovative projects have been developed at some 80 institutions in both developed and developing countries, all with a minimum of organizational delay and administrative expense. Certain of these PARFR efforts could lead to new contraceptive products and fertility regulation procedures well-suited to the special needs of developing countries. Other PARFR projects have proven not to be feasible and have been abandoned.

The original perception of the PARFR potential was, perhaps, somewhat optimistic regarding the amount of time that would be required to bring new methods of fertility regulation from the idea stage to the point of widespread use. Ideas are many and cheap, but the development of the idea to the point of practical usefulness is expensive and time-consuming. Even when promising leads have been uncovered or developed with PARFR assistance, the increasing research demands placed by the regulatory agencies have tremendously increased the amount of work and time and money required to fully develop the lead. Another complicating factor is the desirability and, indeed, the absolute necessity for increasing amounts of PARFR's research efforts to be carried out in developing countries. There is growing concern about the fact that most contraceptive development has been and is being carried out in developed countries (mostly non-US), and there is serious question as to whether the results of such research are truly relevant to the people in developing societies. Recognizing this, PARFR early on began to identify institutions in developing countries where applied research projects could be conducted in appropriate volunteer groups, thereby obtaining data under actual use conditions. On the other hand, the desirability of obtaining FDA approval for new drugs or devices, prior to testing them abroad, has set up a conflict situation for PARFR; consequently much of the original developmental research that PARFR has accomplished has been done in the United States and at relatively greater cost.

Despite these many constraints and obstacles, the PARFR mechanism has been responsible for the development of a significant number of promising new or improved fertility regulation methodologies for both men and women. These include new barrier methods of vaginal contraception; long-acting injectable steroidal preparations; non-surgical methods of permanent contraception for both the male and female; potentially reversible "sterilization" methods for the female and male; improved methods of intrauterine contraception; and other methods that are in the early stages of research and development. The Program has reached the point where several of these new methods of fertility regulation are available for testing in male or female volunteers. These new methods are being given increased Program emphasis by the support of Phase I and collaborative Phase II clinical trials in developing countries and in the United States. The challenge now facing PARFR is to determine, through adequate testing, which methods of fertility regulation are safe, efficacious and acceptable, and which could result in FDA approval and their ultimate availability to developing countries.

## 2. Significance to AID Objectives

It has been well established that there are three general ways in which a society can initiate or extend the practice of fertility regulation: it can

- 1) increase the motivation of the individual members of the society to control their fertility,
- 2) improve and expand family planning and health care delivery systems, and/or
- 3) improve contraceptive technology.

It is equally clear that in order for LDCs to solve their population/development problems, these societies must strengthen certain of their existing capabilities and establish new ones. Among the numerous social, economic and scientific needs of LDCs, the needs for the expansion of applied research capability and the improvement of methods of fertility regulation are of key importance.

Since 1966, the United States Agency for International Development, recognizing that all three of the factors listed above are important and are closely interrelated, has directed its efforts toward the development of programs which would enhance LDC capability in all three areas. In order to deal with the first two factors, it has assisted LDCs in establishing, maintaining and expanding their population/family planning programs. As regards the third factor, there is good evidence that these family planning programs must offer a wide variety of contraceptive methods if they are to make a significant demographic impact. A number of different techniques are needed, because women and men of different ages, with differing needs and different life situations prefer and require different means of

fertility regulation. Therefore, AID has included, in its overall Population Programs, support for research on new means of fertility control and the improvement of existing techniques.

This proposal describes the ongoing PARFR program, designed to develop a variety of fertility regulation methods, especially those most suitable for countries with rudimentary systems of education, transportation, and health delivery. Its mandate is the stimulation and support of applied, goal-oriented contraceptive research and development and particularly research in which the countries themselves participate.

AID believes that the conduct of specific research projects in LDCs has two major benefits. First, the results of such projects could lead to the development of safer and more effective methods of fertility regulation. Second, the carrying out of the projects would, in itself, serve to increase the level of research capability of the individual investigators as well as their institutions. AID has long recognized that many LDC students who have received an excellent education in developed countries often make little use of their training when they go home. This occasions a tremendous loss of valuable manpower and a correlative waste of money. It is, therefore, believed to be essential to identify these individuals and to provide continued support for their research efforts.

Finally, AID believes that if the research projects carried out in the PARFR program are relevant to the needs of the LDCs and particularly if they include LDC participation, then it is more likely that the new fertility regulation methods coming out of the program will make a substantial impact in these countries.

### 3. Program Accomplishments

PARFR is well-established at Northwestern University (office facilities at Northwestern Memorial Hospital) as an active, productive, scientific and administrative organization that effectively provides financial and technical support to U.S. and foreign institutions for applied research projects in the field of fertility regulation.

#### a. Research and Development Program

PARFR has successfully implemented a scientific and administrative mechanism to seek out, by a variety of formal and informal international solicitations, promising research ideas in the field of fertility regulation. In accordance with the perceived needs of developing countries, PARFR has given priority to the development of fertility regulation methods which:

- can be self-administered;
- require infrequent application;
- can be used by the male;
- may be effective on a post-coital or post-ovulatory basis;
- improve techniques for male or female sterilization, especially regarding the possibilities of later reversibility.

Since 1972, PARFR has approved and funded 149 research projects, executing 118 extended research subcontracts and 31 pilot studies. These 149 research subcontracts were awarded to 32 Universities, 12 research institutes, and other institutions in The United States. Fifteen institutions in 10 developing countries (Brazil, Colombia, Egypt, El Salvador, Iran, Jamaica, Mexico, Philippines, South Korea, and Thailand), and 4 institutions in Belgium, Japan and West Germany also have received PARFR support.

Table I summarizes the scientific program of PARFR by grouping all past and present research projects into the seven areas of contraceptive research, as outlined by the Technical Office of AID.

TABLE I

<u>Contraceptive Research Area</u>	<u>No. of Active Projects</u>	<u>No. of Terminated Projects</u>	<u>Total No. of Projects</u>
I. Female Sterilization	7	29	36
II. Male Sterilization	6	14	20
III. Intrauterine Contraception	2	14	16
IV. Systemic Contraception	12	36	48
V. Barrier Contraception	6	11	17
VII. Pregnancy Termination	5	7	12
	<u>38</u>	<u>111</u>	<u>149</u>

Table 2 summarizes the scientific program of PARFR regarding its research funding support in the same seven areas of contraceptive research. Additionally, Table 2 indicates, in a chronological fashion, the expended/encumbered dollar amounts by 3-year contract periods.

TABLE 2

PARFR  
Amount Expended/Encumbered  
Research Subcontracts

<u>Contraceptive Research Area</u>	<u>1972- 6/30/75</u>	<u>7/1/75- 6/30/78</u>	<u>7/1/78- 6/30/81</u>	<u>Total</u>
I. Female Sterilization	\$ 229,871 (20%)	\$ 273,036 (18.5%)	\$ 627,258 (20.2%)	\$1,130,165 (19.7%)
II. Male Sterilization	160,627 (14%)	218,279 (14.8%)	351,890 (11.3%)	730,796 (12.8%)
III. Intrauterine Contraception	47,823 (4.1%)	284,592 (19.3%)	104,081 (3.4%)	436,496 (7.6%)
IV. Systemic Contraception	461,649 (40.2%)	639,170 (43.3%)	1,075,379 (34.7%)	2,176,198 (38%)
V. Barrier Contraception	249,181 (21.7%)	61,797 (4.1%)	372,536 (12%)	683,514 (11.9%)
VII. Pregnancy Termination	-----	-----	572,480 (18.4%)	572,480 (10%)
TOTALS	\$1,149,151 (100%)	\$1,476,874 (100%)	\$3,103,624 (100%)	\$5,729,649 (100%)

Capsule summaries of all current (1977-1980) research projects, as well as those projects terminated prior to 1977 are provided in the Appendix.

PARFR has supported a significant number of new fertility regulation methodologies for both men and women, that offer the promise of widespread use in both developing and developed countries. Brief status summaries of these particularly important PARFR developments are provided below.

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Two systems are under study; a 180-day system and a 90-day system. Preliminary results in female volunteers indicate the acceptability of the 6-month system, and its safety (98M). Additional clinical studies are being planned to document the contraceptive efficacy over the period of 6 months, and to determine the effects of the minute steroid blood levels on menstrual cyclicity. Studies are almost completed that will provide the data necessary for an FDA-IND application for the 90-day system. Phase I clinical studies of this system are in the preliminary stage. An independent manufacturer has agreed to partially support further development of these biodegradable systems.

The scientific research team that has developed the above biodegradable microcapsule system has, with PARFR support, developed a totally unique approach for the administration of long-acting drugs. Steroids or other chemicals have been incorporated into a fiber which can provide for predictable and varying durations of timed release (206, 104N & P9). These fibers are manufactured in a process similar to spinning nylon or other polymers. In close collaboration with PARFR staff, the scientists at Southern Research Institute and the University of Alabama are developing new approaches to fertility regulation by the use of these fibers. As examples: a steroid-releasing active IUD tail; a fiber releasing quinacrine that would cause fallopian tubal closure, and which could be administered via an IUD; a long-lasting IUD that would release minute quantities of steroid, and yet be soft, flexible, and non-irritating to the uterus (219 & P57).

PARFR is supporting the development of a steroid-cholesterol pellet that can be implanted under the skin, and that will provide long-term contraceptive protection for periods up to 6 months. Preliminary laboratory and animal studies indicate the feasibility of this approach (105N). PARFR is in process of mounting Phase I clinical studies to determine the acceptability, metabolic effects and contraceptive efficacy of these steroid pellets. These Phase I studies have received FDA approval.

#### Non-Surgical Sterilization for the Female

PARFR has supported clinical studies on the use of a tissue adhesive (methylcyanoacrylate) injected via a "blind" delivery system. These studies now include 200 women (86N, 200G). These women have been almost totally free of side effects. Preliminary results indicate a tubal closure rate of 80%, following one injection. The investigators are planning additional studies in Brasil, Chile, India, Indonesia and the Philippines with PARFR support, in an attempt to raise the efficacy rate to a level of 95%. If this level can be achieved, the method could supplant most other methods of surgical female sterilization. Importantly, the delivery system can be applied by trained paramedical personnel.

PARFR has supported, since its inception, the development of a potentially reversible method of female sterilization that does not require surgery (63N & 207). The method involves the application of specially designed uterotubal silastic/stainless steel plugs, under direct visualization, through a specially designed hysteroscope and device carrier. Extensive animal testing and preliminary human testing (in Iran) have documented the effectiveness of the plug in preventing conception. Animal studies also have documented the easy reversibility of the procedure upon device removal. Actual human studies are underway in Chicago, but the results are too preliminary to comment upon the efficacy of the devices for the long-term protection against pregnancy, or the potential for reversibility.

#### Non-Surgical Methods of Permanent Contraception for the Male

Early results on the use of a percutaneous injection of a mixture of formalin and ethanol into the vas deferens, under local anesthesia, are highly favorable (220). Side effects and patient complaints have been minimal. Closure of the vas, with one injection on each side, has been accomplished in approximately two-thirds of the male volunteers. The investigator believes that a double injection, bilaterally, will result in closure rates of approximately 90%.

Recently, PARFR has agreed to support clinical studies of a new technique for non-surgical vas occlusion (221C). The technique is simple, and involves the application of a coagulating current through a specially designed bipolar needle that is administered to the vas, under local anesthesia. Preliminary results among 25 men have been 100% successful in producing azoospermia, approximately 6 weeks after the treatment. PARFR will conduct collaborative studies on small groups of male volunteers in Brasil. Should these studies corroborate the earlier finding of efficacy and safety, it is likely that this method will replace standard surgical vasectomy.

#### Intrauterine Contraception

Numerous studies have clearly established that uterine size and shape vary considerably among different individuals. Until recently, however, there has been no way to determine these dimensions in the living individual. Accordingly, IUDs of various types are usually made in two sizes, based merely upon the length of the device (the length of the endometrial cavity can be measured). PARFR has supported the development of an ingenious measuring device that accurately measures total uterine length, and uterine width at varying levels (P51). This information can be translated into a 2-dimensional outline of the uterine cavity by means of mathematical equations. Once this accurate geometric picture is obtained, the most appropriate IUD (dimensions and shape) may then be inserted. It is anticipated that a better-fitting IUD will reduce the most common complications of expulsion, cramping pain and bleeding, and consequent IUD termination. Clinical studies are just beginning in an attempt to correlate IUD event rates with the particular IUD inserted and its conformity to uterine shape and dimensions.

PARFR has established the safety and efficacy of inserting an IUD in women following unprotected intercourse at mid-cycle (84N & 88N). The method offers great advantages over the more routine approach of using estrogens in that side-effects are less, steroid administration is not necessary (with its unknown risks on developing embryos), the IUD insertion can be done as late as one week post-coitally, and the woman can continue for years with the same IUD.

### Contraceptational Agents

PARFR is supporting research in the development of methods (chemical compounds) that will interfere in the production of progesterone by the corpus luteum. These compounds include super-agonists of luteinizing hormone-releasing factor (LH-RH) (114N, 201B & P53), prostaglandin analogues having a unique structure (P55); two synthetic steroid derivatives of estrogen (208); and a group of compounds originally synthesized for their CNS tranquilizing effects. In each of these studies, PARFR has entered into agreement with the relevant pharmaceutical manufacturer to collaborate in the further development and testing of these potentially promising contraceptive approaches. None of the studies are far enough along to comment upon their eventual applicability regarding effectiveness and safety in terminating very early pregnancies. Nevertheless, in each instance, animal studies of selected compounds have been most promising, and hold out the hope that at least one of the approaches could result in a "pill" to be taken by the woman at the time of the "missed" menses. The farthest along is a compound developed by Lepetit Pharmaceutical Company. PARFR has supported animal testing, and the company has supported toxicology testing (100N & 218). Complete results will be available before the end of 1980. PARFR has agreed to support Phase I clinical studies with this compound, assuming that the toxicology studies are negative.

### Male "Pill"

Recently, the Chinese have reported on their studies involving the use of gossypol, a pigment found in the cottonseed. These studies are on-going, and include approximately 10,000 men. Specially prepared gossypol is administered orally on a daily basis over a period of approximately 8-12 weeks, until azoospermia is obtained, following which the maintenance dose of gossypol is administered once a week. The Chinese claim a 99% effectiveness rate in the production of azoospermia and a reversibility rate, upon discontinuance of the drug, of about 92%. Some side effects have been noted, but these were minor and easily treated. PARFR held a workshop in Chicago (March 11, 1980) to which were invited scientists who had worked with gossypol, including four Chinese colleagues. The investigators documented the great variation among animal species and strains to the efficacy of gossypol as an anti-fertility agent and

its safety. In certain animal species - American rats and mice, pigs and chickens, the oral administration of gossypol causes death in a high proportion of the animals. In other species, like Rhesus monkey, gossypol administration in large doses causes no observable toxicity. PARFR was encouraged by this workshop review of current (210) and old research, and has decided to support additional animal studies in subhuman primates. These studies will determine efficacy and toxicity, in accordance with FDA guidelines. In addition, a non-US scientist has started a small clinical trial in men, using Chinese gossypol. Preliminary findings appear to substantiate the Chinese experience. This investigator plans to request PARFR support for a larger clinical study.

b. Workshops and Publications

As one of its major objectives, PARFR reviews and disseminates the findings of applied research in fertility regulation. This objective is accomplished through a variety of mechanisms, including PARFR-organized workshops, symposia and seminars focused on specific topics of fertility control research, by the participation at scientific meetings of PARFR staff and its investigators, by encouraging investigator publication and staff publications on research findings, and by the newly-organized PARFR publication "Research Frontiers in Fertility Regulation."

The following workshops have been organized by and held under the auspices of the Program for Applied Research on Fertility Regulation:

Hysteroscopic Sterilization, Minneapolis, June 22-24, 1973  
Attended by 55 participants representing 10 countries.

Control of Male Fertility, San Francisco, June 19-21, 1974  
Attended by 60 participants representing 5 countries.

Advances in Female Sterilization, Minneapolis, June 15-18, 1975  
Attended by 80 participants representing 12 countries.

Risks, Benefits and Controversies in Fertility Control,  
Arlington, March 13-16, 1977  
Attended by 155 participants representing 19 countries.

Reversal of Sterilization, San Francisco, December 4-6, 1977  
Attended by 83 participants representing 18 countries.

Animal Models for Research on Contraception and Fertility,  
Washington, D.C., May 8-10, 1978  
Attended by 239 participants representing 12 countries.

Pregnancy Termination: Procedures, Safety and New Developments,  
Nassau, Bahamas, May 23-26, 1978  
Attended by 175 participants representing 24 countries.

Vaginal Contraception: New Developments, Guatemala,  
April 25-27, 1979  
Attended by 175 participants representing 38 countries.

Research Frontiers in Fertility Regulation, Mexico City,  
February 11-14, 1980  
Attended by 155 participants representing 24 countries.

Gossypol, Chicago, March 11, 1980  
Attended by 38 participants representing 6 countries.

The participants have found these workshops to be most valuable as have the invited observers, and the scientific/population press. They have served a most valuable function in bringing scientific thinking up-to-date in each of the selected topics. Publication of the proceedings of each of these workshops has been timely, and the scientific community has welcomed these publications. Importantly, the Agency for International Development has obtained a large number of copies of each workshop at the low publisher's cost, for distribution outside the United States.

In addition to its own workshops, PARFR's staff has actively participated in scientific gatherings of a wide variety of organizations, both nationally and internationally. Most recently, PARFR and IFRP collaborated with our Brazilian colleagues in the organization of two workshops in Sao Paulo and Rio de Janeiro. A Portuguese publication of the proceedings was done in an exemplary fashion, and is the first book on recent advances in fertility regulation to appear in that language.

PARFR is currently planning to hold a workshop on recent advances on fertility regulation in Surabaya, Indonesia, in collaboration with IFRP, PIACT, the Government of Indonesia, UNFPA and USAID. This workshop will be held in December, 1980 and a publication of the proceedings is planned.

There is an information gap among researchers in the field of fertility regulation, due to the many and varied scientific disciplines now involved - e.g. polymer chemists, physicists, organic chemists, plastics researchers, engineers, biologists, urologists, gynecologists, etc. Each group having their own sources of information (peer journals), rarely come to know about research developments in other fields; yet, they could be instrumental in the furtherance of new approaches to fertility regulation.

Recognizing this gap, PARFR has initiated a research newsletter, "Research Frontiers in Fertility Regulation," to be issued approximately six times annually, that will summarize state-of-the-art on selected topics of fertility regulation research. The premiere issue is included in the Appendix. Subsequent topics already selected include:

Current Status of Research on Hormonal Contraception  
in the Male

Progesterone Inhibition in Fertility Regulation

Female Sterilization by Pharmacologic Methods

LHRH Agonists and Antagonists in the Female

c. Administrative Accomplishments

The scientific research program including workshops is administered by a small staff composed of a Director of Administration, one full-time and one part-time (80%) scientist/clinician, a Project Controller and three support staff. Through the experience and expertise of the scientific personnel, along with an efficient core-administrative group, the A.I.D. Population Office has been able to extend its own research activities and interests in contraceptive development.

Currently PARFR's functions are to:

1. Periodically solicit research proposals, requiring continual updates of national and international mailing lists, now numbering around 6,000 institutions and investigators.
2. Initiate and provide technical and administrative assistance in developing promising proposals.
3. Bring together domestic and foreign institutions and investigators to collaborate on applied research projects.
4. Process proposals through the established review procedure and prepare, negotiate, and process subcontracts.
5. Administer and monitor funded projects, and arrange periodic site visits as required.
6. Arrange and organize Scientific Advisory Committee (SAC) meetings, recently revised from quarterly to meetings three times a year.
7. Serve as liaison between A.I.D., the SAC, subcontractors, and potential investigators.

8. Maintain a network of contraceptive research consultants.
9. Maintain a network of LDC clinical investigators.
10. Keep abreast of advances in contraceptive technology by attending relevant scientific meetings, and maintaining a library of research articles and other publications.
11. Organize and conduct Scientific Workshops to inform PARFR staff, SAC members, and interested investigators of current progress in contraceptive development. Proceedings of these workshops are prepared and edited by PARFR staff and AID for publication.
12. PARFR has become involved in organizing smaller workshops in LDCs (e.g. Brazil - December, 1979 and Indonesia - December, 1980) on selected topics appropriate to the family planning needs and concerns of the particular country. These meetings are coordinated with other agency support - IFRP, UNFPA, PIACT, etc.
13. Coordinate its activities with other fertility research organizations to avoid unnecessary duplication of research efforts (e.g. attendance at annual WHO and NICCHD meetings).
14. Dissemination of information by distribution of workshop proceedings as well as PARFR's new series (July, 1980) - "Research Frontiers in Fertility Regulation," to PARFR's mailing list, AID, and selected PARFR investigators.
15. Preparation of a semi-annual report to AID.

PARFR administrative costs have always been low in relation to the total costs of the program. In order to accomplish this PARFR continually evaluates the efficiency and effectiveness of its programs, internal staff organization and procedures, with representatives of the AID Technical and Contract Offices.

PARFR staff feels strongly that the individual must be protected as a research subject. Therefore, PARFR staff spends considerable time in review of the patient consent form to assure that the rights of research subjects are protected. Guidelines have been written in accordance with HHS (formerly DHEW) regulations to assist investigators in developing consent forms. Forms have been standardized to make the requirements and documentation more understandable. Every approved proposal submitted to PARFR must comply with federal regulations relating to human subjects investigation. The proposing institution, as well as Northwestern University's Institutional Review Board must approve and assure to PARFR that the rights of the subject are protected prior to the award of a subcontract.

PARFR requested a site-visit of the AID Contracting Officer. On June 26 and 27, Mr. Peter Staples spent two days with the PARFR staff discussing current methods of operation. The site visit was beneficial to PARFR in that they were able to appraise current operations and discuss administrative procedures to further streamline PARFR.

#### 4. Relation to Other Research

The World Health Organization has hosted an annual meeting of agencies conducting or directly supporting research in the bio-medical aspects of family planning. The purposes of these meetings are to review the programs of the agencies in the following areas of research; safety and effectiveness of current methods of fertility control; and the development of new methods. An additional purpose of the meeting is to discuss areas of complimentation, collaboration, replication and relative neglect, as well as general issues or coordination and the overall funding to research in family planning. Questionnaires are sent in advance to the invited agencies, relating to their overall expenditures for research in family planning, and detailed expenditures for the research areas that are the focus of the meeting.

The following agencies participated in the meeting held in September, 1979:

Agency for International Development  
Center for Population Research;  
National Institute for Child Health and Human Development  
Deutsche Forschungsgemeinschaft  
European Medical Research Council  
Ford Foundation  
Indian Council of Medical Research  
International Development Research Center  
International Fertility Research Program  
International Planned Parenthood Federation  
Medical Research Council of UK  
National Institute of Health and Medical Research (INSERM)  
Population Council  
Program for Applied Research on Fertility Regulation (PARFR)  
The Rockefeller Foundation

The total expenditures in 1978 of the above agencies in family planning, including basic and applied research and excluding grants to other agencies and operating costs of the agencies themselves, was \$85 million. Compared to 1977 total, the 1978 total shows an actual drop of about \$4 million. The decrease in funding to the field is in fact greater when one takes into account inflation and the diminished value of the dollar. There was general recognition of a universal tendency for funding for biomedical research on family planning to fall off, based partly on the wide publicity given to the drop in fertility in a few developing countries.

In 1978, approximately \$16 million was spent on currently-available methods of family planning, and approximately \$16 million expended on the development of new methods.

It is painfully obvious to those involved in the field of contraceptive development that the grossly inadequate funding provided by the governments, foundations and pharmaceutical companies has severely restricted continuing research and the eventual pay-off in methods of fertility regulation that hold promise of being more acceptable, more safe, and more widely used. In our present era of consumer concern and governmental regulations, it has been estimated that it would take about 15 years and an expenditure of approximately \$35 million to bring a scientific invention to a commercially available product. Certainly, at this required level of time, effort and money, it is unlikely that new methods of fertility regulation can be developed. Compared to 1978, anticipated expenditures in 1980 by the same international agencies and governments appear to be even further decreased. Unless the funding situation can be turned around, new developments in fertility regulation will consist merely of new packaging of old ideas.

Close and frequent contact by PARFR staff and its Scientific Advisory Committee members with other agencies involved in fertility regulation research has led to coordination and collaboration in several research developments. These informal and formal inter-relationships provide the means to avoid unnecessary duplication of research effort. Additionally, exchange of information has been most helpful in directing PARFR resources to research and development areas not included in the programs of other agencies.

The relationship between PARFR and IFRP forms a natural and logical progression. The former dealing primarily with early development through the phase of early small scale clinical testing, and the latter dealing primarily with large scale clinical testing and more sophisticated epidemiologic or "phase 4" evaluation. In addition PARFR and IFRP staff collaborate on common research interests and support jointly sponsored seminars and workshops.

5. Proposed Work Plan

The Objectives of PARFR are:

- a. To shorten the time between the evolution of a new idea in fertility control and its active application in the field.
- b. To strengthen applied contraceptive research interests in foreign and U.S. institutions, and to focus research interests and attention on the fertility control problem in less developed countries.
- c. To provide scientific, technical and funding assistance in the development of new or improved means of fertility regulation.
- d. To review and disseminate the findings of applied research in fertility regulation.

PARFR will accomplish its objectives by:

- a. Providing funds to United States and foreign institutions for applied research projects with the goal of developing new or improved means of fertility control suitable for use in less developed countries.
- b. Expanding funding support, technical assistance and training to less developed countries for multi-centered, collaborative, clinical testing of new fertility control technologies.
- c. Expanding PARFR-initiated research and development, especially in less developed countries, by providing seed funds for short-term support of promising research ideas that could develop into new methods or techniques of fertility regulation.
- d. Encouraging the adaptation by less developed countries of new or improved developments in fertility regulation by short-term, preferably in-country training in these new technologies, in close collaboration with other AID programs.

- e. Improving the dissemination and review of applied research findings in fertility regulation;
  - 1. through PARFR-organized workshops focused on specific topics of fertility control research;
  - 2. by publishing an information report, "Research Frontiers in Fertility Regulation", that reviews the latest research and development efforts on selected topics in a series of about six issues per year, distributed to an international mailing list of approximately 6,000;
  - 3. through presentations at scientific meetings of PARFR-supported research;
  - 4. by encouraging scientific publications by principal investigators on PARFR-supported research and development.

The Program for Applied Research on Fertility Regulation will be continued at Northwestern University as an applied contraceptive development research program. This program will continue to serve as a flexible mechanism providing financial, scientific and technical assistance for innovative research projects of modest magnitude which will supplement the current AID research program on new means of fertility control.

The PARFR program has reached the point where several new method of fertility regulation, outlined previously, are available for testing in human volunteers. These developments will be given increased emphasis by the support of Phase I and early Phase II clinical trials in LDCs, the U.S. and other selected countries.

The following research areas are given the highest priorities for development by PARFR:

- Self-administered methods
- Long-acting female methods
- Male methods (non-surgical)
- Female Sterilization Techniques
- Male Sterilization Techniques
- Intrauterine Delivery Systems
- Contraception Methods

The principal criteria for PARFR selection of projects are:

The research must be applied with a reasonable expectation of development of a new or improved means of fertility control.

New techniques developed must be suited to the needs of individuals and fertility control programs in the LDCs.

Accordingly, new methods given priority are those which do not rely on medical delivery systems, which require infrequent administration, which minimize supply problems, which decrease requirements for high levels of motivation, which do not require use at the time of sexual activity, which can be self-administered, and which may be effective on a "hind-sight" basis. Additionally, PARFR supports research to improve techniques for sterilization of males and females, especially methods that lend themselves to easy reversibility.

PARFR will continue to utilize its two-step proposal procedure, and supplement this process with PARFR-initiated development projects and pilot study activities.

#### Two-Step Proposal Procedure

##### 1. Informal Proposals

PARFR solicits informal research proposals by a periodic mailing of Request for Proposals (RFP) to a large number of national and international individuals and institutions. Another source of informal proposals is from national and international scientific meetings where PARFR advertises its program with scientific exhibits, distribution of PARFR literature, and discussions with prospective investigators. On occasion, PARFR advertises its program in key scientific journals. AID complements PARFR's mailing of RFPs by requesting AID missions' cooperation in soliciting proposals. Informal proposals are accepted on a continuing basis with no set deadlines. They are screened by PARFR's staff and with AID Technical Office concurrence, formal proposals are requested for those projects which conform to PARFR research objectives. Approximately a third of the informal proposals ever submitted have generated formal proposals.

##### 2. Formal Research Proposals

Formal proposals are reviewed three times a year. PARFR staff prepare written reviews and SAC members are provided copies of proposals and the reviews for their review prior to the SAC meeting. Whenever appropriate, evaluation by outside consultants is also utilized. The full SAC then discusses and votes on each formal proposal. AID Technical Office personnel participates in these meetings. AID approves

or disapproves each proposal recommended for funding. Subcontracts are then prepared and negotiated with the investigator's institution. Funds are provided under conditions of a cost-reimbursable subcontract. In general, projects are funded on a pro-rated annual basis at a maximum level of \$66,000 per year.

### Pilot Studies

Pilot Studies are solicited through the RFP mechanism, via personal solicitation by PARFR staff and SAC members, or as a result of PARFR-initiated activity. Pilot research studies, not to exceed \$10,000 for a one year effective period are selectively placed with promising investigators to assist them in the development of an extended research proposal. This mechanism greatly increases PARFR's flexibility in dealing with the needs of individual investigators, and eliminates the delay in obtaining preliminary research results often required by the SAC prior to award of a formal subcontract for extended research. Such administrative flexibility is valuable in the achievement of the objectives of both AID and PARFR, insofar as new ideas of merit can be afforded preliminary testing with resultant economies of time, money, and administrative effort. Pilot studies are funded by cost-reimbursement subcontracts with AID Technical Office and Contract Office approvals.

### PARFR-Initiated Proposals

PARFR staff, SAC and consultants may identify research ideas suitable for PARFR projects. These research ideas may be generated in any of several different ways. One of the more promising approaches is the PARFR organization of a mini-workshop on a specific topic or problem associated with fertility regulation. Relevant investigators from the U.S and other countries are invited to pool their collective expertise with that of PARFR Staff, AID and selected SAC members in a problem-solving endeavor designed to generate targeted research proposals.

PARFR will continue to use its initiative in moving promising developments from the laboratory and animal testing to early clinical testing. In several instances in PARFR's program, the developer of an innovative methodology or technique has lacked the facilities or expertise to undertake the next research step, and PARFR has played a facilitating role in maintaining the momentum of these promising developments.

## Research in Less Developed Countries

Because of growing concern about the real and potential side effects of the current contraceptive methods, it is clear that new and improved techniques are needed for both developed and developing countries. Moreover, there is considerable misapprehension about the fact that most of the original and ongoing contraceptive evaluation has been and is being carried out in developed countries. Thus, there is serious question as to whether or not the results of such are actually relevant to LDC population using these same methods.

Recognizing these two serious problems, several years ago PARFR began to identify sites in LDCs where applied research projects could be conducted in appropriate patient groups and under actual use conditions, in order to obtain more relevant data. PARFR has now developed a select network of developing country institutions at which there are well trained investigators who have indicated a strong interest in carrying out research on fertility regulation. To date the primary focus has been in Latin America, but, in the future, growing emphasis will be placed on the development of similar programs in Africa and Asia.

As outlined in this proposal, it is planned that an increasingly large proportion of PARFR's research studies, particularly clinical trials, will be done by LDC investigators. PARFR has identified a number of bright, young investigators who have returned to their countries of origin following their training at the Center for Research and Training in Reproductive Biology and Voluntary Regulation of Fertility at the University of Texas Health Science Center at San Antonio, Texas, and who want to continue research in reproduction. Additionally, PARFR has worked with other investigators in developing countries, and they too are participating in the PARFR-supported clinical research network.

This group will carry out research in three general categories. The first of these are projects submitted by individual LDC investigators. Second, network members are being kept apprised of on-going PARFR research. Once a new technique has been judged to be safe and effective by the principal investigator, members of the network can elect to carry out additional clinical studies using this technique. Third, collaborative clinical Phase I and Phase II projects are being developed by PARFR. In such situations, multiple institutions from both developed and developing countries will participate in a collaborative study in order to gather data from a variety of social and cultural settings. The collaborating centers utilize common standardized research protocols and data collection instruments. PARFR staff members and consultants are available, upon the request of LDC institutions, to provide technical assistance and short-term, in-country orientation and training in these new technologies. In certain cases, the PARFR-supported investigator is called upon, while in other cases, collaboration with other agencies and programs proves to be the most feasible and economical approach to take. In all of its projects

in both developed and developing countries, PARFR continues to coordinate its activities with those of related research programs, such as the IFRP, UNFPA, ICCR, PLAMIRH, PIACT, and WHO. In addition, PARFR is continuing its close working relationship with NIH and NICHD.

Several of the current PARFR-supported techniques are, or will soon be, ready for field trials. In order to evaluate their potential usefulness in a variety of clinical situations, studies are being set up in an extensive number of developing countries as outlined in the following table.

<u>Clinical Research Study</u>	<u>Actual or Intended Country Locations</u>
I. Female Sterilization	
a. Tissue adhesive delivered through the FEMCEPT device.	New York, South Korea, El Salvador, Philippines, India, Brazil, Indonesia, Germany and Chile
b. Tubal cauterization by silver acetate-alginate formulations	New York, Brazil, Indonesia
c. A fibrous polymer for the delivery of quinacrine to the fallopian tubes.	Brazil and Chile
d. Reversible female sterilization with tubal hoods	U.S., Belgium, Egypt, India, Philippines
e. Reversible female sterilization with uterotubal junction blocking device	Chicago, Mexico, West Germany and Singapore
II. Male Sterilization	
a. Percutaneous injection of vas deferens with sclerosing agents	New York and Brazil
b. Percutaneous bipolar cauterization of vas deferens	Colorado, New Orleans and Brazil (2 sites)
c. Reversible male sterilization "shug" device	Chicago, Egypt
III. Intrauterine Contraception	
a. Anti-fibrinolytic IUD	West Germany, Egypt, Thailand and the Philippines
b. Graphic assessment of uterine shape	Chicago, Brazil, Chile, Jamaica and Mexico

Clinical Research Study

Actual or Intended Country Locations

IV. Systemic Contraception

- |  |                            |
|--|----------------------------|
| a. Injectable biodegradable 180-day steroid delivery system                  | Alabama, Mexico and Brazil |
| b. Injectable biodegradable 90-day steroid delivery system                   | Alabama, Mexico and Brazil |
| c. Non-biodegradable medicated fibers for the controlled release of steroids | Chile                      |
| d. Biodegradable cylindrical implants for fertility control                  | U.S., Mexico and Chile     |
| e. Implantable pellet of norethisterone and cholesterol                      | New York, Mexico and Chile |
| f. Gossypol as a reversible contraceptive for men                            | U.S. and Brazil            |
| g. Reversible inhibition of sperm motility by oral Contrasperm               | U.S., Hong Kong and India  |

V. Barrier Contraception

- |                                     |  |
|-------------------------------------|--|
| a. Water soluble spermicidal condom | U.S., Indonesia, India, Bangladesh, Philippines and South Korea  |
| b. Collagen Sponge Contraceptive    | Arizona, Texas, New York, Egypt, Tunisia, Philippines and Mexico |
| c. Intravaginal insert (IVI)        | U.S. and Brazil  |

VI. Contraceptational Methods

- |  |   |
|--|---|
| a. Testing of Lepetit Compound DL-105-IT       | Philadelphia, India and U.K.                        |
| b. Testing of Schering CI and CII Compounds    | West Germany and India                              |
| c. Super-agonist and super-antagonist of LH-RH | San Diego, San Antonio, Brazil, Argentina and Chile |

## Workshops

PARFR has successfully organized 10 workshops designed to review current developments in an applied research area and to provide an opportunity to interact with research investigators. The 11th workshop is currently being planned "LH-RH as Male or Female Contraceptives" for April, 1981, in Chicago. PARFR intends to continue these workshops on an annual basis. The proceedings of all workshops are published and internationally distributed by Harper and Row Publishers.

## "Research Frontiers in Fertility Regulation"

At the center of an applied fertility control research program, PARFR is in an excellent position to follow current research in a variety of areas. To overcome the known gap in current research information availability, PARFR publishes reviews of both published and unpublished findings in selected field of fertility regulation research. Selected, knowledgeable investigators are requested to review all pertinent studies in a specific area of fertility control. The material is submitted to PARFR for final review and editing, and subsequent printing. Each review will be approximately 10 pages, prepared in a loose-leaf manner. PARFR using its own mailing list, supplemented by a selected list from the Population Reports Series, distributes approximately 6,000 copies of each issue to individuals, libraries and institutions. The first issue, "Long-acting Steroidal Contraceptive Systems," was distributed in July, 1980, and a copy of this issue is appended.

## Scientific Advisory Committee

In carrying out the objectives of this program, the SAC will continue to play an important role in reviewing proposals, monitoring funded projects and providing scientific consultation to the program. Composed of experts actively engaged in reproductive research, the size of the committee will be limited to the chairman and up to 12 regular voting members representing the scope of scientific disciplines most important to the program. SAC meetings are held three times yearly for the purpose of reviewing proposals and monitoring projects. In addition, SAC members participate in site visits of on-going research projects and provide consultation to prospective investigators in developing research projects.

## 6. Research Methodology

The research methodology of informal and formal proposals is reviewed by PARFR Staff and the Scientific Advisory Committee. If the project involves human subjects, the protocol and informed consent form must be approved by Northwestern University Review Board for Research on Human Subjects.

## 7. Researcher Competence

The PARFR administrative unit is established within the Department of Obstetrics and Gynecology of Northwestern University Medical School and John J. Sciarra, M.D., Ph.D., Professor and Chairman of the Department, serves as Program Director and Chairman of the Scientific Advisory Committee. Dr. Sciarra has generated considerable momentum for this program and much of its success can be attributed to his skill and expertise. His demonstrated credibility in the scientific community, as well as his broad knowledge of reproductive biology and the key workers in this field have contributed significantly to the success of the program.

Dr. Sciarra is a Phi Beta Kappa graduate from Yale, and has obtained both an M.D. and a Ph.D. from Columbia University. Under his leadership as head of the Department of Obstetrics and Gynecology at the University of Minnesota, the department established an outstanding record of research achievement in reproductive biology. Currently, he is Professor and Chairman of the Department of Obstetrics at the Northwestern University Medical School, Chief of Staff of the Prentice Women's Hospital, and Vice President for Medical Affairs of the Chicago Maternity Center. Dr. Sciarra has authored and edited numerous books in the field of reproductive biology and is Editor in Chief of Gynecology and Obstetrics. He is a member of the Board of Associate Editors of "Contraception," and serves on the Editorial Board of "Fertility and Sterility." He has published over 50 papers, and is a winner of the Carl G. Hartman Award of the American Society for the Study of Sterility.

Diane H. Krier serves as the Director of Administration where she is primarily responsible for the administrative functioning of the PARFR program. Ms. Krier joined PARFR on July 1, 1977. She has an M.B.A. (1975) from Loyola University of Chicago with a major in Marketing, and has considerable experience in Personnel, Accounting, Finance, and Education Program Administration from a previous position in a Chicago medical center.

Gerald I. Zatuchni, M.D., M.Sc. serves as the Director of Technical Assistance. He is Associate Professor of Obstetrics and Gynecology at Northwestern University Medical School. His major responsibility is to provide technical assistance and scientific direction for PARFR efforts in contraceptive development.

Previously, Dr. Zatuchni was the Associate Director, Technical Assistance Division, Population Council, Inc., New York. He has been involved in population/family planning and contraceptive development for over 15 years in a variety of roles and locations, having served as Director of the International Postpartum Family Planning Program (New York), Advisor to the Ministry of Health and Family Planning, Government of India (New Delhi, India), Consultant to the Maternal/Child Health Unit, World Health Organization (Geneva, Switzerland), and Resident Representative and Regional Medical Director for the Population Council in Tehran, Iran. Dr. Zatuchni has published over 50 papers on topics related to Obstetrics and Gynecology and Family Planning.

Alfredo Goldsmith, M.D., M.P.H., joined the PARFR staff as Head, Research Project Development on April 1, 1980. Dr. Goldsmith received his M.D. from the University of Chile, Santiago and his M.P.H. in Population Planning from the University of Michigan, Ann Arbor. Dr. Goldsmith's primary responsibility is to provide assistance in project development and to coordinate and monitor ongoing projects.

Dr. Goldsmith formerly served as Associate Director of the International Fertility Research Program. He has been active in the population field since 1965, when he took charge of the Postpartum Family Planning Program of the University of Chile, - a position he held for twelve years. Dr. Goldsmith has served as a consultant for the American Public Health Association, the International Project Association for Voluntary Sterilization, the United Nations Fund for Population Activities, World Bank, the World Health Organization, and other population-related organizations. He has published 5 books, 11 chapters in books, and more than 70 papers in areas related to Obstetrics and Gynecology and contraceptive technology.

PARFR's Scientific Advisory Committee, a group of 12 experts with primary interest and expertise in the areas of reproductive biology and contraceptive development, is composed of individuals representing numerous universities and disciplines, including Obstetrics and Gynecology, Urology, Veterinary Medicine, Biochemistry, Endocrinology, and Reproductive Physiology. The present members are:

John J. Sciarra, M.D., Ph.D. Chairman	Obstetrics and Gynecology Northwestern University
Nancy J. Alexander, Ph.D.	Reproductive Physiology University of Oregon
Robert T. Chatterton, Ph.D.	Steroid Biochemistry Northwestern University
Joseph E. Davis, M.D.	Urology New York Medical College
Edward C. Mather, D.V.M., Ph.D.	Animal Reproductive Physiology Michigan State University
Kamran S. Moghissi, M.D.	Reproductive Endocrinology Wayne State University
Carl J. Pauerstein, M.D.	Obstetrics and Gynecology; Physiology The University of Texas Health Science Center at San Antonio
Ralph M. Richart, M.D.	Obstetrics and Gynecology; Pathology Columbia University
Susan C.M. Scrimshaw, Ph.D.	Social Anthropology University of California at Los Angeles
Aquiles J. Sobrero, M.D.	Obstetrics and Gynecology Northwestern University
Judith L. Vaitukaitis, M.D.	Endocrinology Boston University
A. Albert Yuzpe, M.D.	Obstetrics and Gynecology University of Western Ontario, Canada

Another valuable resource for PARFR has been its 56 consultants (see Appendix). They come from many different areas of the country and represent a wide variety of disciplines. PARFR consultants, assembled over the life of this program, serve to supplement the expertise of the SAC members by reviewing proposals and making site visits to monitor specialized projects.

#### 8. Contribution to Institution Building

PARFR has and will continue to strengthen the applied research programs in LDC institutions and in the U.S. Traditionally, U.S. universities have not been willing to apply their resources to the field of applied contraceptive development; rather, investigators at these institutions have opted for more fundamental reproductive biological research. PARFR has encouraged U.S. institutions by the solicitation of proposals and the development of PARFR-initiated projects.

Fifteen institutions in 15 less developed countries have been strengthened in their research activities by both provision of funds and technical assistance in the development and carrying out of PARFR projects. These funds are utilized for salary support, small equipment purchase, animal purchase and maintenance, and indirect costs. Additionally, over 300 developing country scientists, researchers and clinicians have participated in PARFR workshops. In several instances, family planning authorities have requested PARFR's organizational expertise and support for national workshops on various aspects of fertility regulation. These have included Mexico, Brazil, and India. Currently, PARFR is planning additional workshops in Rio de Janeiro, Brazil and Surabaya, Indonesia.

#### 9. Expected End Results

AID's original mandate to PARFR in 1972 was to develop new and/or improved methods of fertility regulation suitable for use in less developed countries. The program was designed to provide scientific and technical assistance along with small amounts of financial support to investigators, researchers, and clinicians in the U.S. and abroad. To this end, an intensive international effort was made to solicit proposals from the scientific community. AID was also concerned about the length of time it took under their existing program guidelines and administrative procedures to fund small innovative projects. Therefore, the PARFR guidelines were written in a manner that would allow it to solicit, screen and fund research projects in a matter of several months.

Today PARFR continues to provide AID with a flexible, efficient and cost effective approach to the support of projects dealing with fertility regulation. While it has long since been conceded that there will probably never be an "ideal" contraceptive for all circumstances, it continues to be equally true that there is a great need for a broad spectrum of fertility regulation methods which are more convenient to use, less annoying, and which require less complex and expensive distribution systems than do the presently available methods. With this in mind, PARFR has selected for funding projects that meet these criteria. The last few years have seen the development of a number of promising new techniques for both men and women. These include barrier methods of vaginal contraception, long-acting injectables, and non-surgical methods of permanent contraception and potentially reversible "sterilization" for both males and females. In addition, another group of projects in these and other areas are now in the early stages of testing.

As regards the second problem, time, PARFR has been able to shorten considerably the interval between the development and evaluation of a new idea and its active application in a clinical setting. Numerous innovative techniques have been studied at many institutions in both developed and developing countries with a minimum of bureaucratic delay and expense.

Now that PARFR is a well-established widely recognized scientific and educational organization, it is prepared to build upon its earlier work and expand its activities, especially in the area of collaboration with investigators from less developed countries. In line with its original mandate, increasing amounts of support are going into clinical trials in LDC's. In addition, PARFR will continue to put great emphasis on the review and dissemination of the data coming out of its projects. Grantees will be aided and encouraged to present the results of their research at scientific meetings, both national and international.

PARFR will continue to hold several types of meetings for their grantees and other investigators working in allied fields. The highly successful workshop format will be continued. Additionally, small technical meetings will be organized which will serve the dual purposes of informing PARFR about new developments, and of providing PARFR access to scientific thinking on highly selective research areas. Larger and more broadly based meetings of a post-graduate nature will be organized to inform developing country personnel about new developments in fertility regulation technology.

Finally, through its various publications, PARFR will continue to be a source of up-to-date information, both on research coming out of its own program and on the entire field of fertility regulation.

In summary, the development of practical fertility control methods is an important and essential element of the social and economic development of societies. This is a goal to which the United States Agency for International Development in general, and PARFR in particular, continue to be dedicated.

## 10. Utilization Plan

The gap between the acquisition of new knowledge and its practical application has long been a matter of concern to both scientists and development agencies. Of equal concern has been the frequently long lag time between the development of a new technology and its widespread usage. Recognizing these dual and closely allied problems, concurrent with its efforts to find new and better methods of fertility regulation, PARFR has been forming and expanding links to other groups who will take the most promising leads coming out of the PARFR program and continue their development.

These groups belong to both the public and the private sectors. Key among the former group is IFRP, also primarily AID-supported. The link between PARFR and IFRP forms a natural and effective progression from early small scale testing to large scale field trials. In addition, close contact is maintained with other agencies, both national, such as FDA, NIH and NICHD and international, such as UNFPA, WHO, and PIACT.

PARFR is also now working much more closely with the private sector. Highly productive ties have been established with a number of the major pharmaceutical companies, both in the U.S. and abroad. These links have proven to be mutually advantageous, PARFR aiding in early evaluation and industry assuring the continued development and the ultimate availability of successful products to LDCs, via public sector rights established by PARFR and AID.

Additional ways of making both the services of the PARFR staff and the data coming out of the PARFR program more readily available have been established. PARFR maintains an active liaison with other contraceptive development projects and many research workers in the field. This liaison is accomplished by dissemination of research findings through publication of PARFR-supported research, presentation of PARFR research at scientific meetings, and by PARFR scientific exhibits at key national and international meetings.

Finally, PARFR workshops have served to bring researchers together to provide a review and critical analysis of the current status of a particular fertility control modality. Subsequent publication of these workshops has resulted in broad dissemination of the information presented at the meetings.

PARFR PROPOSED FIVE-YEAR BUDGET

July 1, 1981 - June 30, 1986

<u>CATEGORY</u>	<u>81-82</u>	<u>82-83</u>	<u>83-84</u>	<u>84-85</u>	<u>85-86</u>	<u>TOTAL</u>
<u>Administrative Costs</u>						
Salaries	\$ 277,566	\$ 311,291	\$ 328,389	\$ 347,196	\$ 367,883	\$ 1,632,325
Fringe Benefits (14.3%)	39,692	44,515	46,960	49,649	52,607	233,423
Indirect Cost (39% S&W)	108,251	121,403	128,072	135,406	143,474	636,606
Rent	21,606	24,307	27,345	30,763	34,608	138,629
Supplies	65,000	68,500	72,850	78,000	84,500	368,850
Equipment	22,000	25,000	25,000	25,000	25,000	122,000
TOTAL ADMINISTRATIVE	534,115	595,016	608,616	644,014	686,072	3,067,833
Consulting Fees	25,000	25,000	25,000	25,000	25,000	125,000
Travel	50,000	55,000	65,000	65,000	65,000	300,000
Workshops/Publications	85,000	85,000	85,000	85,000	85,000	425,000
Research & Development	2,125,000	2,400,000	2,800,000	3,100,000	3,300,000	13,725,000*
Research Supplies	20,000	25,000	30,000	35,000	40,000	150,000
TOTAL RESEARCH	2,305,000	2,590,000	3,005,000	3,310,000	3,515,000	14,725,000
TOTAL PROPOSED BUDGET	2,839,115	3,185,016	3,613,616	3,954,014	4,201,072	17,792,833
Admin. Costs/Total Budget	18.8%	18,7%	16.8%	16.3%	16.3%	17.2%

Approximate Percentage

Traditional PARFR -type studies including new ideas	51%
Network Studies (US and Abroad)	26%
Development (Product manufacture, FDA required animal toxicity studies, etc.)	23%

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PARFR YEAR I PROPOSED BUDGET, 7/1/81 - 6/30/82

PERSONNEL: PROFESSIONAL STAFF

John J. Sciarra, M.D., Ph.D. Program Director/Scientific Advisory Committee Chairman	10%	1.2 man-months	- 0 -
Gerald I. Zatuchni, M.D., M.Sc. Director of Technical Assistance	80%	9.6 man-months	\$ 40,090
Diane H. Krier, M.B.A. Director of Administration	100%	12.0 man-months	27,500
Alfredo Goldsmith, M.D., M.P.H. Head, Research Project Development	100%	12.0 man-months	50,113
To Be Named Research Development Coordinator	100%	12.0 man-months	50,113

PERSONNEL: NON-PROFESSIONAL STAFF

Ann Conner Nickle Project Controller	100%	12.0 man-months	18,000
Ruvenia Thomas Secretary	100%	12.0 man-months	16,500
Mary Rose Traylor Secretary	100%	12.0 man-months	14,500
Martha Rolon Secretary	100%	12.0 man-months	13,750
Kelley Osborn Publication Coordinator	50%	6.0 man-months	12,000
To Be Named Department Assistant	100%	12.0 man-months	15,000
To Be Named Computer Technician	100%	12.0 man-months	20,000

TOTAL PERSONNEL SALARIES \$277,566

FRINGE BENEFITS (% of Salaries & Wages) 39,692

14.3% x \$277,566

INDIRECT COST (% of Salaries & Wages) 108,251

39% x \$277,566

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<u>RENT TO NORTHWESTERN MEMORIAL HOSPITAL</u> (Including utilities and maintenance)	\$ 21,606	
<u>SUPPLIES</u>	65,000	
<u>EQUIPMENT</u>	22,000	
<u>TOTAL ADMINISTRATIVE</u>		\$ 534,115
<u>CONSULTING FEES</u>		
SAC Meetings (12 x \$386 x 3)	\$ 13,896	
Site Visits, Proposal Reviews and Project Development	<u>11,104</u>	
Total Consulting Fees		25,000
<u>TRAVEL</u>		
Foreign	35,000	
Domestic	<u>15,000</u>	
Total Travel		50,000
<u>WORKSHOPS/PUBLICATION</u>	85,000	
<u>RESEARCH AND DEVELOPMENT</u>	2,125,000	
<u>RESEARCH SUPPLIES</u>	20,000	
<u>TOTAL RESEARCH</u>		2,305,000
<u>TOTAL PROPOSED BUDGET (YEAR I)</u>		<u>\$2,839,115</u>

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BUDGET JUSTIFICATION

Estimates of PARFR Research and Development Costs  
(in thousands of dollars)

<u>Contraceptive Research Area</u>	<u>1981-82</u>	<u>1982-83</u>	<u>1983-84</u>	<u>1984-85</u>	<u>1985-86</u>	<u>Total</u>
I. Female Sterilization	\$ 350	\$ 400	\$ 500	\$ 600	\$ 650	\$ 2,500 (18.2%)
II. Male Sterilization	225	275	325	350	350	1,525 (11.1%)
III. Intrauterine Contraception	225	250	300	325	375	1,475 (10.7%)
IV. Systemic Contraception (Male & Female)	750	800	900	1,000	1,100	4,550 (33.2%)
V. Barrier Methods	250	325	350	375	375	1,675 (12.2%)
VI. Pregnancy Termination	325	350	425	450	450	2,000 (14.6%)
<b>TOTALS</b>	<b>\$2,125</b>	<b>\$2,400</b>	<b>\$2,800</b>	<b>\$3,100</b>	<b>\$3,300</b>	<b>\$13,725</b> <b>(100%)</b>

The proposed plan of work will continue to emphasize PARFR developments in accordance with past trends of expenditures in each of the six major contraceptive areas. Each area includes several projects, ranging from animal studies, toxicology studies, developmental requirements, and studies required for the purposes of receiving FDA approval for clinical studies. The indicated figures allow some minor flexibility for research and development of new ideas not presently being undertaken. It should be noted that 62.5% of the budgeted amounts for the entire 5-year period are in the areas of sterilization and systemic contraception which include male and female methods.

The estimated research and development costs are based upon PARFR's present subcontractual expenditures in the specific projects. Additional costs are now required to support animal and toxicological studies in a specific development area leading towards FDA approval for an IND. Costing of Phase I and early Phase II collaborative clinical trials are also included. It should be noted that some developments during the next five years will be taken over by interested groups, either public or private, and hence, PARFR's costs should eventually decrease in that particular research area.

The estimated research and development costs for 1981-82 (1st year of this proposal), represents an approximate 60% increase in R & D costs, as compared to the budget for 1980-81. PARFR has initiated clinical trials of PARFR developments; for the most part, these clinical trials are to take place in developing countries with collaborating U.S. centers. The financial requirements for supporting these clinical trials far exceed PARFR initial development costs. Another major reason for the budget increase is the absolute requirement for PARFR to support whatever animal and toxicology studies are required by the FDA for IND submissions. To cite one example, the funding necessary for IND approval of the 90-day NET injectable steroid system approximates \$150,000; an additional amount of \$200,000 is required for the support of studies leading to FDA approval for Phase II clinical trials. Accordingly, the indicated increases in the PARFR budget for R & D costs is necessary if PARFR is to reach its goal of shortening the required time between the evolution of a new contraceptive method and its availability to developing countries.

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BUDGET JUSTIFICATION  
PERSONNEL

	<u>81-82</u>	<u>82-83</u>	<u>83-84</u>	<u>84-85</u>	<u>85-86</u>	<u>TOTAL</u>
John J. Sciarra 1.2 mm (10%)	- 0 -	- 0 -	- 0 -	- 0 -	- 0 -	- 0 -
Gerald I. Zatuchni 9.6 mm (80%)	\$ 40,090	\$ 40,090	\$ 40,090	\$ 40,090	\$ 40,090	\$ 200,450
Diane H. Krier 12.0 mm (100%)	27,500	30,250	33,275	36,603	40,263	167,891
Alfredo Goldsmith 12.0 mm (100%)	50,113	50,113	50,113	50,113	50,113	250,565
Research Development Coordinator 12.0 mm (100%)	50,113	50,113	50,113	50,113	50,113	250,565
Ann Conner Nickle 12.0 mm (100%)	18,000	19,800	21,780	23,958	26,354	109,892
Ruvenia Thomas 12.0 mm (100%)	16,500	18,150	19,965	21,961	24,157	100,733
Mary Rose Traylor 12.0 mm (100%)	14,500	15,950	17,545	19,300	21,230	88,525
Martha Rolon 12.0 mm (100%)	13,750	15,125	16,638	18,301	20,131	83,945
Kelley Osborn 6.0 mm (50%)	12,000	13,200	14,520	15,972	17,569	73,261
Department Assistant 12.0 mm (100%)	15,000	16,500	18,150	19,965	21,961	91,576
Computer Technician 12.0 mm (100%)	20,000	22,000	24,200	26,620	29,282	122,102
Biostatistician 12.0 mm (100%)	- 0 -	20,000	22,000	24,200	26,620	92,820
TOTAL SALARIES	<u>\$277,566</u>	<u>\$311,291</u>	<u>\$328,389</u>	<u>\$347,196</u>	<u>\$367,883</u>	<u>\$1,632,325</u>

Salaries:

Eight professionals are included among PARFR personnel: the Program Director/Scientific Advisory Committee Chairman, the Director of Technical Assistance, the Director of Administration, the Head of Research Project Development, the Project Controller, the Research Development Coordinator (vacant), the Publications Coordinator, and the computer technician (vacant). There are three support staff members among PARFR's current staff. One position is being requested in this proposal for a Department Assistant.

The salaries listed above indicate the man-months anticipated for each position per year, the percentage of effort that each individual will devote to the work under this contract, and the anticipated salary for each position. Ten percent annual increases in salaries have been incorporated in salary estimates to allow for yearly merit increases and occasional cost of living increases which are provided in accordance with Northwestern University policies. Individuals at government maximum have remained at that amount even though the potential maximum may increase during the 5 year period of the contract.

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<u>Fringe Benefits:</u>	<u>1981-82</u>	<u>1982-83</u>	<u>1983-84</u>	<u>1984-85</u>	<u>1985-86</u>	<u>Total</u>
14.3% of S & W	\$39,692	\$44,515	\$46,960	\$49,649	\$52,607	\$233,423

The current Fringe Benefits rate for Northwestern University employees is 14.3% of the total Salaries and Wages (effective 9/1/79). It is expected that this rate will increase during the course of the 5-year proposed period, but an estimate is not available at this time. Northwestern University has requested that the current rate be used for the entire proposed program period.

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<u>Indirect Costs:</u>	<u>1981-82</u>	<u>1982-83</u>	<u>1983-84</u>	<u>1984-85</u>	<u>1985-86</u>	<u>Total</u>
39% of S & W	\$108,251	\$121,403	\$128,072	\$135,406	\$143,474	\$636,606

The current negotiated overhead rate for Northwestern University is 39% of the total Salaries and Wages (effective 9/1/79-8/31/81). This is in accordance with FMC 73-6 negotiated as of May 14, 1979. This rate may change over the course of the proposed program period.

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<u>Rent:</u>	<u>1981-82</u>	<u>1982-83</u>	<u>1983-84</u>	<u>1984-85</u>	<u>1985-86</u>	<u>Total</u>
	\$21,606	\$24,307	\$27,345	\$30,763	\$34,608	\$138,629

PARFR occupies 1,708 square feet on the 10th floor of Passavant Pavilion of Northwestern Memorial Hospital (NMH). For the period of 7/1/78-6/30/79, PARFR paid NMH rent of \$17,506 (\$10.25/sq. ft.). For the period of 7/1/79-6/30/80, PARFR paid \$19,215 (\$11.25/sq. ft.).

NMH is now proposing a rate of \$21,606 for 7/1/80-6/30/81 (\$12.65/sq. ft.). This is a 12.5% increase over the previous year. We are projecting a 12.5% increase for the other years.

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<u>Supplies:</u>	<u>1981-82</u>	<u>1982-83</u>	<u>1983-84</u>	<u>1984-85</u>	<u>1985-86</u>	<u>Total</u>
Postage	15,000	17,000	17,850	20,000	21,500	91,850
Periodicals/Books	10,000	10,000	11,000	11,000	12,000	54,000
Telephone	15,000	16,000	17,000	18,000	19,000	85,000
Duplicating/ Printing	10,000	10,000	11,000	12,000	12,000	55,000
Office Supplies	15,000	15,000	16,000	17,000	20,000	83,000
<b>TOTAL SUPPLIES</b>	<b>\$65,000</b>	<b>\$68,500</b>	<b>\$72,850</b>	<b>\$78,000</b>	<b>\$84,500</b>	<b>\$368,850</b>

All expendable office supplies are included in this category. Items included are office machine rental and maintenance, telephone costs, postage costs, printing and duplicating, medical journals and books, and general office supplies such as Xerographic paper and supplies, file folders, binders, and the like.

A number of factors contribute to the size of the line-item for supplies. Multiple copies of individual documents are needed for SAC members, AID personnel, University personnel and subcontracting institutions. PARFR is an international and nationwide organization, telephone costs are high. PARFR needs frequent large mailings to organize workshops, publication distribution, and solicitation of proposals. PARFR maintains a library for which selected medical publications are sought and purchased. PARFR distributes copies of its new publication "Research Frontiers in Fertility Regulation" to a mailing list of 6,000. PARFR also distributes copies of workshop publications to selected individuals.

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<u>Equipment:</u>	<u>1981-82</u>	<u>1982-83</u>	<u>1983-84</u>	<u>1984-85</u>	<u>1985-86</u>	<u>Total</u>
	\$22,000	\$25,000	\$5,000	\$3,000	\$3,000	\$58,000

PARFR proposes to computerize our data management system which would: 1) provide files of research proposals submitted to PARFR; 2) process data relevant to external and internal reports; 3) maintain bibliographic files of publications originated from subcontractors' work and/or other sources, related to subject matters of interest to PARFR; and 4) facilitate a rational distribution of information among PARFR members.

Computerization would include: 1) Hardware - a minicomputer based system, including large storage capacity for sequential filing. Input-output devices with video-hard copy alphanumeric displays and graphics and communication capabilities. 2) Software - operating system, data management oriented. PARFR may be able to attach a computer system within our Lexitron Word Processor.

PARFR plans to increase its staff, therefore funds are needed for additional office furnishings. In order to provide adequate organized storage of accumulated PARFR documents, additional shelving and cabinets will become necessary.

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<u>Consulting Fees:</u>	<u>1981-82</u>	<u>1982-83</u>	<u>1983-84</u>	<u>1984-85</u>	<u>1985-86</u>	<u>Total</u>
SAC Meetings (12 x 3 x \$193 x 2 days)	\$13,896	\$13,896	\$13,896	\$13,896	\$13,896	\$ 69,480
Additional Consultants	\$11,104	\$11,104	\$11,104	\$11,104	\$11,104	\$ 55,520
TOTAL CONSULTING FEES	\$25,000	\$25,000	\$25,000	\$25,000	\$25,000	\$125,000

PARFR relies heavily upon the expertise of its consultants for assistance in subcontract funding decisions and in monitoring ongoing projects. The Scientific Advisory Committee (SAC) currently has eleven approved members (with a twelfth member soon to be approved). SAC meets three times per year to assist PARFR staff in review of proposals submitted for funding, monitoring of funded research, and planning of research programs. Government maximum daily rate is \$193/day.

In addition, the Program has developed a group of approved consultants with expertise in areas of reproductive biology and related clinical areas to supplement the expertise of the staff and Scientific Advisory Committee. These consultants are routinely used for proposal review, technical report review, and site visits, in addition to or as substitutes for members of the Scientific Advisory Committee and Staff. This pool of consultants is continually open to expansion with the approval of the AID Technical and Contract Offices.

Since the number and types of subcontracts sponsored by the Program varies from time to time, it is impossible to anticipate accurately the number of consultants and the number of man-days of services which will be required, the budget reflects an approximation. PARFR reimburses \$50 per proposal review. Each consultant's fee is approved individually, usually based upon his or her present annual income. The consultant rate per day, dependent on salary, ranges from \$60/day to a maximum of \$193/day. The fee does not include travel and transportation costs. These are provided by the Program separately and are included in the Budget in the items identified as Travel.

<u>Travel:</u>	<u>1981-82</u>	<u>1982-83</u>	<u>1983-84</u>	<u>1984-85</u>	<u>1985-86</u>	<u>Total</u>
PARFR Staff and SAC Members-Program Development (25 trips x \$400)	\$10,000	\$11,000	\$13,000	\$13,000	\$13,000	\$ 60,000
SAC Meetings (16 x 3 meetings)	15,000	16,000	18,000	18,000	18,000	85,000
Site Visits (20 domestic x \$400)	8,000	10,000	12,000	12,000	12,000	54,000
(10 foreign x \$1500)	15,000	16,000	20,000	20,000	20,000	91,000
Additional Travel	<u>2,000</u>	<u>2,000</u>	<u>2,000</u>	<u>2,000</u>	<u>2,000</u>	<u>10,000</u>
TOTAL TRAVEL	\$50,000	\$55,000	\$65,000	\$65,000	\$65,000	\$300,000

A slight increase is projected for the first three years. Travel expenses are provided for PARFR staff, consultants, and investigators for travel to domestic and foreign locations, to evaluate projects which are funded or might be funded, travel to meetings, and travel to meetings of related organizations to speak on behalf of PARFR. No dependents are included in these Budget items since PARFR activities do not require individuals to be away from home for sufficient periods of time to require their dependents to travel with them. Likewise, no provision is made for household effects to be shipped and/or stored.

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<u>Workshops/ Publications:</u>	<u>1981-82</u>	<u>1982-83</u>	<u>1983-84</u>	<u>1984-85</u>	<u>1985-86</u>	<u>Total</u>
PARFR Publications	\$35,000	\$35,000	\$35,000	\$35,000	\$35,000	\$175,000
Workshops	50,000	50,000	50,000	50,000	50,000	250,000
TOTAL WORKSHOPS/ PUBLICATIONS	<u>\$85,000</u>	<u>\$85,000</u>	<u>\$85,000</u>	<u>\$85,000</u>	<u>\$85,000</u>	<u>\$425,000</u>

PARFR routinely sponsors annual scientific workshops on new techniques of fertility regulation at which leading national and international investigators are brought together to present their experiences and to exchange ideas. The workshops are designed to review current developments in the applied research area and to provide an opportunity to develop research programs suitable for funding by PARFR. Approximately 80-175 invited participants attend each workshop. Speakers are provided with economy air fare and hotel accommodations during the course of the workshop. No honoraria are provided. Individuals invited as "observers" are requested to pay their own transportation and living expense. Individuals who participate in workshops and are personnel of AID or other government agencies are not financially supported by PARFR.

The proceedings of each workshop are published in hard-cover form. PARFR's series "Research Frontiers on Fertility Regulation" will be published 6 times a year.

The Workshops/Publications budget is based directly on experience with past workshops. An increase in publications cost is anticipated due to the increasing volume of material generated by the workshops, rising publication costs, and a desire to keep retail cost of our publications reasonable. This cost increase is not projected in this budget presentation. If costs increase too much, the Research Frontiers on Fertility Regulation series may have to be cut to 4 issues per year instead of 6.

UNIVERSITY OF MINNESOTA  
 May 31, 1972 - June 30, 1975  
 FINANCIAL ACCOUNTING OF  
 PRIME CONTRACT  
 AID/csd-3608

	<u>Budget</u> <u>5/31/72 - 6/30/75</u>	<u>Expended</u> <u>5/31/72 - 6/30/75</u>
Salaries	\$ 187,839	\$ 188,538
Fringe Benefits	30,952	21,237
Indirect Costs	49,522	51,270
Supplies	27,240	32,920
Equipment	11,500	11,133
Facility Rental	19,400	19,264
Consultant Fees	26,350	20,164
Travel	98,050	63,087
Workshops	115,000	86,117
Subcontracts	2,783,670	1,024,841
TOTAL:	<u>\$3,349,523</u>	<u>\$1,518,571*</u>

\* Unexpended funds transferred to Northwestern University  
 AID/csd-3608 as of 7/1/75.

NORTHWESTERN UNIVERSITY  
1975 - 1980 FINANCIAL ACCOUNTING  
OF PARFR PRIME CONTRACTS

<u>Categories</u>	AID/csd-3608 at Northwestern University		AID/DSPE-C-0035 at Northwestern University		Planned Committments for the Period <u>9/1/80-6/30/81</u>
	<u>Budget 7/1/75-6/30/80</u>	<u>Expended/Encumbered 7/1/75-6/30/80*</u>	<u>Budget 7/1/79-6/30/81</u>	<u>Expended/Encumbered 7/1/79-6/30/81</u>	
Salaries		\$ 372,927	\$ 386,134	\$ 365,968	
Fringe Benefits		51,269	55,217	52,245	
Indirect Costs		131,095	150,596	141,846	
Supplies		141,544	117,800	90,920	
Equipment		27,995	2,600	347	
Alterations & Moving Costs		14,213	- 0 -	- 0 -	
TOTAL ADMINISTRATIVE	\$ 739,043	739,043	712,347	651,326	
Consulting Fees		40,973	35,200	20,442	\$ 6,600
Travel		143,860	115,000	55,120	45,000
Workshops/Publications		191,663	135,000	61,603	65,000
Subcontracts		3,242,321	2,262,453	1,039,862	1,120,000
Pilot Studies		138,245	150,000	74,212	35,000
TOTAL RESEARCH	3,773,469	3,757,062	2,697,653	1,251,239	1,271,600
GRAND TOTAL	\$4,512,512	\$4,495,105	\$3,410,000	\$1,902,565	\$1,271,600
Percentage Admin/Total	16.4%		20.9%		

\* Funds were appropriated only through 6/30/79. Subcontracts were able to be written for work through 6/30/80.

Σ To date, all final invoices have not been submitted.

11. Budget Analysis

PARFR requested an annual budget of approximately \$4.2 million over the five years. We are requesting approval at a level of \$2.839 million for FY1981 and an average of about \$3.6 million over the five years. This compares with the FY1980 funding of \$1.91 million. We believe this reflects a realistic pattern of growth which takes into consideration:

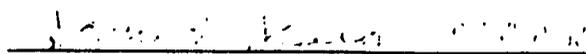
- 1) the increasing amount of good quality traditional "new idea" type research,
- 2) collaborative phase I and II studies in the U.S. and in developing countries of successful PARFR developments, and
- 3) developmental costs including product manufacture and long-term animal toxicity studies necessary for FDA approval.

The program continues to be highly productive with a low percentage of costs going to administration.

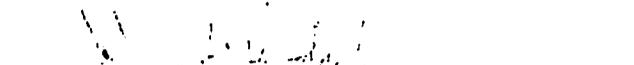
12. Proposing Office General Evaluation

PARFR operates a vigorous and effective research program which is responsive to AID's needs. The PARFR program has reached a stage of maturity in which a number of important developments are on the threshold of practical value to developing country family planning programs. These include two intravaginal methods of contraception, long-acting injectable progestin contraceptives, a non-surgical (MCA) technique for female sterilization, a non-surgical technique for male sterilization by percutaneous vas thermocoagulation, and potentially reversible sterilization methods. The proposal contains adequate provision to carry developments such as these into the more advanced stages of early collaborative clinical trial and to carry out other "developmental" activity necessary for ultimate usefulness in family planning programs. At the same time PARFR will continue to emphasize early "new idea" research. Careful AID monitorship and communication with IFRP will continue to ensure that PARFR does not duplicate IFRP's extensive clinical phase III testing network and more sophisticated epidemiologic safety studies.

In general, the proposing office considers this program to be a successful, valuable, productive biomedical research program. It provides an efficient and effective mechanism for supporting projects in this area and for stimulating developing country and U.S. talent in the field. We strongly recommend its approval.

  
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Signature of Monitor, J.D. Shelton

  
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Signature of Duff G. Gillespie  
Chief, Research Division

  
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Signature of J.J. Speidel  
Acting Director, Office of Population