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**MIDTERM EVALUATION OF THE  
CONTRACEPTIVE  
RESEARCH AND DEVELOPMENT  
(CONRAD) PROGRAM**

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## Glossary

A.I.D.	U.S. Agency for International Development
AIDS	Acquired immune deficiency syndrome
CA	Cooperating Agency
CD:RI	Contraceptive Development: Research India
CONRAD	Contraceptive Research and Development Project
CTO	Cognizant Technical Officer
EVMS	Eastern Virginia Medical School
FDA	Food and Drug Administration
FHI	Family Health International
FSH	Follicle stimulating hormone
FTE	Full-time equivalent
FY	Fiscal year
GnSIF	Gonadotropin surge inhibiting factor
GnRH	Gonadotropin releasing hormone
ICCR	International Committee on Contraception Research (Population Council)
IND	Investigational new drug application
IRB	Institutional Review Board
IVF	<u>In vitro</u> fertilization
LDC	Less developed country
NIH	National Institutes of Health
NICHD	National Institute of Child Health and Human Development

<b>Ob/Gyn</b>	<b>Obstetrics/Gynecology</b>
<b>PARFR</b>	<b>Program for Applied Research on Fertility Regulation</b>
<b>PERT</b>	<b>Program evaluation review technique</b>
<b>PI</b>	<b>Principal Investigator</b>
<b>POPTECH</b>	<b>Population Technical Assistance Project</b>
<b>PY</b>	<b>Project year</b>
<b>R&amp;D</b>	<b>Research and development</b>
<b>RFA</b>	<b>Request for application</b>
<b>RIA</b>	<b>Radioimmunoassay</b>
<b>STS</b>	<b>Senior technical staff</b>
<b>TAC</b>	<b>Technical Advisory Committee</b>
<b>VSB</b>	<b>Vaginal spermicidal barrier</b>
<b>WHO</b>	<b>World Health Organization</b>

## Executive Summary

### Overview

At its midpoint, the Contraceptive Research and Development (CONRAD) program has moved rapidly and successfully to initiate numerous activities in contraceptive research. The several mid-course corrections identified in this evaluation are designed to assist the program to shift resources from the intramural to the extramural program, to broaden the portfolio of the extramural program, and to improve the management and administration of the total program.

CONRAD, with total authorized funding of \$28 million, is operating under a five-year Cooperative Agreement between the U.S. Agency for International Development (A.I.D.) and the Eastern Virginia Medical School (EVMS). This midterm evaluation was to identify the accomplishments, strengths, weaknesses, and problems of the program and to consider whether the project had been conceptualized and designed in a manner that would permit it to meet its objectives efficiently and effectively.

### Strengths

The CONRAD program has already begun to make its mark in the world of contraceptive research, through the excellence of some of its intramural research (conducted in-house), its funding of over 40 extramural subprojects (with outside institutions), and the holding of two international workshops, with publication of proceedings either accomplished or under way. Excellent staff were recruited and put in place very quickly. The intramural program is making good progress in a number of areas of contraceptive research, such as the GnRH antagonist subproject, which involves suppression of gonadotropin secretion through the use of the compound Nal-Lys-GnRH antagonist and reproductive immunology efforts, which focus on identifying, characterizing and isolating sperm and egg-based antigens germane to fertilization. Research on spermicide and virucide screening is also under way supported in part by the National Institute of Child Health and Human Development as part of a new initiative by CONRAD on the mechanism and prevention of the heterosexual transmission of HIV. An excellent Technical Advisory Committee (TAC) has been assembled to help guide the work of the program and the subprojects developed seem appropriate, falling into areas in which research is needed and scientifically feasible. The program has established excellent working relations with other organizations, both national and international, that are involved in contraceptive research and development.

### Weaknesses

Project weaknesses are primarily related to the over-emphasis on the longer-term leads in the research portfolio. This bias is evident in both the intramural and extramural components. In particular, the clinical research component of the intramural program has had a slower start than anticipated, but staff and facilities are now in place to accommodate a heavier load of subprojects if they can be identified.

## **Design Issues**

A major problem identified is that project management has not kept to the project design, which had mandated that two-thirds of project resources available for research would go to the extramural component and one-third to the intramural. The purpose of this mix was to ensure that the extramural outreach efforts, which were thought to be the most cost-effective way to develop new contraceptive leads, were supported by in-depth in-house scientific expertise, not to build an intramural research institution. It has turned out to be more expensive and time-consuming than anticipated to conduct in-house research, and considerable additional staff and a number of core laboratories have been added to support this work. Thus, at midpoint, about half of project resources are going to support intramural research, which, because of the research strengths of the intramural staff, is primarily on long-term leads.

By comparison, the extramural component is not receiving the attention anticipated from the intramural staff. In particular, the expectation that they would play an active role in soliciting and monitoring extramural subprojects has not materialized. The TAC, too, has not been actively involved in seeking out new subprojects.

## **Management Issues**

The project has gotten somewhat off course (especially with regard to the balance between intramural and extramural, and between near-term and long-term subprojects) in large part because of a lack of firm management control. Planning of allocation of staff time and project resources is inadequate, and staff have not routinely attempted either to articulate goals that are to be met or to identify progress indicators to measure movement towards those goals. Likewise, monitoring of allocation of both time and funds needs improvement; the budgeting system does not allow attribution of staff costs and core labs to intramural subprojects and, therefore, the project has been unable to track the true expenditures on intramural subprojects as it can for extramural subprojects. It is highly likely that if a better tracking system had been in place, the program would not have gotten so far off track as it has. The lack of management oversight can be traced, in part, to the Project Director being extremely overextended, compounded by the decision not to fill the position of Director of Administration after it became vacant early on.

## **The Future**

The evaluation recognizes that because CONRAD is a research project, goal setting must be a flexible process whose priorities can change in response to research developments. The evaluation also recognizes that scientific staff of the calibre gathered together in the CONRAD program have multiple demands on their full time that has diverted their attention from the prime goals of this project.

The evaluation's major recommendation is that the program now take stock and make the difficult decisions necessary to permit reallocation of resources from intramural to extramural efforts and from longer to nearer-term subprojects. Specific programmatic changes suggested include more vigorous efforts to solicit a wider range of extramural and clinical subprojects and a careful reevaluation of the level of resources now devoted to intramural subprojects. At the same time, a major

**tightening of financial and staff planning and monitoring is recommended. First priority should go to improving the management and administration of the program, perhaps by hiring a Director of Administration, and external consultants should be brought in if necessary to assist staff develop a planning system that ensures that objective setting, strategy formulation, workplans, budgeting and reporting are part of a coherent system that makes clear the role of each staff member.**

# 1. Introduction

## 1.1 Project Background

### 1.1.1 Project Overview

The Contraceptive Research and Development (CONRAD) program, now at its midpoint, is one of three A.I.D.-funded efforts to support the development of new and improved family planning methods for use in developing countries. The program was created under a five-year Cooperative Agreement (September 30, 1986 to September 30, 1991) between the U.S. Agency for International Development (A.I.D.) and the Eastern Virginia Medical School (EVMS). With a total authorized funding level of \$28 million, CONRAD represents a major increase in A.I.D.'s support for this purpose. The program also takes a new organizational approach, including both an intra- and extramural component, on the assumption that this mix would provide the critical mass of views, expertise, approaches, and hands-on experience to enhance the likelihood of bringing new family planning methods to market.

### 1.1.2 Field of Contraceptive Development: Overview

Only a handful of public sector agencies are currently involved in the field of contraceptive development. In addition to CONRAD, A.I.D. supports Family Health International (FHI), which primarily conducts Phase III and IV trials (involving up to thousands of volunteers) on products developed elsewhere. The Population Council, which carries out research internally, and internationally through the International Committee for Contraception Research (ICCR), also receives some support from A.I.D. The other major public sector organizations are the World Health Organization (WHO) Special Programme of Research in Human Reproduction and the Contraceptive Development Branch of the Center for Population Research, National Institutes of Health, and several national research councils, including the Indian Council for Medical Research, all of which support biomedical research on reproduction and fertility regulation.

The CONRAD project is the successor of the program for Applied Research on Fertility Regulation (PARFR) of Northwestern University in Chicago. Unlike PARFR, which was exclusively a program that supported extramural research, CONRAD also supports a group of in-house scientists who have the dual responsibility of carrying out in-house research and overseeing extramural subprojects like that of PARFR. The rationale of mixing an intra- and an extramural program arose from the increasing scientific complexity of research and development in the area of human reproduction. Scientific advancements in highly specialized areas such as immunology, molecular biology, bioengineering, delivery systems and polymer chemistry require that staff overseeing any extramural program must be conversant with developments in all these areas. Moreover, the interrelationship between the two program components was expected to provide a synergism that would significantly accelerate overall progress.

### 1.1.3 Project Design

#### Principal Activities

To facilitate achievement of the overall project goal, the Cooperative Agreement envisions two principal areas of activities:

- Research; and
- Technical leadership and information dissemination.

With respect to research, CONRAD's niche within the overall field of contraceptive research includes the so-called mission-oriented or fundamental applied research, which falls somewhere between truly basic research and more advanced applied research and which is conducted to fill in gaps needed to bring an approach to the stage of clinical trials. Excluded from CONRAD's workscope is the support of basic, reproductive events research that is conducted simply to understand reproductive science and processes. CONRAD's primary role is to support research and development (R&D) activities beginning with targeted basic research studies which utilize animals and continue through the first two phases (I and II) of clinical trials. (Thereafter, typically Phase III work would be passed on to FHI.)

With respect to technical leadership and information dissemination, the Cooperative Agreement calls for a) convening of international and regional workshops, seminars, conferences and meetings and b) publication of proceedings of workshops, reviews of research findings, and a periodic bulletin or newsletter.

To accomplish the project objectives, the Cooperative Agreement listed 22 illustrative activities that might be undertaken.

### Project Evaluation Criteria

The Cooperative Agreement makes clear that project success will depend on how closely it adheres to its highest priority activity: moving leads through the necessary steps required to conduct Phase I and II clinical trials. Thus, the Agreement states that ultimately, the success of the CONRAD program will be judged on one criterion: the number of leads that reach the stage of Phase III clinical evaluation.

### Distribution of Resources

The project design calls for a preponderance of project resources to be devoted to extramural efforts: Two-thirds are expected to be applied to the extramural program and one-third to the intramural.

The intramural resources are to cover cost of in-house research projects, including staff salaries. The extramural funds are to cover subprojects with collaborating scientists and institutions and associated CONRAD staff salaries and operating expenses. The EVMS proposal, which won the CONRAD award, indicated it would try to achieve a ratio of one-quarter intramural to three-quarters extramural.

## **1.2 Evaluation Assignment**

### **1.2.1 Purpose of the Evaluation**

This midterm evaluation was designed primarily to assess the achievements and strengths of the CONRAD program to date, to identify any areas (weaknesses) requiring mid-course corrections, and to make recommendations as to what those corrections should entail. Specific areas to be investigated included whether the project had been designed and conceptualized in ways that would permit it to meet its objectives and whether it was being implemented according to the requirements of the Project Agreement.

Specific areas designated for in-depth examination included:

- The extent to which designated research priorities were being adhered to;
- The allocation of funds between intra- and extramural activities;
- The process of solicitation and monitoring of the extramural subprojects; and
- The adequacy of overall administrative and management structure and procedures.

(See Appendix A for full Scope of Work.)

### **1.2.2. Team Composition**

A four-person team carried out this evaluation. Together, they brought to the evaluation extensive knowledge of contraceptive development and biomedical research in family planning; extensive research experience in topics being investigated in the CONRAD program, including both applied fundamental and clinical research; experience in funding external biomedical research projects; and expertise in management and administration. Team members were

- Samuel A. Pasquale, M.D., Associate Dean for Clinical Affairs, UMDNJ-Robert Wood Johnson Medical School, New Brunswick, N.J. (team leader);
- Mahmoud Fahmy Fathalla, M.D., Ph.D., Professor of Obstetrics and Gynecology, Assiut University, Egypt; and Director-Designate of WHO Special Program of Research in Human Reproduction, Geneva;
- E. Edward Rizzo, management consultant and former Deputy Director of the Development Administration Division, A.I.D. and;
- Koji Yoshinaga, Ph.D., Reproductive Sciences Branch, Center for Population Research, National Institute of Child Health and Human Development, National Institutes of Health.

Jeffrey Spieler, Project Cognizant Technical Officer (CTO) in the Research Division, Office of Population, participated as a resource person for the entire evaluation period, and Dorothy Wexler, POPTECH project, participated as the report coordinator.

### **1.2.3 Evaluation Format**

The evaluation took place primarily over a four-day period (March 21-24) and involved the following:

- A one-day briefing at A.I.D. in Rosslyn, VA meeting with Office of Population staff and visiting CONRAD's extramural program, which is also located in Rosslyn.
- Three days at CONRAD headquarters in Norfolk, Va., inspecting the facilities, being briefed by CONRAD Senior Technical Staff (STS), meeting associate technical and administrative staff, and (during the final day) preparing a first draft of the technical sections of this report (see Appendix B for list of persons interviewed).

The management specialist had spent two additional days in Norfolk and one day in Rosslyn prior to the arrival of the rest of the team.

As part of the evaluation, teams members reviewed documents provided by A.I.D. and the CONRAD program (see Appendix C). These were supplemented during the evaluation by briefing papers provided by, and requested from, CONRAD staff.

Despite the short period of the evaluation, the team was confident that it had been provided an excellent overview of the CONRAD program, thanks to the full cooperation of the STS and the full-time involvement of the CTO. Prior to its departure, team members had a final session with STS to discuss its overall impressions of the program. These could be summarized as follows: Overall, the project has been very successful in recruiting its staff and getting numerous activities going, including more than 40 extramural subprojects, about 10 intramural projects, conducting two international workshops and publishing one workshop proceedings and two bulletins. Areas that need improvement include strengthening and widening the portfolio of the extramural program, decreasing the emphasis on the intramural program and improving the management and administrative aspects of the project, including financial and program planning. The evaluation team expressed its full confidence in the CONRAD program's ability to successfully conduct this well-conceptualized and exciting project.

## 2. Research

### 2.1 The Intramural Applied Fundamental Research Program

#### 2.1.1 Overview

The Applied Fundamental Research component can be counted as a major strength of the CONRAD program. It is composed of six subprojects, plus some pilot research that has not been formalized as a subproject (see Table A in Appendix D and Section 2.1.3). Thanks to the excellent quality of the work, the budget size, the number of participants, and the availability of space, this component has been successfully established as an important component of the CONRAD program. The activity of the subprojects is enhanced by four service facilities (core laboratories).

The subprojects aim at the development of new contraceptives by two means:

- 1) inhibition of gonadotropin secretion by administration of compounds or by immunological means, and
- 2) inhibition of fertilization by preventing the union of sperm with the ovum using antibodies to sperm antigens or spermicidal drugs.

#### 2.1.2 Evaluation of Each Subproject

##### 1) GnRH Antagonist

The GnRH (gonadotropin releasing hormone) antagonist subproject, a major activity with Year 2 costs estimated at \$416,000, appears very successful but expensive. The scientific mechanism involves suppression of gonadotropin secretion through administration of compounds. In the early stages of development of this approach, the GnRH antagonist compounds were found to have inherent histamine-releasing side effects. Improvements resulted in the currently available "third generation" GnRH antagonists, with little of these negative side effects.

The CONRAD subproject studies have been conducted on the effects of Nal-Lys-GnRH antagonist on the hypothalamus-pituitary-ovarian axis of female monkeys. Weekly injections of Nal-Lys GnRH antagonist to ovariectomized monkeys have resulted in a long-term continuous suppression of gonadotropin secretion. In vitro studies indicated that gonadotropes did not have a residual loss of their responsiveness to GnRH challenge after the suppression of gonadotropin release by the antagonist and subsequent removal. In vivo studies using cycling monkeys revealed that Nal-Lys GnRH antagonist given prior to ovulation (when estradiol level is less than 200 pg/ml) prevented ovulation without luteal tissue formation in the follicle in which ovulation was prevented. Concomitant administration of a synthetic progestin with Nal-Lys GnRH antagonist will mimic the normal cyclic ovarian hormonal pattern without ovulation. The finding is very promising with relation to possible development of a new female contraceptive method. If the toxicological studies (conducted by NICHD) are successful, clinical trials could be initiated within one year.

##### 2) FSH Suppression in Male Primates

The subproject on the immunological suppression of FSH (follicle stimulating hormone) in male primates (with Year 2 costs estimated at \$111,000) is still at its initial stages and no data have been obtained as yet. The goal is to confirm some of the reported results of the Moudgal-Raj project on FSH suppression in male bonnet monkeys by immunizations, and to

investigate whether immunization of male monkeys with human FSH, instead of ovine FSH as used in the other project, will yield the same or better results. It is not clear how the monkey in vitro fertilization (IVF) procedures being developed will benefit this project until the monkey IVF test method is well established. The hemizona assay method appears to benefit this project.

3) Inhibin/GnSIF

This project is a combination of two subprojects seeking to isolate and purify substances that might be used as the basis of contraceptives -- inhibin for males and gonadotropin surge inhibiting factor (GnSIF) which might suppress ovulation in females. The merger followed the departure of the principal investigator (PI) for the inhibin project. Research on a molecular-based sperm binding to zona protein assay is also being conducted in conjunction with these subprojects (see Section 2.1.3). This is the intramural program's single most costly endeavor with Year 2 costs estimated at \$581,000.

Inhibin investigations have been under way for years in a number of laboratories around the world, and the CONRAD program therefore adopted an existing methodology<sup>1</sup> to obtain 5-15 mg of pure inhibin from 300 ml of porcine follicular fluid. This inhibin has been characterized chemically and its biological activity tested. Currently, inhibin purification from one liter of porcine follicular fluid is under way. Antibody production has been initiated, but no antiserum useful for radioimmunoassay (RIA) has been obtained.

In contrast to inhibin, GnSIF has been studied by only a few investigators. CONRAD's efforts are being carried out in collaboration with The Population Council. The CONRAD program has succeeded in separating the inhibin fractions and the GnSIF fraction on a heparin-Sepharose column. Further purification and characterization of GnSIF will be carried out.

4) Reproductive Immunology

A second major effort is in the area of reproductive immunology. The overall objective of this subproject (with Year 2 funding at \$314,000) is to identify, characterize, and isolate sperm or egg-based antigens germane to fertilization. The research approach appears to be making three important contributions. The first relates to the types of antigens being isolated: Although antisperm antibodies have been raised in a variety of laboratories, this project is emphasizing that the antigens should have a role in fertilization. The second is the endeavor to obtain the antigen by using molecular biology technology. The third unique aspect is the recent development of a new test method for sperm-egg binding ability (the hemizona assay method).

The objective of this project is very important for the CONRAD program. The molecular biological approach for production of the antigens appears to be the right approach. The development of the hemizona assay method will accelerate inter-project collaboration, not only within the CONRAD program, but also between the intramural and extramural projects.

5) Spermicide screening program (2 projects -- part of AIDS research supported, in part, by NICHD)

These two subprojects are one activity that involves the screening and evaluation of spermicides and other compounds for their effect on sperm function. The compounds are also being evaluated under an extramural program which is assessing their virucidal properties (anti-HIV). The investigation also includes the effects of sex steroid hormones on transmission of HIV

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<sup>1</sup>The methodology of Dr. Nicholas Ling of the Salk Institute has been adapted slightly for this work.

and the presence of blood cells in semen samples collected from different parts of the world. Another area being studied is the implication of the spermicidal effect of methylene blue. Preliminary efforts were directed toward establishing the hemizona assay.

### **2.1.3 Core Laboratories**

To provide the specialized yet commonly used techniques required to support the intramural research subprojects, four core laboratories have been established as follows: 1) animal husbandry 2) radioimmunoassay (RIA) 3) tissue culture, and 4) cellular and molecular biology.

The animal husbandry and the RIA core laboratories serve all the subprojects, the former by providing animal care for experimental purposes and carrying out minor experimental procedures as required and the latter by carrying out the radioimmunoassays that are common to much of the research. Experimental costs for the animal husbandry core are pooled for all projects and per diem charges are paid to EVMS's Animal Resources Section for housing. The radioimmunoassay core charges \$2.75 for a routine specimen analysis performed in duplicate. Centralization of these commonly used services is cost-effective and useful to maintain high standards required for research. The RIA core lab is also providing services to extramural projects, e.g., NET assay for clinical trials.

The tissue culture core laboratory is used somewhat differently; it carries out the actual experiments called for in a given subproject. In this case, each experiment is budgeted in the core lab in which it is carried out.

The cellular and molecular biology core laboratory represent yet another function served by the core laboratories. In this laboratory, new pilot studies are being carried out to purify and characterize bioactive protein molecules: specifically, in this case, of ZP3, a sperm receptor zona pellucida protein and of sperm antigens germane to fertilization. Both efforts will contribute to establishment of a method to produce pure sperm antigens useful for immunocontraception. Because this research has not been formalized as a subproject, the approval process required for full-fledged intramural subprojects, including approval by the CTO, is not used (see Section 2.1.4).

A core administrative unit provides administrative support for all four core labs. In addition, each core lab has its own manager.

### **2.1.4 Staffing and Costs of Intramural Program**

It is extremely difficult to develop a clear picture of how either staff time or program expenditures are allocated among intramural projects. The problem begins at the budgeting stage: the Principal Investigator (PI) for each subproject develops detailed budget estimates for one or more years for that activity. These are approved by the Program Director and the A.I.D. CTO, but there is no input from the fiscal control group in the Accounting Section to comment on the accuracy of the cost factors and assumptions.

The program, however, does not appear to monitor allocation of expenditures on subprojects with any great precision. Records are kept of the amount of time of professional, technical staff and core technicians on subprojects, but is not clear how accurate these records are, especially for part-time staff. The system breaks down further because in addition to staff time spent directly on subprojects, the accounting system also charges a proportion of STS time, and of between eight and ten supporting staff time, to intramural subprojects, although they may have no involvement with some of these activities. For example, the Director of Clinical Research has a

small portion of his salary charged to each of the major basic research subprojects, although he is not involved with them at all. This is the result of the distribution of STS time spent in overall management and review of the CONRAD intramural program.

This accounting system appears to be adding to the high costs of each subproject. Because of the questionable nature of these figures, it is impossible, however, to draw any meaningful conclusion as to whether intramural subprojects are being carried out in a cost-effective manner.

### Recommendations

1. Continued support should be provided to the following subprojects: GnRH antagonist, reproductive immunology, FSH suppression in male primates (although very little progress has been made to date), and the GnSIF component of the inhibin/GnSIF subproject.
2. **The level of resources allocated to intramural subprojects should be reevaluated. One suggestion is that the inhibin subproject might be contracted out as an extramural activity.<sup>2</sup> Another alternative might be to phase out this area of research entirely in view of the existence elsewhere of this line of research.**
3. Pilot research studies, such as those to purify and characterize bioactive molecular proteins, which are carried out in the core laboratories, should be treated as separate subprojects; budgets for each should be developed and approved in accordance with the procedure for all intramural subprojects. This would involve submitting each subproject to the CTO, in accordance with the terms of the Cooperative Agreement.
4. **An in-depth review should be undertaken to establish the real costs as well as the staffing levels necessary to operate the core labs and the intramural research subprojects.** Such a review should help inform the program decision-makers as to which of these in-house activities are cost-effective and deserve continued support and which are less cost-effective and might be abandoned.
5. Consideration should be given to centralizing the administrative core lab under CONRAD's central administration.

## 2.2 Clinical Research

### 2.2.1 Cooperative Agreement

#### Project Design

The Clinical Research program is charged through the Cooperative Agreement with conducting Phase I and II clinical trials of new methods of fertility regulation. According to the Cooperative Agreement, studies will primarily involve pharmacodynamics, pharmacokinetics, and preliminary safety and efficacy in relatively small numbers of human volunteers. New drugs, devices, and other potential methods of fertility regulation are to be studied. Additionally, although not specified in the Agreement but approved by the CTO, the Clinical Research program will cooperate with FHI as a Phase III study site when time and space permit.

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<sup>2</sup>Recommendations or parts of recommendations in bold face are considered major recommendations (see Chapter 6 for complete listing).

To accomplish these charges, the Agreement indicated that the Clinical Research program must have available adequate personnel and space, and that medical personnel should be experienced in conducting clinical trials and knowledgeable in contraceptive research and techniques and FDA requirements. Additionally, the Clinical Research program is encouraged to establish with the extramural program clinical trial centers in both the United States and other countries, including LDCs, where clinical trials may be undertaken quickly and efficiently.

Among the 22 illustrative activities listed in the Project Agreement, in which the Clinical Research program was expected to participate include 1) actively seeking out, identifying, and developing projects, or soliciting proposals (extramural research); 2) keeping abreast of research and development activities being undertaken by the private sector (e.g., pharmaceutical companies) worldwide; 3) providing technical assistance and encouragement to LDC investigators and institutions to prepare (clinical) proposals and to have the facilities required to participate in single or multicentered studies; 4) developing and maintaining a roster of worldwide investigators who are capable and ready to undertake specific projects as required; and 5) establishing a working relationship among worldwide centers capable and ready to participate in single or multicenter clinical trials.

### Evaluation of Design

The establishment of a clinical research center at CONRAD together with a network of clinical trial centers was a highly appropriate aspect of the project design. Their existence should ensure rapid, accurate evaluation of new methods of fertility regulation by personnel experienced in contraceptive techniques, and should thus lead to faster development of promising methods of fertility regulation. It should also ensure cost-effectiveness by allowing for quick initiation of studies and early termination of ineffective, unsafe, or poorly accepted methods.

## 2.2.2 Facilities and Staffing

### Facilities

With respect to facilities, up to now, clinical trials have been conducted in space also utilized by other members of the EVMS Department of Ob/Gyn. Particularly during periods of heavy usage by these faculty,<sup>3</sup> this arrangement has limited the space available for coordinators of clinical research and nurse practitioners who counsel volunteers.

The space problem appears to have been solved, since the program has recently been assigned new space dedicated to CONRAD's clinical research. The space will provide offices for the Director and clinical research staff and thus allow privacy for consultation with study volunteers. Additional space near the offices will be converted to examination rooms to be utilized by the program. These offices and examination rooms are presently scheduled for occupancy May 1, 1989. This new space should allow for greater flexibility in conducting studies, and better accommodate volunteers' and researchers' schedules. The only drawback is that they are now physically separate (three floors down) from the other Ob/Gyn activities. This may raise problems with respect to utilizing Ob/Gyn staff time.

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<sup>3</sup>These occur regularly for "cycles" of women who are enrolled in the Institute's in vitro fertilization program.

The new space is more suitable for Phase II and III studies than for Phase I pharmacokinetics studies. The program, however, has arranged to utilize sleep rooms physically located at Norfolk General Hospital to conduct those studies for which overnight facilities are required.

### Staffing

The program's staffing appears fully adequate; it includes a Director (90 percent of his time charged to CONRAD); administrative assistant/secretary (90 percent); coordinator of clinical research (90 percent); assistant coordinator of clinical research (100 per cent); clinical practitioner (30 percent); and a medical office assistant (75 percent). Additional members of the program not funded through CONRAD include a transcriptionist, two clinical practitioners, and a work-study student. The Director serves as the PI on all CONRAD-supported studies. Co-investigators have included one physician partially supported by CONRAD (5 percent) and residents, fellows, and faculty from the EVMS Department of Ob/Gyn who receive no CONRAD funding.

Involvement of these co-investigators could be a particularly strong aspect of the CONRAD program, as it offers the opportunity to encourage young physicians to become interested in contraceptive research and to educate them in appropriate techniques of research. At present, however, this opportunity appears to be slipping by. Studies are generally conducted by the nurse practitioners under the supervision of the Director who conducts the study. It is not standard practice (in studies of "non-invasive" methods) for every volunteer to be seen by a physician, either the PI or the co-investigators. Not only does this practice represent a lost opportunity; it is technically questionable.

The Director of the Clinical Research program has worked in gynecological endocrinology for many years, but is not working at full potential for the CONRAD program. The clinical coordinator also has had considerable experience in clinical trials involving contraceptives. The rest of the staff were relatively inexperienced before joining this program.

## 2.2.3 Performance of Clinical Research Program

### Clinical Trials

The current level of CONRAD-supported clinical activity is quite low at present; there are only three CONRAD or FHI-supported clinical trials now under way (see listing on next page and Table A, Appendix D). The staff are, however, also conducting six trials supported by pharmaceutical companies. In addition, the Director of the Clinical Research program is responsible for monitoring and evaluating extramural clinical projects. The clinical program has also done a preliminary study, a vaginal spermicidal barrier (VSB) pharmacokinetic study, which involved 29 volunteers.

Over the next 12 months, CONRAD anticipates supporting an additional 9 Phase I studies, one Phase II and one Phase III FHI study (see Appendix E for projected lists). The addition of Phase III trials, although not part of the CONRAD Cooperative Agreement and charge, will be particularly welcome as these long-term stable trials will help keep up staff interest and expertise. It is understood that Phase III studies should not be conducted if they interfere with the main work of the CONRAD program. It is not clear that much effort has been made to date to develop new protocols or develop collaboration centers for these new studies.

**CONRAD-supported Studies**

<b><u>Study</u></b>	<b><u># Volunteers</u></b>	<b><u>Status</u></b>
1. Phase II Comparative Study of VSB vs the Conventional Diaphragm	60	24 Enrolled
2. Evaluation of the Safety and Pharmacokinetics of Biodegradable Norethindrone Pellets Implants Phase I (Sponsor FHI and CONRAD)	35 initial 15 additional	35 Enrolled

**FHI-supported Studies**

*(The second study below is part of the second study listed above.)*

<b><u>Study</u></b>	<b><u># Volunteers</u></b>	<b><u>Status</u></b>
1. Phase III - NET 90 Day Injectable: Norethindrone (NET) Serum Concentrations, Safety, and Effectiveness of 65 mg and 100 mg of 90-day norethindrone	100 39 active	100 Enrolled
2. Measurement of Alpha-Reduced Metabolites of Norethindrone in Plasma (FHI/EndoCon, Inc.)	42	3 Enrolled

**Monitoring Extramural Subprojects**

The following five extramural subprojects were being conducted:

- 1) Barrier methods (VSB) with evaluation of nonoxynol-9 and chlorhexidine for action, persistence, and effect on vaginal flora, and Phase I trials with acetaminophen-4 guanidiobenzoate;
- 2) Male sterilization with Phase I evaluations of the shug vas deferens blocking device;
- 3) Female sterilization with Phase I evaluation of the Meeker tubal plug and clip device;
- 4) Male systemic methods with funding of studies to evaluate sublingual and injectable delivery of testosterone, the evaluation of the requirement for azoospermia to have an effective method based on suppression of sperm production with testosterone enanthate in normal men; and
- 5) Phase I studies evaluating LHRH antagonists as potential male contraceptives.

The Clinical Research program director is monitoring only one of these subprojects (#1).

### Relationships with LDC and U.S.-based Centers

The Clinical Research program is trying to establish relationships with clinical centers in LDCs. Senior technical staff have made a site visit to Santiago, Chile to discuss establishing a site for clinical studies on methods for breastfeeding women, but for a number of reasons, this effort has been progressing slowly. Site visits have also been made to Thailand and Indonesia and plans exist for further talks that could evolve into relationships with centers in these countries.

There appears to be some question as to what role CONRAD should be playing with respect to LDC centers. In the Program Director's view, it is a weakness of the CONRAD project that it has not yet succeeded in establishing clinical study centers in LDCs. Since a number of highly qualified centers of excellence in clinical research already exist in LDCs, however, it appears unnecessary for CONRAD to establish any new centers. Rather, CONRAD should continue to attempt to develop relationships with existing centers that could be used for clinical trials when the need arises. CONRAD could also benefit from collaboration with other international agencies such as FHI and WHO, which support a network of collaborating centers in developing countries.

In the U.S., CONRAD, through its well-known and highly respected scientific staff, has made numerous contacts with investigators interested in fertility regulation. Nationally, however, clinical investigation with new contraceptives is decreasing as a result of many different forces beyond the scope of the CONRAD program including a decrease in private sector spending in contraceptive research, issues related to product liability insurance, and the availability of trained clinical researchers.

### Issues

The prime explanation for the relatively limited activity by the Clinical Research program is that finding projects ready for Phase I and II trials is highly dependent on factors beyond the control of the investigator. For example, with respect to the nine Phase I CONRAD studies anticipated to begin during the next 12 months, problems with formulation, animal toxicology, stability, drug release rates, or many other problems could result in delays or termination of any of the projects.

There have been some managerial consequences of the low level of activity. For one, it has not been deemed necessary thus far to plan carefully or track allocation of staff time through such management tools as time line or Program Evaluation Review Technique (PERT) charts. Therefore, the allocation of CONRAD-paid staff time on various activities is not easy to identify. In view of the low level of activity, it appears that the Director of the Clinical Research program does not devote 90 percent of his time to CONRAD program work, but it is impossible to confirm this. If the work level were to expand as envisioned, the need for better planning would grow considerably. There will always be peaks and valleys in the Clinical Research program workload, but better planning will help ensure that these are accommodated.

A second consequence has been that it has been difficult to provide the amount of training needed to improve the contraceptive research skills of some of the inexperienced clinical staff.

On balance, however, CONRAD's slow start in the area of clinical activity was expected. Most of the subprojects in CONRAD's intramural applied fundamental research portfolio were envisioned as needing many years to reach clinical trials. Moreover, until adequate facilities

were available and staff fully trained, it would have been unwise to embark on too ambitious a program. Further major delays, however, in this area would be the basis for some concern.

The same uncertainty exists with respect to extramural clinical projects, but here more active solicitation of projects ready for clinical trials might make a difference (see Section 2.3). The Clinical Research program, however, has not played the active role in soliciting these projects, leaving the task primarily to the Director of the Extramural Program.

### Recommendations

6. **The Clinical Research program staff and extramural program staff should increase its efforts to solicit extramural project that are at Phase I or Phase II trial stage.** Two suggestions on how to proceed are:
  - **CONRAD may wish to utilize consultants to encourage the submission or development of proposals.** For instance, the private sector frequently employs individuals who are responsible for product licensing; scientists are utilized to evaluate proposals presented by the Product Licensing Team. A similar approach could be taken by CONRAD, with the Clinical Research program evaluating proposals from a clinical standpoint concerning their merit for study.
  - **The Technical Advisory Committee (TAC, See Section 2.3) has clinicians with expertise in contraceptive clinical research who could be utilized effectively to bring in new proposals.** This would require increased contacts with appropriate TAC committee members. A subcommittee of TAC might be an appropriate mechanism (see also Recommendation 19).
7. Time line or Program Evaluation Review Technique (PERT) charts of planned clinical trials should be drawn up to allow for the appropriate staffing level for each trial. These should be developed as the basis of the careful evaluation of protocols and realistic identification of tasks to be performed with each trial.
8. Physician involvement in clinical trials should be increased, including trials of non-invasive methods.
9. Efforts directed toward LDC clinical centers should focus on development of relationships with clinical centers at which appropriate clinical trials may be performed. As such centers are enlisted, they should be encouraged, when possible, to adhere to common protocols, case record forms and should be monitored appropriately by CONRAD personnel to attempt to obtain data for FDA approval and in as many countries as feasible.
10. Efforts to establish any new LDC centers should be discouraged. The program should utilize already existing LDC centers of excellence, and should collaborate with other agencies that have supported the development of such centers.
11. CONRAD should develop a roster of potential clinical investigators within the United States and abroad and communicate with such people frequently.
12. Clinical protocols and collaborating centers should be developed now for the Phase I and II studies anticipated to begin within the next 12 months.

## 2.3 Extramural Program

### 2.3.1 Overview

The expectation of the program design was that an extramural component would tap the wide spectrum of expertise and scientific energy in existence at universities, hospitals, research institutes and private companies worldwide. The goal was that the subproject proposals submitted or solicited would represent the most appropriate contraceptive development leads that required funding. The importance attached to this component was reflected in the decision to accord it two-thirds of the total funds available for research projects.

### 2.3.2 Portfolio

#### Project Mix

The 42 active subprojects since the beginning of the extramural program can be divided into the eight program areas shown in Table 1.

Although it is difficult to make a precise judgment on whether this constitutes an adequate mix, the portfolio generally seems well chosen. The subprojects appear to fall in areas where research is needed; they seem scientifically feasible including projected time and cost; and they seem to be in areas that are not already saturated by research efforts. Whether the mix will remain appropriate, however, is not entirely clear. In particular, AIDS-related research, which is receiving the largest proportion of funding of any area, could possibly divert the extramural program from its original mission of contraceptive research and development. Given the public health importance of the subject and the selective research agenda, however, the emphasis on this program area is justifiable. It is important, nonetheless, to make sure that it does not result in any reduction of the efforts directed to contraceptive development research activities--which, after all, is CONRAD's primary mission.

Table 1

#### SUBPROJECTS BY PROGRAM AREA

<u>Program Area</u>	<u>Number of Awards</u>	<u>U.S. Dollars</u> (in thousands)	<u>Percentage</u> <u>of Expenditures</u>
Applied Basic	4	45	1
Sterilization	5	144	4
Drug Delivery	5	389	8
Male Systemic	3	385.8	11
Gonadal Factors	4	461.1	13
Immunology	10	479.2	13
Barrier/Spermicide	7	746.5	21
AIDS	<u>5</u>	<u>1046.0</u>	<u>29</u>
TOTAL	43	3696.6	100

With respect to how well the subproject portfolio is meeting the overriding program goal of funding projects that may result in new products in the near future, the record appears more questionable. An analysis of all subprojects (both regular and pilot funded to date [see Table

4) shows that only two projects can be categorized as near-term (at the point of Phase II clinical trials), with 14 as medium-term (at or close to Phase I studies) and 27 as long-term (or undergoing laboratory studies) (see Table 2).

Table 2

**EXTRAMURAL PORTFOLIO, LONG-, MEDIUM- AND SHORT-TERM PROJECTS**

	<u>AIDS</u>	<u>Barrier</u>	<u>Delivery Systems</u>	<u>Steril.</u>	<u>Immuno.</u>	<u>Male Syst.</u>	<u>Non-Ster. Gon. Fac.</u>	<u>App. Basic</u>	<u>Total</u>
Near-Term	-	1	-	-	-	1	-	-	2
Medium-Term	-	2	5	5	-	2	-	-	14
Long-Term	5	4	-	-	10	-	4	4	27

To a large degree, the heavy emphasis on long-term efforts represents the state of the art. On the other hand, there may be additional opportunities in such areas as reversible or non-surgical sterilization and barrier methods that could evolve sooner into contraceptive products.

### 2.3.3 Project Management

The extramural program is administered by CONRAD staff in the Rosslyn office and includes a Director, Project Administrator, Administrative Assistant, and a Chief Accountant (located in Norfolk). The physical separation of the Rosslyn office from Norfolk does not seem to present any significant problems, particularly in view of the advanced system of communication presently in place between the two facilities. A Washington area location also has the significant advantage of strengthening liaison with A.I.D. and other agencies such as NIH and FDA.

A Technical Advisory Committee (TAC) has been established to assist the CONRAD program in several key areas, most important of which are to review proposals that have been submitted and to help establish research priorities and strategies. In addition, it was expected that the TAC would help solicit proposals and monitor and evaluate technical reports of funded projects.

Currently, 11 members serve on the TAC representing a broad mix of disciplines. Meetings originally held three times per year are now held semi-annually and are attended by all CONRAD Senior Technical Staff (STS), A.I.D. staff and consultants as needed, as well as collaborating agency representatives.

### 2.3.4 Solicitation, Review and Monitoring of Subprojects

#### Solicitation of Proposals

**Strategy.** It was envisioned that the TAC would play a key role in establishing priorities for extramural research and development of research strategies and that the strategy in turn would govern the solicitation of subprojects. Perhaps because the TAC meetings are very short (1 1/2 days) and now occur only twice annually, these meetings have not proved to be a very effective forum for planning. Although the universe of available subprojects is a clear constraint, it is possible that if more attention were directed to planning at the TAC meetings, with full

involvement of the STS and TAC members, would serve to increase the energy level directed to solicitation of near- and medium-term subprojects.

**Performance.** It was envisioned that, although the chief burden for soliciting extramural subprojects would fall to the Director of the Extramural Program, these efforts would be supplemented by those of STS (in particular, the CONRAD Director and the Director of Clinical Programs) and TAC members. It was also expected that the solicitation process would be active, capitalizing on the multiple contacts of the TAC and STS in the scientific community and involving personal contact and promotion. To date, however, the solicitation process has primarily been passive. Proposals are solicited by means such as announcements in journals, newsletters, mailings, and attendance at conferences. Both STS and TAC members acknowledge that they could do more in soliciting subprojects, but cite time constraints as a deterrent.

The need for more active solicitation is evident. The extramural staff could easily process for funding a larger number of formal proposals than the project funded in 1988. Indeed, consideration is being given to revising the position of Project Administrator (whose current occupant is leaving) to make it a more technical role capable of assisting in the development and technical monitoring of subprojects. It is recognized that a more active approach focusing on attracting proposals for near-term activities might serve to redress the imbalance among near-, medium-, and long-term subprojects.

To encourage the submission of proposals, CONRAD has a very flexible approach to the types of submissions it will consider. It accepts not only formal proposals (full proposals as described in CONRAD guidelines), but also informal proposals (initial submission limited to a few pages) (see Table 3). It also encourages pilot projects (funded up to \$15,000) as well as regular projects (funded over \$15,000) (see Table 4).

The use of informal proposals appears sound, giving the STS and TAC a wide selection of potential proposals from which to choose. A total of 128 proposals have been received to date, the preponderance (78) informal. The informal route serves two purposes: it saves the time of busy researchers (subproject recipients) in preparing proposals and the members of STS and the TAC in reviewing them; and it serves to reduce the number of formal proposals that are turned down, and the inevitable disappointment and negative reaction that accompanies any such rejection.

The pilot project mechanism is also working well. The main purpose is to provide investigators an opportunity to obtain preliminary data or otherwise demonstrate feasibility of an approach that would justify the submission of a regular full proposal. About one-third of the pilot submissions have fallen into this category and of these, two have resulted in submission of proposals for regular projects. In addition, pilot projects include small grants for applied and for mission-oriented fundamental research. At present, at approximately a 2:1 ratio (28 regular and 15 pilot), the portfolio represents a reasonable mix of regular and pilot subprojects.

The range of funding has varied widely among the regular projects. Among subprojects budgeted over the project life at over \$100,000, four had budgets between \$100,000 and \$200,000; six between \$200,000 and \$300,000; and three between \$300,000 and \$500,000.

As called for in the Cooperative Agreement, the current research portfolio includes some LDC subprojects including one in Argentina (\$15,000), one in Chile (\$14,850), and one in Brazil (\$36,556). This is a level lower than that anticipated.

**Table 3**

**PROPOSALS FOR SUBPROJECTS:  
FORMAL AND INFORMAL**

<u>Formal</u>		<u>Informal</u>	
Total Submitted	50	Total Submitted	78
Funded	19	Funded directly	9 *
Pending	6	Progress to regular proposal/funded	1 **
Not funded	25	Progress to pilot proposal/funded	1 ***
		Pending	21
		Not accepted	46

\* *Seven were inherited from PARFR and two transferred from The Population Council.*

\*\* *Also included under the 28 regular projects in Table 4.*

\*\*\* *Also included under 15 pilot projects in Table 4.*

**Subproject Review**

Tables 3 and 4 also suggest that the review process is rigorous and the STS and TAC have been careful to rule out inappropriate or poorly conceived proposals. Overall, a total of 71 proposals have not been funded. Of these, the majority (60 percent) have been informal proposals, with the other 40 percent including formal proposals for regular subprojects (32 percent) and proposals for pilot projects (8 percent).

Overall, the TAC deserves high marks for the job it does in providing a peer review mechanism for project proposals. Its membership reflects the disciplines needed for the current activities of the program, with the possible under-representation of two areas: the perspectives of women and of developing countries. With respect to possible conflict of interest, very few funded projects have been or are being carried out by TAC members, but this is an issue that must be kept under review. The participation of representatives of Collaborating Agencies such as the Population Council, FHI, NICHD, and WHO in the TAC meetings is also helping to avoid unnecessary duplication of research efforts as well as promoting synergistic research efforts. The STS and TAC

**Table 4**

**SUBPROJECTS:  
REGULAR AND PILOT**

	<u>Regular</u>	<u>Pilot</u>	<u>Total*</u>
Funded	28	15	43
Pending	6	1	7
Not Funded	25	6	31

\* *Eleven of these have been extended and requests for extension for four others are pending.*

ensure that appropriate attention is given to voluntarism and the protection of human subjects; all clinical trials adhere to FDA requirements with regard to informed consent and Institutional Review Board (IRB) approval.

### Subproject Monitoring

Technical monitoring of the extramural projects is divided among the five STS, generally according to their areas of technical expertise. Typically, it should include review of progress reports and their submission to TAC, supplemented by site visits and technical help in solving problems as necessary. Primarily because of the areas supported, the burden has been distributed unevenly, with one staff member responsible for 17 out of 42 projects (representing 51 percent of the dollar value) whereas other senior staff hold 19 percent, 12 percent, 10 percent and 8 percent of the portfolio's dollar value. Because few of the STS have been able to give enough time to monitoring, in general there has been little or no on-site supervision or technical assistance (see Table B in Appendix D). In some cases, however, the intramural program monitor has worked closely with extramural investigators (e.g., in preparation of monoclonal antibodies).

### 2.3.5 Overall Conclusions

1. The extramural program portfolio appears well chosen (i.e., subprojects are addressing needs, they are not redundant with other activities underway elsewhere, and they appear feasible). On the other hand, the portfolio is tilted too heavily in the area of long-term subprojects.
2. TAC has been very helpful to CONRAD in providing a peer review mechanism, as well as in reviewing progress of funded projects. The Committee has been of less help in some of the other functions, such as development of such projects, development of overall and specific research strategies and the establishment of overall program priorities. One constraint may be the short duration of TAC meetings.

### Recommendations

13. **Efforts need to be increased to solicit extramural proposals, particularly those that are near-term.**
14. The mechanism of solicitation of proposals needs to be strengthened and to be more proactive. The following means are suggested.
  - **All of the STS need to be more actively involved in the process.**
  - **The extramural program (Rosslyn office) would benefit if the Project Administrator were replaced with a technical person (rather than another administrator). This would free the Extramural Program Director to do more active solicitation of proposals.**
  - **The TAC as a committee and as individual members could also play a more active role. Consultants might also be enlisted to assist with solicitation (see also Recommendation 19).**
15. The process of technical project monitoring, including site visits, could be strengthened by more inputs from the STS, utilization of the services of TAC members, and recruitment of consultants as necessary.

16. In future appointments to TAC, an active effort should be made to include among members with the required experience, more women and members with developing country experience.
17. Consideration should be given either to increasing the duration of the TAC meetings or to supplementing the meetings with smaller group meetings (with other members coopted as needed for the subject) to allow the Committee to address more effectively its other functions related to establishment of priorities, development of research strategies, and particularly for development of such projects for which proposals can be solicited.
18. More attention should be devoted to soliciting projects from LDC investigators and otherwise to increasing the contribution of developing county scientists and institutions.

## **2.4 Interrelationship Between Extra and Intramural Programs**

### **2.4.1 Ratio between Extra- and Intramural Program Spending**

At this stage in the life of the project, it is clear that the extramural program is consuming a smaller proportion of the resources than the three-quarters anticipated in the Cooperative Agreement. For Year 1 (10/1/86 to 9/30/87), expenditure on the extramural program was estimated at \$1,997,598, compared to \$1,267,402 for the intramural program. For Year 2 (10/1/87 to 9/30/88), of total expenditures of \$4,050,972, expenditure for the extramural program was \$2,051,604 compared to \$1,999,368 for the intramural program (see Sec. 5 for analysis of funding) or 51 percent of the total.

### **2.4.2 The Balance of Long-, Medium-, and Near-Term Subprojects**

An overview of the combined CONRAD portfolio, including both intramural and extramural subprojects, indicates that the bias toward long-term subprojects found in the extramural portfolio also characterizes the combined portfolio. Graph 1 provides an analysis of the combined portfolio, both current and total, broken down into eight research areas. Immunology, with a total of 10 extramural subprojects, combined with two intramural subprojects, represents the area with the largest number of subprojects, followed by barrier/spermicide subprojects (8), drug delivery (7) and non-steroidal gonadal factors and AIDS (both with 6). When these areas are characterized in terms of near-, medium- and long-term subprojects (see Graph 2), it is clear that the emphasis on immunology, in combination with subprojects in gonadal factors and AIDS, and to a lesser degree in applied basic and barrier/spermicides, brings the total of long-term subprojects to 33 out of a total of 54 subprojects. This compares with only five near-term and 14 medium-term subprojects.

Because the number of intramural subprojects is relatively few, their influence does not greatly affect the total numbers of subprojects in each research area. From the perspective of funding, however, their effect is enormous (see Graph 3). In three long-term areas -- immunology, gonadal factors and basic applied research--almost all program costs were being absorbed by the intramural program. Two of these areas -- immunology and gonadal factors -- were budgeted at the highest level of any area (with a combined total of about \$1.2 million). If the budget for Year 2 for subprojects in applied basic research and AIDS were added, the combined total for long-term subprojects would be over \$2 million. In areas that are more promising over the near-term, the largest Year 2 expenditure is that of drug delivery, with somewhat less going to barrier methods, and very little to the two areas in which there are no intramural subprojects: male pharmacological methods and sterilization.

### 2.4.3 Conclusions with Regard to Project Design

A.I.D.'s rationale in emphasizing the extramural component was based on its view that contraceptive development can occur most cost-effectively by supporting the research of investigators worldwide coupled with an intention not to build a research institution that would utilize all the funds available to support its own activities.

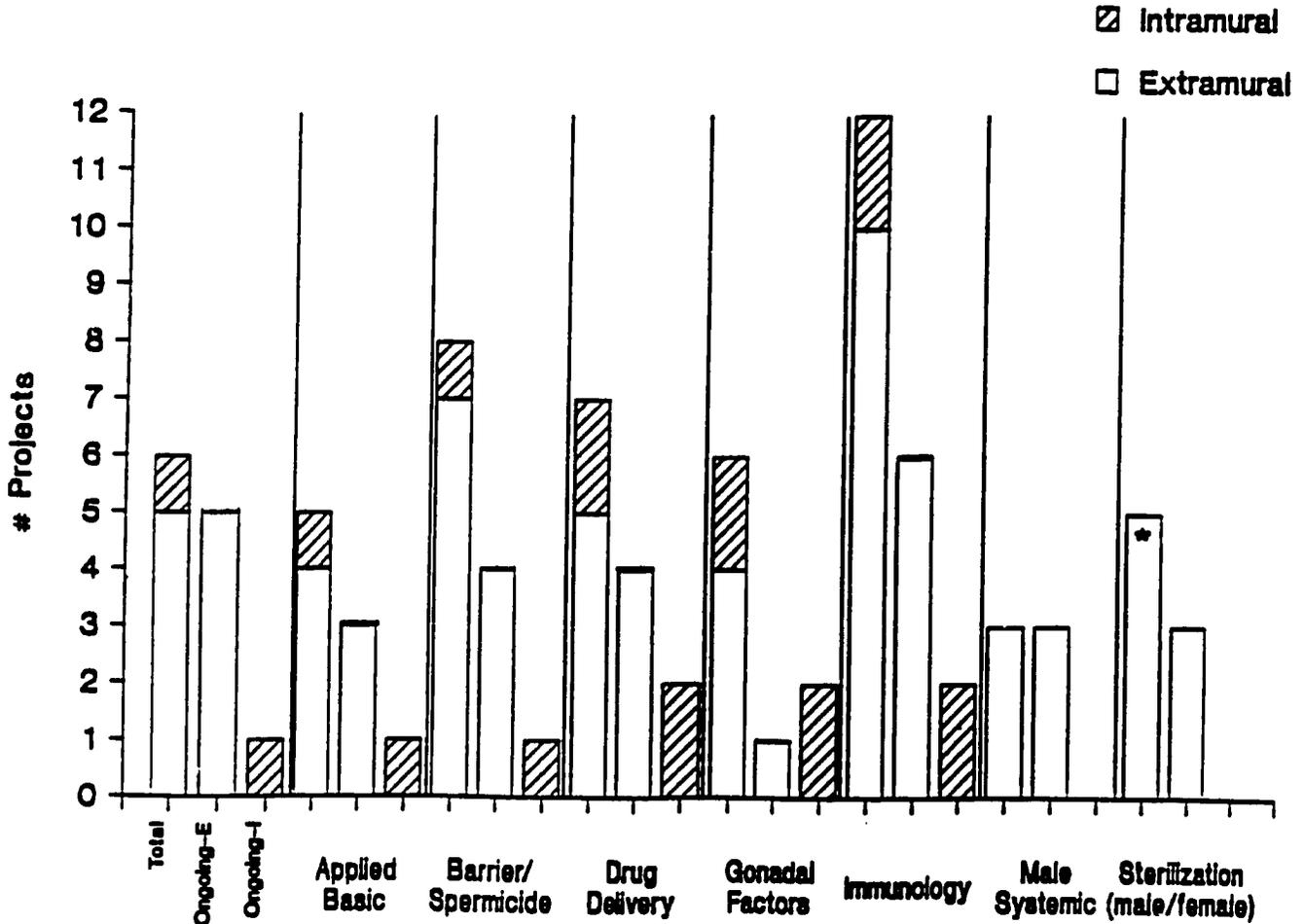
This decision was valid conceptually and project experience is proving its appropriateness. The wisdom of the decision to create an intramural component is being amply demonstrated by the exciting scientific work now under way by CONRAD staff in Norfolk. At the same time, one of the main reasons that the project's overall portfolio is skewed towards long-term activities is that this is where the strengths of the in-house staff lie. The initial intention was that the extramural component would provide the desired depth and breadth to the project portfolio, including seizing every available opportunity to fund near-term opportunities. Unless the Director of the Clinical Research program becomes more active in this area, solicitation through the extramural program will remain the principal way in which the project can strengthen its involvement with near-term activities. The evaluation team believes it remains entirely proper that the extramural component should be accorded a larger proportion of project resources than the intramural.

#### Recommendation

19. CONRAD management and A.I.D. should reexamine the portfolio of intramural and extramural subprojects in light of their objectives for near-term versus longer-term payoffs. It may not be either appropriate or possible to achieve the 2-1 ratio (extramural, two-thirds and intramural, one third) set forth in the Project Agreement, but efforts are clearly needed to increase the level of extramural funding, and clinical trials of near- and medium-term needs. At the same time, it is important to ensure that intramural spending does not encroach on funding for extramural subprojects.
20. A thorough review is needed of the proper staffing level for intramural projects that takes into consideration the program levels desired, the funds available, the cost-effectiveness of the core labs and the productivity and morale of the staff.

Graph 1

# CONRAD PROGRAM Intramural and Extramural Subprojects by Area



AIDS

\* One male and one female method

Graph 2

## Extramural and Intramural Subprojects by Development Process Stage

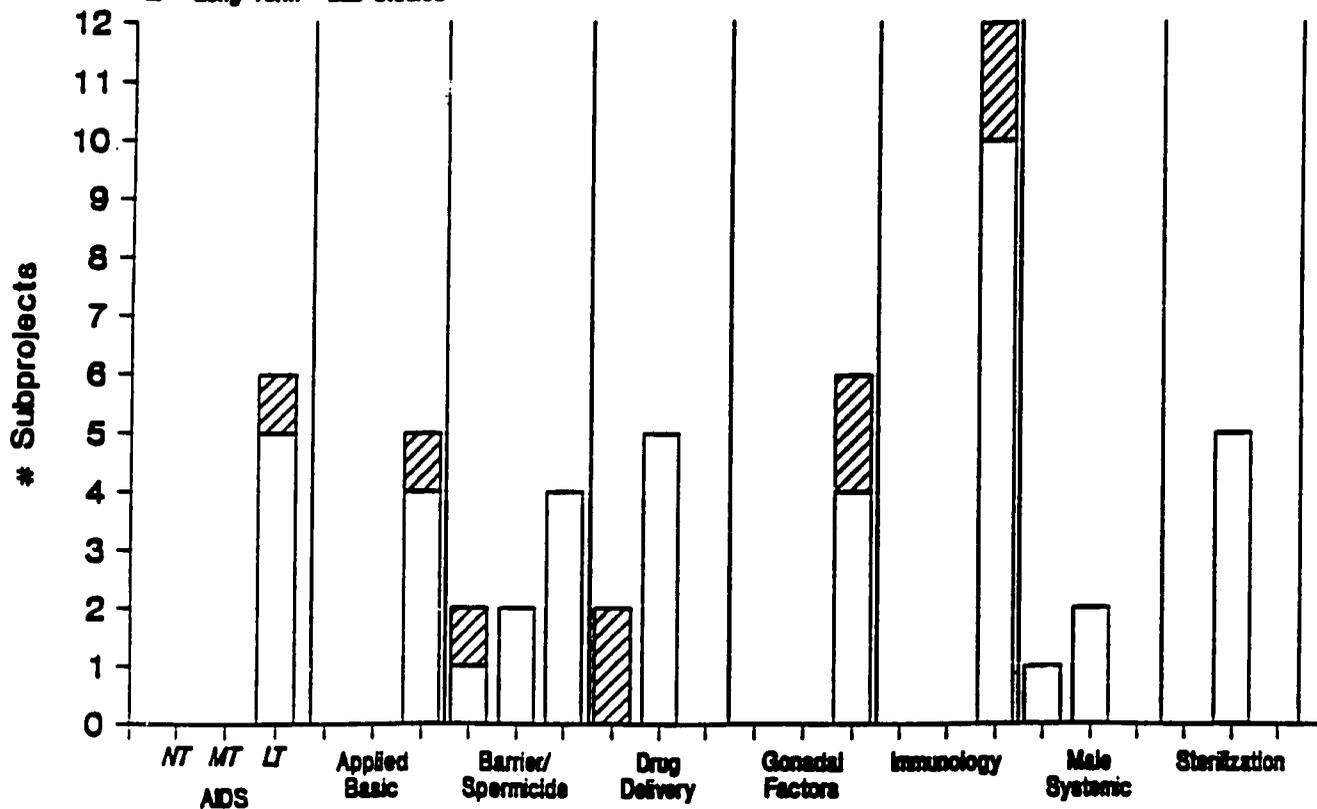
*NT - Near Term Phase II Clinical Study*

*MI - Middle Term Phase I or Close to Term*

*LT - Long Term Lab Studies*

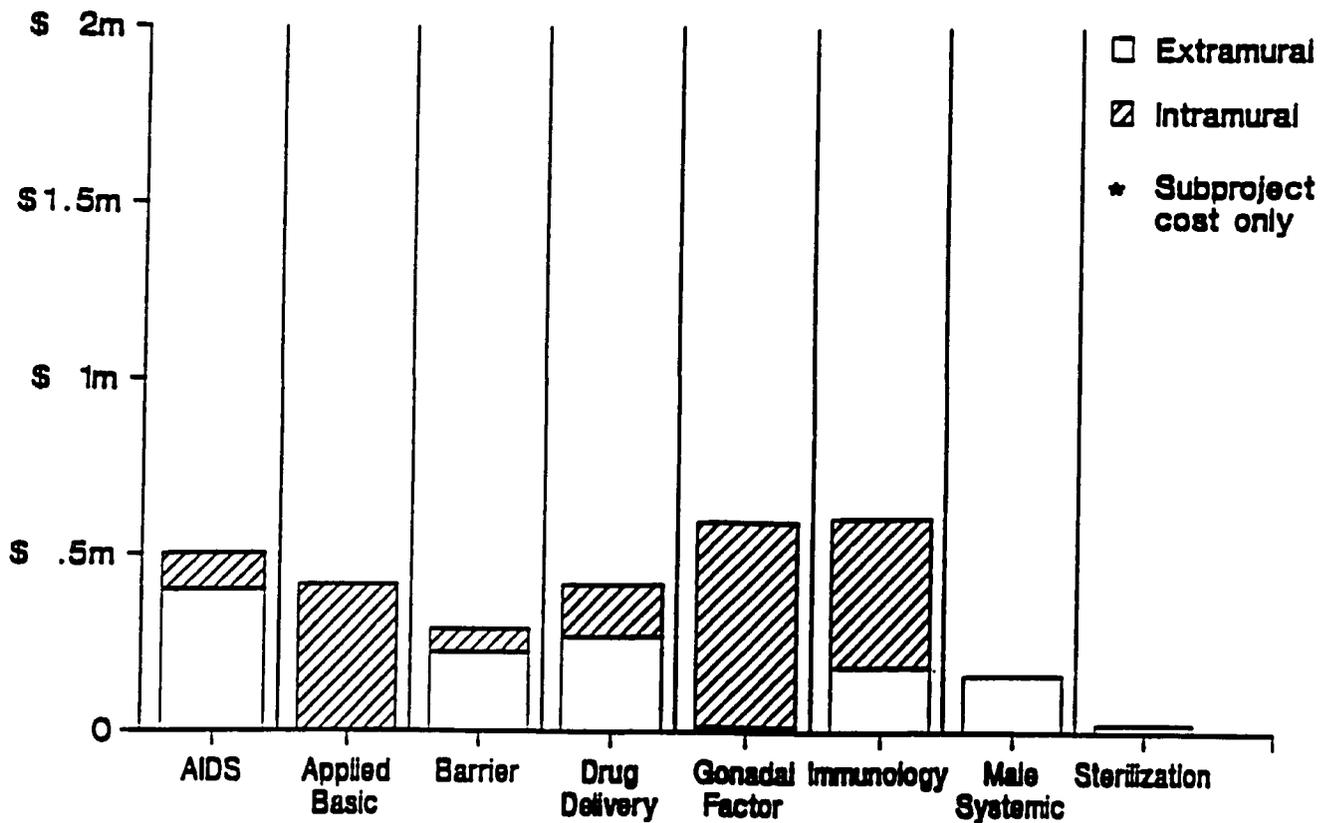
□ Extramural

▨ Intramural



Graph 3

### Intramural and Extramural\* Program Costs by Area Year 2 Budget (10/1/87 - 9/30/88)



**3. Technical Leadership and  
Information Dissemination**

### **3. Technical Leadership and Information Dissemination**

#### **3.1 Technical Leadership**

The CONRAD program is to be praised for its efforts in accordance with the Cooperative Agreement in establishing good relations with other organizations involved in contraceptive research and development. Among these are Cooperating Agencies (CA) supported by A.I.D. (e.g., FHI and The Population Council), other national programs (e.g., NICHD), international programs (e.g., WHO) and private industry. Representatives of CAs attend TAC meetings, and STS of CONRAD attend relevant advisory committee meetings of other agencies. Collaboration with FHI is active in the area of clinical trials of new long-acting methods. AIDS-related research is supported, in part, by NICHD. Collaboration with The Population Council is active in the area of non-steroidal gonadal factors. CONRAD funded the U.S. center participating in the WHO multicenter study on systemic hormonal methods for male contraception.

#### **Recommendation**

21. Opportunities for collaboration with other agencies should continue to be explored and exploited, particularly in areas that might be relevant to the extramural and clinical research programs. Possibilities might include 1) collaborating with agencies such as WHO for joint funding of projects of mutual interest; 2) participating in multicenter clinical trials sponsored by other collaborating agencies on leads of mutual interest, and 3) supporting studies in the networks of clinical research centers in developing countries that collaborate with other international agencies.

#### **3.2 Information Dissemination: Workshops, Bulletins and Publications**

##### **3.2.1 Workshops**

The Cooperative Agreement stipulates that the program will be responsible for organizing and convening an annual international workshop. In accordance with this stipulation, CONRAD has held two international workshops and plans at least two more. The first CONRAD international workshop was held on January 6-8, 1988 on the topic of Nonsteroidal Gonadal Factors: Physiological Roles and Possibilities in Contraceptive Development. The proceedings were published as a book and mailed to the 120 participants as well as a total of about 800 people around the world. The second international workshop was held on February 1-3, 1989 on the subject of the Heterosexual Transmission of AIDS, and proceedings are in preparation. The third international workshop is scheduled for November 27-29, 1989 in San Carlos de Bariloche, Argentina, on the topic of Gamete Interaction: Prospects of Immunocontraception. The workshop is co-sponsored by the WHO Special Program of Research, Development, and Research Training in Human Reproduction. A fourth workshop is being planned for 1990 on the topic of Barrier Contraception and STDs.

Workshops are a good medium for exchange and dissemination of information. They also enhance the visibility of the program. On the other hand, they are labor-intensive; they are placing a heavy demand on the time of the STS and support staff involved, and therefore they may be detracting from other higher priority activities. It may be possible, however, to make adjustments that would reduce STS' time and make the workshops more relevant to the program's research goals, particularly in terms of soliciting new near-term leads.

### 3.2.2 Publications

Two issues of the CONRAD Communique, a newsletter, have been published and widely circulated. The principle, format, and contents are excellent. In addition, an impressive list of publications has been authored or co-authored by the STS and supported by the CONRAD program (43 published or accepted articles). As might be expected, fewer papers have been produced through the extramural program -- 10 papers published or accepted. A continuing problem has been the late submission of or failure to clear through the CTO, all items whose publication is supported by CONRAD. A.I.D. has an obligation to clear all publications financed with A.I.D. money.

#### Recommendation

22. The workshop mechanism should be utilized to a greater degree for the generation and solicitation of research projects. This could be accomplished if the number of participants were limited and more focus given to soliciting proposals from included potential investigators. In addition, when proceedings of international workshops are distributed, a brochure about CONRAD should be included together with an invitation to submit research proposals in the area of the topic of the workshop or other areas as described in the brochure.
23. The need to convene an annual international workshop should be abandoned if it is directly interfering with progress in other program areas.
24. The Communique should continue as a medium for dissemination of information.
25. All publications acknowledging CONRAD support should be cleared with the CTO before publication in accordance with A.I.D. regulations.

## **4. Management and Administration**

### **4.1 Overview**

From a management perspective, CONRAD is a complex program. The range of research efforts, both applied research and clinical trials, covering many disciplines, organizations, and principal investigators spread out among many institutions, makes an unusual demand on the management mechanisms for planning, control, funding, communication, coordination and staffing.

The program has made a strong start. Scientific staff has been assembled, the TAC has been created, basic procedures necessary for internal operations have been established, good internal communication processes begun, and channels opened between CONRAD and an array of other scientific organizations. All this has made it possible for CONRAD to begin quickly to develop its strong intra- and extramural portfolios.

Perhaps because of the sheer volume of work and the rapidity with which it has gone forward, however, staff have been unable to focus sufficiently on some aspects of management--for example, on program and financial planning and on monitoring the balance between intramural and extramural subproject expenditures. If more attention had been paid to planning to achieve the agreed 2 to 1 ratio between extra- and intramural subprojects (i.e., two-thirds of resources allocated to extramural subprojects and one-third to intramural), and if expenditures for each of these two categories had been more rigorously tracked, it is possible that the project would not have strayed as it has from this stipulated balance. Other areas of management needing improvement are organizational structure and staffing.

### **4.2 CONRAD as Part of the Jones Institute**

One of the most exciting aspects of the CONRAD program is that it operates in the context of another larger and more diverse organization--the Jones Institute for Reproductive Medicine, the place where the first successful in vitro fertilization in the U.S. took place. Research is being carried out here on the entire range of reproductive medicine, which gives CONRAD scientists immediate access to scientific experts in allied fields of infertility, menopause therapy, and pre-embryo genetic diagnosis. CONRAD staff attest to the value of the lively scientific interchange that this wider scientific and medical setting allows.

From a management standpoint, however, this arrangement adds to the complexity that already exists. CONRAD is a program within an organization, not an organization itself. Since most of the persons working in CONRAD hold other responsibilities in the Institute, the program cannot be organized as an independent and vertical structure. Some of the difficulties encountered in the project can be attributed to the overlapping nature of the jobs of many staff.

### **4.3 Staffing**

#### **4.3.1 Overview**

Overall, an excellent staff has been assembled. Each member demonstrates a dedication to the research tasks, evidenced by both the long hours worked and the scientific output that in turn has resulted in a considerable volume of research publications. Many staff, however, have a large number of demands on their time, both CONRAD and non-CONRAD-related, and some may lose track of program priorities in the press of other duties.

### **4.3.2 Original vs. Current Levels**

The current staffing level is four times above the original level envisaged in the Cooperative Agreement. As of October 1, 1989, the full-time equivalent (FTE) staff level is projected to reach 48.25, compared with the 12 FTE envisioned in the Cooperative Agreement. The increases have been steep, with 29.8 FTE on staff by the end of the first year, rising again to 47.05 by October 1988. Since then, however, the increase has leveled off. Over the same period, the total Institute staff had grown much faster than CONRAD and is now almost twice the size (see Graph 4).

The growth in staff can be ascribed entirely to the requirements of the intramural program, including additional staff needed for the Core Laboratories and increased numbers of support staff (administrative assistants and secretaries). For instance, six FTE research assistants and four research associates, three lab managers, and three lab aides have all been added to conduct research, supported by two additional secretaries, four administrative assistants and two accountants (see Table 5). By contrast, no increases have been made in STS nor in staffing for the extramural program.

The resulting increase in technical and administrative staff has greatly changed the overall configuration of staff by generic function: i.e., according to whether staff are classified as scientific personnel involved in applied research, technical back-up, clinical, extramural, or administrative. The initial plan had anticipated that administrative staff (with over 40 percent of the total FTEs) and technical staff (over 15 percent) would account for slightly over half the staff and that they would be supervised by the other half, consisting of the applied research scientific staff (nearly 25 percent), and extramural and clinical research staff (each under 10 percent).

The current breakdown is markedly different. Technical staff has replaced administrative personnel as the largest category (with 45 percent), followed by administrative (with 33 percent). Together, these two categories account for a total of 78 percent of all the staff. Supervisory staff have been reduced to less than a quarter of the staff, with applied research staff accounting for 43.3 percent, clinical for 8.4 percent, and the extramural director for only 2 percent (see Table 6, page 30).

Increases in staff have been accepted incrementally by A.I.D., based on justification by the Program Director and intramural PIs that they are essential for specific subproject. Because research is a labor-intensive process, the failure to provide for the technical and administrative staff needed for this work has been acknowledged as a flaw in the original project design.

### **4.3.3 Extramural and Intramural Staff**

The intramural staff is far larger than the extramural staff. Forty-three out of a total of forty-six (FTE) staff are involved in intramural efforts.

The extramural staff, however, appears adequate for its major tasks -- soliciting and managing the extramural subprojects and control of the budgeting process. The recommended replacement of the current Extramural Project Administrator by a more technical person should increase the ability of this division to carry out its prime functions of soliciting and monitoring subprojects (see Section 2.3.4). A three-person accounting staff located in Norfolk works closely with the extramural program in the budget-development process, although it also services other parts of the CONRAD program and thus only a portion of its activities can be attributed to the extramural program (see Section 4.4.3).

Graph 4

### Growth of the Jones Institute for Reproductive Medicine

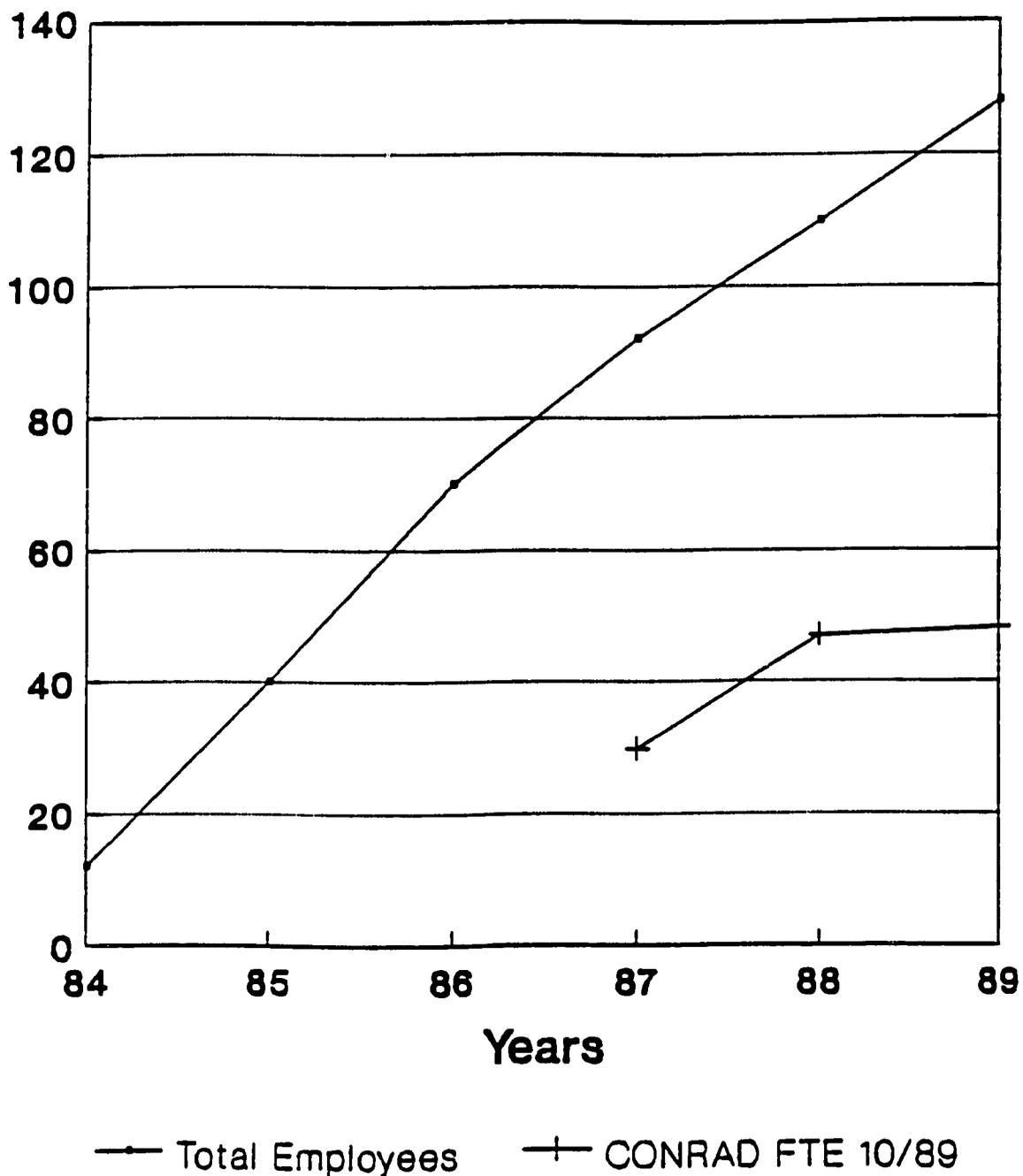


Table 5

STAFFING OF CONRAD

Original Plan				Current Staffing Level			
Position	No.	Funded	FTE	Position	No.	Funded	FTE
Program Director	1	100%	1	Same	1	90%	.90
Bio Med Scientist	1	100%	1	Bio Med Senior	1	90%	.90
Clinical Scientist	1	100%	1	Clinical Scientist	1	90%	.90
Product Developer	1	100%	1	Extramural Director	1	100%	1
Project Administration	1	100%	1	Vacant	1	100%	1
Bio Engineer	1	25%	.25	Andrology Professor	1	20%	.20
Immunologist	1	25%	.25	Asst Professor	2	86%	1.72
Soc Scientist	1	25%	.25	Asst Professor	1	45%	.45
Editor	1	25%	.25	Editor	1	95%	.95
Technical Assistants	2	100%	2	Research Associate	6	100%	6
Secretaries	3	100%	3	Secretaries	5	100%	5
Bookkeeper	1	100%	<u>1</u>	Secretary	1	19%	.19
			12	Accountants	3	100%	3
				Lab Director	1	80%	.80
				Program Development	1	90%	.90
				Admin Assistants	4	100%	4
				Research Assistants	6	100%	6
				Research Assistant	1	14%	.14
				Senior Fellow	1	35%	.35
				Fellow	1	100%	1
				Admin to Director	1	95%	.95
				Lab Managers	3	100%	3
				Lab Aides	3	100%	3
				Animal Technician	1	100%	1
				Clinical Assistant	1	90%	.90
				Clinical Associate	1	100%	1
				Med Office Assistant	1	75%	.75
				Nurse Practitioner	1	30%	<u>.30</u>
							46.30

**Table 6**  
**CURRENT STAFFING BY FUNCTION**

<u>Position</u>	<u>No.</u>	<u>Funded</u>	<u>FTE</u>	<u>Code</u>	<u>FTE By Percent</u>
Administrator	1	100%	1	Admin	
Editor	1	95%	.95	Admin	
Secretaries	5	100%	5	Admin	
Secretary	1	19%	.19	Admin	
Accountants	3	100%	3	Admin	
Admin Assistants	4	100%	4	Admin	
Admin to Director	1	95%	<u>.95</u>	Admin	
			15.09		32.6
Extramural Director	1	100%	<u>1</u>	Engr	
			1		2
Clinical Assistant	1	75%	.75	Med	
Clinical Associate	1	100%	1	Med	
Nurse Practitioner	1	30%	.30	Med	
Clinical Scientist	1	90%	.90	Sci	
Med Office Asst	1	90%	<u>.90</u>	Tech	
			3.85		8.4
Program Director	1	90%	.90	Sci	
Bio Med Professor	1	90%	.90	Sci	
Andrology Professor	1	20%	.20	Sci	
Assistant Professor	2	86%	1.72	Sci	
Assistant Professor	1	45%	.45	Sci	
Lab Director	1	80%	.80	Sci	
Senior Fellow	1	35%	.35	Sci	
Fellow	1	100%	<u>1</u>	Sci	
			6.32		13.7
Research Associate	6	100%	6	Tech	
Program Development	1	90%	.90	Tech	
Research Assistants	6	100%	6	Tech	
Research Assistant	1	14%	.14	Tech	
Lab Managers	3	100%	3	Tech	
Lab Aides	3	100%	3	Tech	
Animal Technicians	1	100%	<u>1</u>	Tech	
Sub-Total			<u>20.04</u>		<u>43.3</u>
Totals			46.30		100

## **4.4 Organizational Structure**

### **4.4.1 Description**

The Cooperative Agreement did not specify a particular organizational structure for the program. Rather, it listed the positions of Program Director, the Director of Administration and a number of specialist skills (see Table 5). The organizational structure of the CONRAD intramural program follows largely a functional form. Staff are grouped into basic research, clinical research, core laboratories, and various administrative units (see Appendix F). The extramural program, on the other hand, is organized in terms of its clientele: the external recipients of subprojects. Thus, the extramural program must lean on the intramural staff for functional expertise in such areas as solicitation and monitoring, according to the needs of a particular subproject. The needed technical staff are not always available, however, nor do they necessarily give the same priority to their time allocation as the extramural program requires. This horizontal interface between the needs of the extramural program with the staff in basic and clinical staff is a source of friction among CONRAD staff.

The core labs of the Jones Institute are under the supervision of the Associate Scientific Director and this provides a clean and workable span of control, a reasonable aggregation of similar activities and an apparent good responsiveness to the users. This need not change. (See Section 2.1.3 for additional comments on core labs.)

The situation with respect to overall administration is more questionable, largely because the position of Director of Administration is vacant and the normal function of this position, including budgeting, have been dispersed. The ramifications of the absence of an individual with oversight responsibilities for administration is explored in Section 4.4.3 below.

### **4.4.2 Role of Program Director**

One of the key flaws of the CONRAD organization is that the Director has too many roles and too large a span of supervision. As well as being responsible for managing the CONRAD project, this individual is the Scientific Director of the Institute and a professor on the faculty. There is a clear and all-embracing assignment of responsibility to the Program Director: He is responsible for all the activities of CONRAD. There is no ambiguity about his authority and the span of his responsibilities. The CONRAD program, however, represents only 35 percent of the total Institute staff (46 FTEs out of a staff of 130), around 30 percent of its budget (an average budget of \$4 million against the Institute's 1989 budget of \$13.7), and about 65 percent of the research projects (51 out of a total of 77).

In order to maintain the kind of talent employed in CONRAD and the Institute, the Director must raise between \$600,000 and \$800,000 per year in addition to the funds received from A.I.D. This requires constant effort to find research sponsors, mostly from foundations and pharmaceutical companies. In 1989, an estimated \$4.2 million of the Institute budget is expected to be revenue from non-CONRAD research projects. Raising these funds is a burden that falls mainly on the Director: He will have solicited 15 of the 27 research grants anticipated between 1984 and 1991.

In addition to this activity, the Director must supervise the non-CONRAD staff, conduct his own research as Principal Investigator, deal with the other officials of the EVMS, and establish and maintain relations with a host of external organizations such as The Population Council, NIH, FHI, A.I.D., as required by the Cooperative Agreement.

As a scientist, the Director authored or co-authored 71 original articles, reviews and chapters from 1987 to 1989, only some of which were CONRAD-supported. This is in addition to numerous lectures and attendance at various professional societies.

The consequences of this overload are apparent. The Director cannot spend sufficient time on CONRAD. Many of the staff at Norfolk are not receiving the time and guidance needed for their tasks. Even senior staff do not have ready access to the Program Director. Many of the details of implementation are not being attended to.

Moreover, with the upcoming retirement of the leadership of the Jones Institute, the demands on the program Director can only be expected to become greater in the future. It is a tribute to the Director and his capacity for work that he has done as much as he has. His output as Scientist and Director of Science for the Jones Institute is phenomenal. Some way, however, must be found to make the scientific and management functions of CONRAD more feasible and to accommodate the various responsibilities of the Director.

#### **4.4.3 Senior Technical Staff (STS) Responsibilities**

The individual senior staff have both supervisory and technical responsibilities. As supervisors, most have a manageable number of people reporting to them (the Director of the Extramural Program, the Director of Core Labs, and the Clinical Research Director). The Director of Basic Research has a large number of persons reporting directly and may need an internal realignment to ease that task.

Concerning the technical monitoring responsibilities assigned to senior staff, the tasks fall more heavily on some staff than others. Because of the press of other activities, it has proved impossible for some STS to execute these responsibilities as originally envisaged (see Section 2.3.4 and Table B, Appendix D).

#### **4.4.4 Absence of Director of Administration**

Considerably more problematic is the CONRAD administrative structure. One of the key positions stipulated in the Cooperative Agreement was Director of Administration. The individual hired for this position resigned after about a year. Instead of hiring a replacement, the Program Director assigned the functions to various persons. At present, administrative duties are dispersed: Budgeting is primarily the responsibility of the Director of the Extramural Program and accounting staff report to him; the central secretarial staff report to a Personnel Assistant who reports directly to the Program Director; and the Program Director himself has an Administrative Assistant.

Assigning the function of budgeting to the Director of the Extramural Program in Rosslyn appears to have given rise to some staff frictions. Not only does the arrangement appear cumbersome, with a top management staff function physically separated from the activities with which it is intimately related. The arrangement also has the appearance of putting one of the coequal STS in a position of affecting the resource allocation of his peers. In fact, the Director of the Extramural Program acts only in an advisory capacity with respect to the total amount allocated to the intramural budget, with decision-making power resting in the hands of the Program Director and the CTO. The perception deserves recognition, however, that budgeting is not fully integrated into the organizational structure of CONRAD.

With respect to the secretarial staff, in general there is a reasonable balance between workload and staff levels. In most cases, secretaries are serving eight or more persons, but there appears to be no problem in allocating workload. Administrative Assistants in the Fundamental Research Program and the Clinical Research program perform part-time secretarial duties in support of staff in those programs.

Although individual administrative activities continue to be carried out in a competent manner, the absence of an individual with administrative oversight responsibilities has had the following repercussions on overall program management.

- The Director's span of supervision has been unnecessarily expanded.
- There is no individual on the CONRAD staff who is technically qualified in administration and management procedures.
- The administrative and financial management functions have been dispersed and this in turn has required that an already overworked Program Director has had to become involved in coordinating details of administration.

#### 4.4.5 Conclusions

It is clear that the current management structure for CONRAD is inadequate. More help is needed for the Director, in both scientific and administrative areas, some of which can be achieved by delegation. Since the unit of management is the subproject, a project management system is necessary -- one that emphasizes synergy and flexibility rather than hierarchical lines of authority and responsibility. Since staff frictions derive from a number of causes not all related to structure or funding, some outside facilitation may be useful together with coaching as necessary on management and supervisory techniques. This reformulation effort should receive high priority, because dissatisfaction with the present situation has been evident to the CONRAD staff and the CTO for some time and the pressures are growing for some resolution.

#### Recommendation

26. The management of CONRAD should be reformulated with special attention to ways in which the Director can be assisted in discharging his functions, both administrative and scientific. Consideration should be given to filling the vacant position of Director of Administration with an individual versed in administration and financial planning. The position would involve overseeing the financial functions of accounting, fiscal control, cash flow projections and budgeting. It would be advisable to move the financial management function from Rosslyn to Norfolk and to assign it to the Director of Administration in conjunction with supervision of the accounting, fiscal control and program tracking systems. This will be particularly important if the budgeting and reporting systems are to be integrated into program and subproject management system. Consideration should also be given to identifying ways in which the scientific duties of the Director can be delegated in his absence (see Recommendations 33 and 38).
27. A subproject and program management system should be developed that groups efforts and roles around objectives. Each unit needs to be organized to permit inputs by staff from various areas according to the desired end result.
28. If recommended efforts to expand the extramural program are implemented (e.g., through shifting some of the workload to other STS and use of consultants -- see Recommendations

13 and 14), different forms of coordination between Rosslyn and Norfolk staff may need to be tried.

29. **The management reformulation should proceed in close coordination with the other system changes recommended, particularly the planning and financial management changes (see Recommendations 33 and 35). Team building and supervisory development should be part of the process to assist in reducing frictions and integrating staff efforts.**

#### **4.5 Management of Staff Time**

A.I.D.'s Request for Application (RFA) had called for full-time dedicated staff, but because of the realities of A.I.D. salary ceilings, it was essential to budget STS at less than 100 percent (one is budgeted at 100 percent, two are budgeted at 90 percent and one [non-key] at 20 percent).<sup>3</sup> Although it should not be the case, this compromise may be undercutting the original objective. Like the Program Director, the other STS have professional calls on their time in addition to CONRAD and are accorded the usual prerogatives of faculty members for a large measure of independence in allocating their own time. There is no question that all the professional and technical staff are hard-working: Many put in an average of about 60 hours a week. The issue has more to do with time management. It is not entirely clear what proportion of their time STS are devoting to CONRAD activities as compared with non-CONRAD duties, nor is it clear whether they are allocating their time spent in CONRAD-related activities in program priority areas. One priority area that has clearly been neglected has been development and monitoring of extramural subprojects (see Section 2.3). There is a serious general concern, however, that the RFA condition calling for full-time dedicated staff is not being fulfilled.

This conclusion is based on two findings: The first is that time reports are not completely satisfactory and they may not be used properly; the second is that little direction has been provided from the top to ensure that STS are spending their time strictly according to program priorities.

##### **4.5.1 Time Reporting**

###### **Time Accorded to CONRAD**

With respect to time allocated to the CONRAD program, the issue of the program's time keeping system has been raised by A.I.D., first at the pre-award audit and then in the April 1987 Management Review. The major problem is that it is difficult to gauge whether the time reports made out by staff provide an accurate picture of the time allocated to CONRAD duties. Staff are required to keep a daily record of hours worked in support of various programs (e.g., intramural, extramural) as well as other non-CONRAD activities (see Appendix G). Since each employee knows what portion of time is paid by CONRAD, there is a natural tendency to report the hours expected each week rather than to keep accurate records. This is not meant to imply that there is intention to provide incorrect data; busy scientists and technicians, however, tend to view the labor distribution report as a chore undertaken for the benefit of future auditors or the Accounting Unit and may not accord it the attention that it deserves.

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<sup>3</sup>Staff are budgeted at less than 100 percent to enable CONRAD to supplement their salaries for work done in the remaining time available. This has been necessary because government salary ceilings are well below the level that these individuals could earn in the private sector.

### Time Accorded among Program Activities

A second problem stemming from the somewhat questionable data on time sheets is that the program has no good measure of the amount of time going into the intramural program as compared with the extramural program. The Labor Distribution report for FY88 indicates that 80.5 percent of total time charged to CONRAD is going for intramural efforts. This seems high, given that only 49 percent of resources were estimated to have been devoted to the intramural program. It certainly is higher than the one-third of program resources supposed to be allocated to the intramural program.

A related problem is that the format of the time sheet itself does not require staff to track time spent on individual subprojects and, therefore, does not serve as a tool for the accounting staff to attribute staff costs to subprojects. These time sheets, if properly used, could serve as an aid to the program in knowing where its most precious asset -- time -- is being used. If used by line management for significant decisions, time reporting would more likely be taken seriously by staff.

#### 4.5.2 Inadequate Direction on Time Allocation

Both with respect to allocation of time between CONRAD and non-CONRAD activities and among CONRAD priorities, there seems to have been an inadequate effort on the part of STS to focus sharply on how they might best mesh their activities with the priorities of the CONRAD program and how such a focus might affect their use of discretionary time. Part of the reason is that, until recently, staff had not attempted to develop a clearly articulated consensus on program priorities. In addition, the Program Director does not regularly discuss with the STS how their time might be allocated in order to determine if this is what is wanted and how it fits with the priorities. Without such discussions, staff have had little by way of a yardstick against which to measure allocations of their individual time.

During the evaluation, an effort was made on the part of CONRAD staff to develop a priority listing of some of the key functions of staff in terms of their relevance or importance to the overall mission of CONRAD. The results are shown below. Most relevant activities were listed in Column A, those of second-level importance were listed in Column B, and the rest were shown as non-CONRAD activities. This was an excellent beginning and the Program Director plans to continue to refine the practice in the coming months.

#### PRIORITY RANKING OF PROJECT ACTIVITIES

Activity	Column A	Column B	Non-CONRAD
Solicitation of Subprojects	x		
Monitoring of Subprojects	x		
TAC meetings	x		
Workshops	x	x <sup>1</sup>	
STS business	x		
Intramural publications	x	x <sup>1</sup>	
Clinical projects	x		
Extramural projects adm	x		
Training		x	
Coordination w/ Other Agencies		x	
LDC Centers		x	
Roster of Investigators		x	
Disseminate Tech Info.		x	
Newsletter		x	
Grant writing			x
Teaching			x
Clinical Care			x

<sup>1</sup>Staff did not reach a consensus on priority that should be accorded to workshops and intramural publications.

## Recommendation

30. **The Program Director should continue the practice of determining the relevance of activities to overall CONRAD goals and establishing some mechanism for comparing desired time allocation with actual time spent. The preliminary list developed is one method that could be used.** If there were consensus on such a list, various staff members could periodically keep their own record--perhaps for a week or two -- and then compare actual time spent with desired allocation. When this is done with a supervisor, it can serve as a planning tool in rearranging priorities. It is important that any such time supervision should be done with due deference to professional independence while seeking a balance between personal preferences and program needs.
31. **The present labor distribution report should be revised to show each of the intramural subprojects.** This would help determine where most of the effort is going and also help the Accounting Unit in its cost analysis. **It should be utilized by STS and the Program Director for determining how best to use staff time. Periodic sample reviews should be made of the accuracy of the report and employees oriented on the purpose and use to be made of the instrument.** This change would appear feasible from the perspective of the Accounting Unit.

## 4.6 Program Planning

### 4.6.1 Measures of Progress

As a research program, CONRAD cannot plan in the methodical way that non-research programs do: It is impossible to predict the inputs and technology that will be needed to develop scientific leads and eventually new products. It is possible, however, in open-ended research programs to define what constitutes progress and how progress is to be measured.

The program's tendency to overspend on the intramural program and longer-term subprojects may be attributed in part to the lack of any commonly agreed-upon list of progress indicators that might serve to guide and check program activities. CONRAD staff are well aware that their mission is primarily to bring products to Phase I, II, and III trials and that their success in this area will be given higher marks than their efforts to hold conferences or publish papers. This general understanding, however, has not been translated into an articulated set of interim goals or progress indicators.

The list of such indicators produced by the STS in the course of the evaluation (see below) reflects staff's willingness to scrutinize its work more carefully. The inclusion of a weighting factor to reflect the relative importance of each variable suggests that the staff is prepared to judge itself sternly (indeed, perhaps too sternly) with respect to adhering to the priorities it sets forth. The list itself should not be considered definitive; it is the process itself that is important -- the joint effort of staff to develop a set of short-term measures that can be used to focus program efforts. Continuing the process should help keep the program on target, particularly if, in time, numerical targets are added to each of the factors.

**PRIORITY RANKING OF PROGRESS INDICATORS**

<b>FACTORS</b>	<b>WEIGHTING</b>
Products reaching Phase III trials . . . . .	15
Products reaching Phase II trials . . . . .	10
Products reaching Phase I trials . . . . .	6
FDA clinical trial approvals (Investigation of new drug [IND]) . . . . .	3
Pre-clinical patents approved . . . . .	2
Pre-clinical licenses . . . . .	2
Number of original publications . . . . .	1
Number of workshops and proceedings . . . . .	3
LDC Centers developed . . . . .	3
Fellows trained . . . . .	1
Newsletters . . . . .	1

**Recommendation**

32. **A.I.D. and the CONRAD staff should jointly develop progress indicators, based on the Cooperative Agreement. These should be used for periodic score-keeping and appraisal of the progress to be followed by corrective action, if necessary. Staff should also periodically review the indicators themselves and revise them, if appropriate. In addition, A.I.D. and CONRAD should develop, if possible, some targets to be used in the periodic workplan reviews and approvals.**

**4.6.2 Strategies and Workplans**

The original concept in the Cooperative Agreement was that semi-annual reports would be submitted to A.I.D. containing summaries of activities, results, accomplishments and problems in program development. The precise format for such reports were to be developed later in conjunction with the CTO. The April 1987 Management Review stipulated that the semi-annual reports were to be made in conformance with the Cooperative Agreement concept, plus an annual strategy (term undefined), reports of site visits, and a schedule of travel and meetings.

The semi-annual reports are largely progress reports on individual projects and administrative matters, with a mixture of comments from the last TAC meeting and comments on possible changes in direction for the extramural projects. They also contain plans for the next six months in each program area but no "strategies," which can be defined as the linkage between objectives or milestones and workplans. Several elements of an effective program planning process are missing:

- 1) **A concept and operational definition of "strategy" and how strategies can be linked to six-month reports and follow-on plans.**
- 2) **A process for relating progress reports and the most recent TAC meeting to assist CONRAD staff and A.I.D. to set strategies and program objectives for the next period.**
- 3) **A process to go from strategies and objectives to a workplan and financial plan for the next period.**

- 4) **Definition of key indicators for tracking progress and establishment of key controls to assure movement in accord with desired direction (see Section 4.6.1).**

The absence of a clear linkage among objectives, strategies, workplans and budgets has contributed to the problems in project implementation identified earlier: the inappropriate balance among the extramural and the intramural budgets, the unanticipated growth of intramural staff, and some of the staff frictions. If A.I.D. and STS were to spend more time dealing with overall program strategies and plans, it is likely they could free themselves from the need to micromanage project activities that has, in fact, diverted them from this very activity. Because this is a demanding process, however, and because of the continued press of day-to-day business, it may be necessary to enlist external assistance if the process is to be instituted.

#### **Recommendation**

33. **Management assistance should be provided to CONRAD (and A.I.D.) in formulating a program planning process that links objective setting, strategy formulation, workplans, budgeting and reporting into a coherent system that facilitates carrying out the responsibilities of each party. The development of the planning system requires the involvement of both parties so that the process is understood, accepted and utilized by the key A.I.D. and CONRAD personnel carrying out the Cooperative Agreement.**

### **4.6.3 Subproject Management**

In the absence of overall progress indicators and of strategies and well-developed workplans, the process of planning is being shifted by default to the subproject level, and the overall program direction tends to be a reflection of what is happening at this level. In both the extramural and the intramural programs, the planning and management process could be improved. Although there appears to be a more systematic effort in the extramural program than in the intramural to define procedures of planning and control, even in the extramural program there are concerns about the need for more vigorous solicitation, the lack of time spent by STS on technical monitoring, and the need for more planning to determine the program mix of subprojects (see Section 2.3). Management control is even less stringent in the intramural program, particularly with respect to reviewing cost estimates used for budgets (see Section 5.1.1). The result is that subproject management is now being carried out without sufficient reference to overall program goals.

With the initiation of a total of over 50 subprojects (intra- and extramural), the management workload, particularly for the Director, has become very complex and may have to be reduced. One way to do this might be to establish progress indicators and milestones for both substantive actions and resource utilization (personnel, funds, equipment, etc.) to facilitate tracking actual progress and deviations from expectations. The Program Director could then focus mostly on those subprojects and specific activities that have deviated from plan. This system is called "Management by Exception" because it helps focus management attention on the departures from expectations rather than on those activities that are proceeding as expected. Normally about 80 percent of an organization's activities are proceeding satisfactorily while 20 percent require attention. Thus, the system allows management time to be more efficiently utilized.

#### **Recommendation**

34. **CONRAD should review and revise its subproject management procedures to link with the overall program planning described in Recommendations 28, 30, and 31. The review should encompass all aspects of the extramural and intramural programs, the need for technical**

**direction, financial planning and control, and the possibilities of adopting a management method that would help reduce the workload on senior staff.**

## 5. Financial Management

### 5.1 Financial Management

#### 5.1.1 Program Budgets and Reports

Overall budgeting for the CONRAD program begins with budgeting, accounting and fiscal control at the subproject level. For extramural subprojects, the system for budgeting, accounting and fiscal control appears sound. For the intramural subprojects, however, the process is more questionable because of the lack of input from the fiscal control group in the Accounting Section (see Section 2.1.4). A more serious problem is that the budgeting process has not required attribution of costs of salaries, equipment, travel and core labs to individual subprojects. Instead, a hybrid approach has been used, based on a prototype five-year budget contained in the Cooperative Agreement (see Table 7, page 42). Despite several requests by the CTO to reconstruct the financial reports and the budgets to show the total funds going into intramural and extramural subprojects, this has not been done. The result has been that the CONRAD management has not been fully aware of the real costs of any of the intramural subprojects or of the comparative aggregate costs of the intramural and extramural programs. Without doubt, this is one reason that program management has strayed from the stipulation that it devote two-thirds of its resources to the extramural program.

Table 8 (see page 43), which shows that extramural and intramural spending was about equal in FY 1988, represents the first effort by the Accounting Unit to produce a report allocating expenditures to intra- and extramural subprojects. As a backup to the aggregates in Table 8, the Accounting Unit also developed a more detailed breakdown of costs by intramural subprojects by allocating salaries, supplies, travel, etc. to the two categories.

This approach also throws new light on the relative cost of staff and core labs to the overall cost of the intramural subprojects. CONRAD's standard budgeting procedure shows that in FY 1988, the proportion of staff costs to overall program costs was a modest 25 percent (see Table 9, page 44).

Total intramural salary and benefits costs (\$698,471) represent 35 percent of total intramural costs (\$1,999,368). From a different perspective, if salaries and benefits for the intramural program alone in FY 1988 were compared to the costs of intramural subprojects for that year (\$440,994): for every dollar spent on intramural subprojects, another \$1.58 was spent for salaries and benefits for the staff involved in those subprojects (the PI, research workers and technicians). If the total cost of salaries, benefits, and core labs were compared to the costs for intramural subgrants, the ratio would be 2:1 (see Table 10).

One explanation of the high costs of salaries, benefits and core labs may be that the scale of projects is uneconomic. Thus, it could be that increasing the value of the projects would not increase salaries and lab costs proportionately. This would have to be examined. If increases were to appear justified on the basis of economies of scale, however, there would be a further imbalance between the extramural and intramural portfolios. It appears that the intramural projects are more labor-intensive than extramural subprojects and that staff costs represent a large proportion of the overall subproject costs. This apparent difference would disappear, however, if one were to count up staff costs funded under extramural subprojects which are proportionately just as high as those for intramural projects.

Table 7

CONRAD Five-Year Budget as Estimated in Cooperative Agreement

	9/30/86- 9/30/87	9/30/87- 9/30/88	9/30/88- 9/30/89	9/30/89- 9/30/90	9/30/90- 9/30/91	TOTAL
SALARIES	\$ 862,991	\$ 868,881	\$ 915,547	\$ 943,014	\$ 971,304	4,581,737
FRINGE BENEFITS (14.1% of Salaries)	121,642	123,332	129,092	132,968	136,954	646,025
Maintenance/Supplies Rent/Phone/Postage/ Periodicals & Books	171,245	176,382	181,674	187,124	192,728	909,164
CAPITAL EQUIPMENT	96,050	-0-	-0-	-0-	-0-	96,050
OFFICE FURNITURE	42,000	-0-	-0-	-0-	-0-	42,000
Travel: Foreign & Domestic	133,500	130,405	134,317	138,347	142,497	679,066
Fees: TAC & Consultants	87,500	51,500	53,045	54,626	56,375	302,956
Workshops & Publications	200,000	206,000	212,180	218,845	225,102	1,061,827
Intramural Subgrants	284,708	293,250	302,048	311,100	320,442	1,511,558
Intramural Consolidated CORE LABS	67,770	125,900	183,900	181,999	179,999	749,611
Extramural Subprojects	837,747	2,878,511	3,234,682	3,678,627	3,600,313	14,249,890
Total Direct Costs	2,905,194	4,886,164	5,366,865	5,846,376	5,825,584	24,829,884
INDIRECT COSTS	897,106	615,019	633,169	652,474	672,048	3,170,116
Total CONRAD Funds	3,802,300	5,501,183	6,000,034	6,498,850	6,497,632	28,000,000

<sup>1</sup> Maximum reimbursement on this line item is established at \$3,000,000 (See Article IV- Overhead Rate), below.

Table 8

CONRAD ACTUAL BUDGET

Run date: 03/23/89  
 Filename: MGTREV89  
 Period: 10/01/86-09/30/87 YR 1  
 Period: 10/01/87-09/30/88 YR 2

	Year 1			Year 2		
	10/1/86- 9/30/87	INTRAMURAL	EXTRAMURAL	10/1/87- 9/30/88	INTRAMURAL	EXTRAMURAL
<b>EXPENDITURES:</b>						
Salaries	645,000	428,784	216,216	862,900	612,291	250,609
Fringe	90,945	60,459	30,486	121,433	86,180	35,253
Indirect	474,075	315,156	158,519	624,361	466,106	158,255
Supplies	70,000	50,412	19,588	76,185	59,530	16,655
Rent & Maintenance	55,000	18,971	36,029	78,190	46,190	32,000
Capital Equipment	95,000	81,864	13,136	9,712	9,712	
Office Furniture	36,500	21,756	14,744	23,681	18,365	5,316
Travel	80,000	35,000	45,000	85,000	60,000	25,000
Consultant Fees (w/TAC)	30,000	0	30,000	40,806	0	40,806
Workshops & Publications	0	0		116,028	0	116,028
Intramural Subgrants	215,000	215,000		440,994	440,994	
Intramural Core Labs	40,000	40,000		258,825	200,000	58,825
Extramural Projects	1,143,480	0	1,143,480	1,282,857		1,282,857
CD:RI	270,000	0	270,000	30,000		30,000
<b>Total</b>	<b>3,245,000</b>	<b>1,267,402</b>	<b>1,977,598</b>	<b>4,050,972</b>	<b>1,999,368</b>	<b>2,051,604</b>
<b>ALLOCATION OF INCOME:</b>						
AID/SAT/FCR/R	2,975,000			3,273,572		
CD:RI	270,000			30,000		
AID/India	0			280,000		
AID/NIH	0			467,400		
<b>Total</b>	<b>3,245,000</b>			<b>4,050,972</b>		

Table 9

**RATIO OF SALARIES AND FRINGE BENEFITS  
TO OVERALL EXPENDITURES**

Salaries and fringe benefits	\$ 984,333
Total CONRAD expenditures	\$4,050,972
Percent Salaries to Total	24 percent

Table 10

**INTRAMURAL SUBPROJECTS:  
COSTS OF SALARIES, CORE LABS, AND SUBPROJECTS**

Salaries and Benefits	\$698,000
Core labs	\$200,000
Intramural subgrants	<u>\$440,994</u>
Percent salaries to grants	158.4 percent
Percent salaries/core labs to grants	204 percent

**Recommendations**

35. **Financial reports and budgets should reflect costs by program and by cost categories. The formats for these management instruments should be developed with professional assistance in close coordination with the senior staff of CONRAD and the A.I.D. CTO to assist in management decisions. In turn, the budget and financial reports should be an integral part of the program planning system (see Recommendation 33).**

The format for a program budget could vary somewhat from that shown in Table 8. For example, the cost for activities such as workshops and conferences could be shown as a separate program element. Likewise, the central management of CONRAD could be shown as a separate element, although it would be preferable if it were divided among other program areas, particularly extramural and intramural.

In addition to changes in format, financial reporting along program lines should be made to the CTO quarterly and incorporated into the semi-annual plans. The exact structure of the program budget should be carefully designed to assist management to track and decide on key aspects such as the amount of investment in central and supporting staff, the balance of intra- and extramural programs, and the relative cost-effectiveness of investment in the balance of the two program areas.

36. **A detailed study is needed to examine whether intramural subproject costs could be reduced further without harming quality or the current level of subprojects. This study could also determine what balance of investment in the two kinds of portfolios would best advance the objectives of the program as a whole (see also Recommendation 19).**

### 5.1.2 Obligations and Expenditures

Current budgets are a mixture of expenditures for past years FY87 and FY88 together with a projection of obligations for the current and future years -- FY89-91. Obligations and expenditures are different concepts that produce different figures. The result is that the program's five-year budgets contain non-comparable figures.

Another issue is that A.I.D. makes distinctions between commitments, expenditures, and balance of funds available,<sup>4</sup> but does not make clear the difference between commitment and obligation. CONRAD makes a distinction between expenditures, obligations and "encumbrances" (or unliquidated obligations), and its budgets contain a number of these encumbrances reflecting funds that have been obligated to extramural projects beyond the current fiscal year: i.e., at this point, funds have already been approved for ongoing extramural subprojects representing commitments, for year 4 of \$721,541, and for year 5 of \$355,000. Because these have not been vouchered, A.I.D. does not recognize these as commitments and the danger (hypothetical at least) is that, should funds run short, A.I.D. might not recognize these as bona fide obligations.

#### Recommendation

37. Budgets and financial reports should deal separately with obligations and expenditures and project these separately. It may also be necessary to clarify with A.I.D. the concepts and definitions of obligations, commitments and encumbrances.

### 5.1.3 Project Budgeting and Control

Although it has not been utilized optimally, the accounting system is detailed enough to track actual expenditures for each subproject and to detect variances from budget. The fiscal controls for all subprojects are thorough and well integrated between the CONRAD program and the EVMS. The one major weakness -- the time reporting system -- has not significantly hindered the overall accuracy of the Accounting Unit's work.

#### Recommendation

38. The current budgeting and reporting systems at the subproject level should be integrated to facilitate management. Consideration should be given to developing a tracking system that integrates substantive progress measures with resource utilization (personnel and funds) along with a variance analysis method (departure from expected levels of resource use) that will permit management to focus upon the departures from expected progress.

## 5.2 Program Funding

The Cooperative Agreement set forth a five-year budget with a total negotiated maximum funding of \$28 million. Based on A.I.D.'s estimate of funds that will be available, program management has prepared a revised five-year budget showing projected expenditures of \$23,190,000, a drop of \$4,810,000 (see Table 11 and Table C, Appendix D). The projection shows increases in funding for years 3 and 4, but a sharp reduction in year 5, associated with the scheduled end of the project.

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<sup>4</sup>These distinctions are made in the Cooperative Agreement Article VI.1.a.

The seriousness of the anticipated shortfall is difficult to assess. Judged on the basis of actual expenditures compared with original estimates, it would not appear grave. During project year 1, expenditures were \$253,000 below the level anticipated and in year 2, expenditures were nearly \$1.5 below the expected amount. If this trend were to continue, project spending could easily be accommodated within the lowered ceiling.

Two developments could easily disturb this situation, however. If efforts to increase the clinical trials portfolio are successful, this will put a great strain on the budget as these activities are very costly. Also, if efforts to increase the extramural budget dramatically are successful, the reduced availability of funds could represent a constraint for other project activities.

The concern is more acute with respect to the extramural budget. Based on planned solicitations over the next three project years, the extramural staff predict a portfolio valued at \$2,355,761 in year 3, \$2,746,541 for year 4 and \$2,725,000 for year 5 (see Table D, Appendix D). Compared with CONRAD's estimated budget for these three years, the result would be an overall shortfall for those three years of \$2,350,135.

Table 11

CONRAD BUDGET  
Dollars (000)

	FY87	FY88	FY89	FY90	FY91	TOTAL
Original Budget	3,502	5,501	6,000	6,499	6,498	28,000
Actual Expended	3,245	4,051	0	0	0	
CONRAD Projected			5,624	5,700	4,570	23,190
Sustained FY88 rate			4,051	4,051	4,051	19,449
Funds received or projected*	4,750	6,940	5,000	3,000	3,500	23,190

\* These funds come from S&T/POP/R; CD:RI, USAID India; and NIH.

## 6. Future Directions and Major Recommendations

### 6.1 Overview

#### 6.1.1 Accomplishments

Overall, the CONRAD program has made a very good start. It has begun to make its mark in the world of contraceptive research, through the excellence of some of its intramural research, its funding of over 40 extramural projects, and the holding of two international workshops, with publication of proceedings either accomplished or under way. The fine staff were recruited and put in place very quickly. The intramural basic research program is making some good progress in a number of areas of contraceptive research. The clinical trials division that has been established has the capability of carrying out Phase I and II trials as solicited. A well-chosen Technical Advisory Committee (TAC) has been assembled to help guide the work of the extramural program, and the subprojects developed also seem appropriate, falling into areas in which research is needed and scientifically feasible.

#### 6.1.2 Program Balance

At this point, with the realization that it is not conforming to the agreed-upon balance between intra- and extramural programs, the CONRAD program has reached a crossroads. If the imbalance is to be redressed, difficult decisions will need to be made with respect to both funding and use of staff time.

There are three ways that a larger proportion of funding could be shifted to the extramural program: 1) spending for extramural projects could increase; 2) spending for intramural activities could decrease; or 3) some combination of the two can be worked out.

The implications of each are discussed below.

#### Funding

- 1) Increasing the Extramural budget. To achieve a 2 to 1 ratio, the extramural budget would have to double to \$4 million per year in FY89. If there is no reduction in the intramural program, this would mean a total annual budget of \$7.6 million for FY89 rather than the \$5.6 million now estimated. It is very unlikely that this amount of money will be available. Moreover, an increase of this magnitude in the extramural budget may not be feasible, given the difficulty in soliciting projects.
- 2) Decreasing Intramural Spending. Even if one or more intramural subprojects were dropped from the portfolio (e.g., see Recommendation 2), an increase in clinical trial subprojects could wipe out the cost reduction and indeed elevate intramural costs to above present levels. Furthermore, the large number of staff and the core labs that were found essential for the intramural research activities now may represent fixed investments that are difficult to cut. It may even be true that if the level of intramural research were increased, these investments might be used more cost-effectively.
- 3) A combination of options 1 and 2. Neither option pursued alone can be expected to achieve the desired results and, therefore, combining both may well represent the best solution.

It is important to keep in mind that the ratio of 2 to 1 was arbitrary and is viewed by A.I.D. as more of a signpost to keep the CONRAD program on track than a rigid requirement to be met. The more appropriate criterion for establishing the balance would seem to be whatever combination of projects would be most cost-effective in meeting the program targets for bringing products to the market. The data thus far, however, seem to support the need for some increase in extramural spending, an increase in intramural clinical trials of near-term leads and a decrease in long-term intramural projects.

### Staffing

Staffing is a crucial issue in the equation -- its quantity, quality, synergy and cost must all be taken into account in considering how the level of staff effort devoted to the extramural program can be increased. The issue can be viewed in the same way as was the shift in funding: Specifically,

- 1) Fewer staff hours could be allocated to intramural programs. This might involve a reduction in personnel funded under CONRAD or an assumption of a larger share of CONRAD personnel costs by the Institute. Efficiency studies looking at the cost per unit of core laboratory output, or per intramural project output, might help in making decisions on how staff might be reduced. A better staff record keeping system might give a clearer picture of whether professional and technical staff time is apportioned to projects according to need and again, provide some guidelines as to how time might be used more efficiently. The degree to which these mechanisms would reduce staff time allocated to intramural programs is not clear.
- 2) Increased staff time could be allocated to extramural programs. Recommendations calling for use of consultants and allocation of some additional STS time to the extramural program could increase the level of effort allocated to the extramural program.
- 3) A combination of 1 and 2. Efforts will need to be made in both areas if the needed staff effort is to be redirected in any substantial degree to the extramural program.

An important proviso in moving forward in these areas is that productivity in a scientific endeavor may depend more on factors of morale, interest, dedication, commitment, the excitement of synergistic team efforts, and the anticipation of professional recognition, than on any effort at reorganization. The effect of these recommended changes on the overall morale of the team will need to be taken into account as management decisions are being made.

A second consideration is that staffing levels cannot be treated as an independent factor. It should be part of a more thorough examination when A.I.D. and the CONRAD management determine overall program and funding levels, priorities, and revised management procedures.

## 6.2 Major Recommendations

In the immediate future, the CONRAD program staff, with A.I.D., should begin to develop a revised strategy, based on the principal recommendations contained in this report. The process should start by undertaking two major reviews recommended earlier. Based on its overview of the program's overall portfolio and staffing, the CONRAD program could proceed to implement the principal recommended actions in programming and management. (A complete list of recommendations contained in the report is provided as Appendix G.)

- 1) CONRAD management and A.I.D. should reexamine the portfolio of intramural and extramural subprojects in light of their objectives for near-term versus longer term payoffs. It may not be either appropriate or possible to achieve the 2 to 1 ratio set forth in the Project Agreement, but efforts are clearly needed to increase the level of extramural funding and clinical trials of near- and medium-term leads. At the same time, it is important to ensure that intramural spending does not encroach on funding for extramural subprojects (#19).<sup>5</sup>
- 2) A thorough review is needed of the proper staffing level for intramural projects that takes into consideration the program levels desired, the funds available, the cost-effectiveness of the core labs and the productivity and morale of the staff. Such a review should be related to the recommendations summarized below regarding overall program management system and organizational streamlining.

### Priority Programming Changes

From a programming standpoint, the following recommendations are offered as the most likely to lead to a greater emphasis on the extramural program and on near-term subprojects:

- 1) Active solicitation of extramural proposals needs to be increased, particularly those that are near-term. This could involve increasing the participation of STS and TAC members, hiring consultants, and replacing the extramural program administrator with a technical person (#13 and #14).
- 2) The Clinical Program Director should increase his efforts to initiate intramural clinical trials and the overall program should solicit more extramural subprojects that are at the Phase I and II trial stages. This could involve more use of TAC members and hiring of consultants (#6).
- 3) The level of resources allocated to intramural subprojects should be reevaluated. One suggestion is that the inhibin subproject might be subcontracted out as an extramural activity. A second is that the inhibin research could be phased out entirely (#2).

### Management

The complex set of interrelated management changes recommended in this report will need to be carried out if these priority program moves are to be successfully implemented. To some degree, these recommendations need to be viewed as a package in which the implementation of one will depend on the successful execution of others. All are linked, but priority should be accorded to those that are starred. (This is the intent of Recommendation 27.)

### Project Organization and Administration

- \* 4) The management of CONRAD should be reformulated with special attention to ways in which the Director can be assisted in discharging his functions. The vacant position of Director of Administration should be filled by an individual versed in administration and financial planning. The position would involve overseeing the

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<sup>5</sup>Numbers at the end of these recommendations refer to the number of the recommendation in the report.

financial functions of accounting, fiscal control, cash flow projections and budgeting. It would be advisable to move the financial management function from Rosslyn to Norfolk and to assign it to the Director of Administration in conjunction with supervision of the accounting, fiscal control and program tracking systems. This will be particularly important if the budgeting and reporting systems are to be integrated into the program and project management system (see below, Major Recommendations 10 and 11) (#28).

- 5) A subproject and program management system should be developed that groups efforts and roles around objectives. Each unit needs to be organized to permit inputs by staff from various units according to the desired end result (#27).

#### Goal Setting, Planning, and Monitoring

- \* 6) Management assistance should be provided to CONRAD (and A.I.D.) in formulating a program planning process that links objective setting, strategy formulation, workplans, budgeting and reporting into a coherent system that facilitates carrying out the responsibilities of each party (#3).
- \* 7) The Program Director should continue the practice of determining relevance of staff activities to overall CONRAD goals and establishing some mechanism for comparing desired time allocation with actual time spent. The preliminary list developed is one method that could be used (#30).
- \* 8) A.I.D. and the CONRAD staff should jointly develop progress indicators, based on the Cooperative Agreement. These should be used for periodic score-keeping and appraisal of the progress, to be followed by corrective action if necessary (#32).
- 9) CONRAD should review and revise its subproject management procedures so that they conform to the overall program planning described in principal Recommendations 6, 7, and 8. The review should encompass all aspects of the extramural and intramural program systems, the need for technical direction, financial planning and control and the possibilities of adopting a management method to help reduce the staff workload.

#### Financial Management

- \* 10) Financial reports and budgets should reflect costs by program and by cost categories. The formats for these management instruments should be developed with professional assistance in close coordination with the senior staff of CONRAD and the A.I.D. CTO to assist in management decisions. In turn, the budget and financial reports should be an integral part of the program planning system (#35).
- \* 11) The current budgeting and reporting systems at the subproject level should be integrated to facilitate management. Consideration should be given to a tracking system that integrates substantive progress measures with resource utilization (personnel and funds) along with a variance analysis method (departure from expected levels of resource use) that will facilitate management control (#38).

- 12) **An in-depth review should be undertaken to establish the real costs as well as the staffing levels necessary to operate the core labs and the intramural research subprojects. (#14)**
- 13) **A detailed study is needed to examine whether intramural costs could be reduced further without harming quality of the current level of projects (#36).**
- 14) **The present Labor Distribution Report should be revised to show each of the intramural projects. It should be utilized by all staff and the Program Director for determining how best to use staff time. Periodic sample reviews should be made of the accuracy of the report (#31).**
- 15) **Budgets and financial reports should deal separately with obligations and expenditures and project these separately. It may also be necessary to clarify the concepts and definitions of obligations, commitments and encumbrances (#38).**

## Appendices

## **Appendix A**

### **Project Evaluation Plan - CONRAD**

Appendix A

PROJECT EVALUATION PLAN - CONRAD

XI. Issues and Questions to be Considered by the Evaluation Team

- A. Recent and Current Funded Extramural and Intramural Subprojects Portfolio:
- Likely pay-off for ultimate LDC use
  - Appropriate mix of subprojects in terms of pilot versus formal projects; intramural versus extramural projects; portfolio in terms of near-, medium- and long-term focus; etc.
- B. Research Priorities:
- Appropriate? Too restrictive? Too loose?
  - Are all priority areas being pursued? Have any major opportunities been missed?
  - Have unsuccessful projects been phased out? What should be phased out if resources should be limited?
  - How has the USAID/India buy-in affected the program?
  - How has the Interagency Agreement with NIH for AIDS-related research affected the program?
- C. Project Planning:
- How are projects developed and/or solicited? Can the process be improved?
  - Are the review mechanism for pilot, informal and formal proposals appropriate and efficient?
  - Are LDC projects encouraged? How many LDC projects have been funded?
- D. Technical Advisory Committee (TAC):
- Is membership appropriate in terms of numbers and disciplines?
  - Is current mechanism effective? Can it be improved?
- E. Staff and Facilities:
- Norfolk and Rosslyn facilities
  - Intramural and extramural technical and administrative staff and staff responsibilities
- F. Program Management and Administration:
- What is the management structure of the Program, including the chain of command? Is it appropriate? Can it be improved?
  - Who is responsible for the day-to-day operation and decision making regarding the total program?
  - Does the lack of a senior administrator adversely affect the Program?
  - Are there sufficient support staff?

- G. Workshops, Publications and Information Dissemination:
- Completed and planned workshops
  - Newsletter and brochures
  - Publications of research supported by CONRAD (intramural and extramural)
- H. Funding Level:
- Is current funding adequate to maintain the program? Adequate to meet major new opportunities? What can be said about the difference between the amount of funds provided each year and the expenditures and commitments (pipeline)?
  - Will the program suffer, and in what ways, if it receives \$22 million instead of the negotiated \$28 million?
  - Is the budget breakdown between line items reasonable? Is the staff level of effort appropriate? Is the mix between funds for intramural versus extramural projects appropriate? How does the budget compare to what was projected when the project was designed by A.I.D. and to the budget in the cooperative agreement? What was the actual budget in the first two years and what is projected for the third year and the last two years?
- I. Relationship with Other Efforts in the Field of Contraceptive Development:
- Relationship with other cooperating agencies supported by A.I.D. (e.g., FHI, Population Council)
  - Relationship with other programs (e.g. NICHD)
  - Relationship with international programs (e.g. WHO)
  - Relationship with private industry, private foundations and PVOs
  - What impact has the CONRAD Program had on the activities of other programs?
- J. CONRAD Assessment of A.I.D. in Administering the Cooperative Agreement. CONRAD'S relationship and experience with:
- the CTO
  - other staff in ST/POP/R
  - staff of ST/POP
  - staff of Office of Procurement (Contracts Office) and Financial Management

## **Appendix B**

### **List of Persons Interviewed**

## **Appendix B**

### **LIST OF PERSONS INTERVIEWED**

#### **CONRAD STAFF**

Anibal Acosta, Director, Fellowships and Andrology  
Nancy J. Alexander, Director, Applied Fundamental Researchy  
Cindy Anderson, Nurse Practitioner, Clinical Research  
Ted L. Anderson, Assistant Professor  
Lydia Antolin, Chief Accountant  
David Archer, Director, Clinical Research  
Rebecca Bacon, Clinical Research Associate  
Gregg Bloomquist, Administrator for Program Development  
Douglas Danforth, Assistant Professor  
David Fulgham, Project Officer, Applied Fundamental research  
Henry L. Gabelnick, Director, Extramural Research  
Sarah Gould, Administrator for the Director  
Gary D. Hodgen, Program Director  
Barbara Murphy, Administrator for Personnel and Physical Operations  
Barbara Ross, Clinical Research  
Robert Williams, Director, Intramural Core Laboratories

## **Appendix C**

### **List of Documents Consulted**

## Appendix C

### LIST OF DOCUMENTS CONSULTED

A.I.D./w/POP Management Review 4/29/87

Cooperative Agreement No. DPE-3044-A-00-6063-00, July 1986

CONRAD Financial Status Report July-Dec 1988

CONRAD Position Descriptions for Key Staff

CONRAD Staffing, CONRAD External Review, March 1989

Contraceptive Research and Development (CONRAD), April 1986, Request for Application (RFA) A.I.D. 1st/HP-6000,

Extramural Project Distribution 3/22/89

Extramural Project Selection and Management Procedure

Extramural Projects by Program Areas 3/20/89

Extramural Project Summary by Quarters 3/14/89

Guidelines for Submission of Research Proposals

Hodgen, Gary D., Overview of CONRAD Program: Midterm Evaluation Review

Interagency Agreement 1-Y01-HD-7-1229-00 between A.I.D., S&T and NIH, NICHD

Labor Distribution Report FY 1988

Medical College of Hampton Roads Foundation, Annual Report 1988

Minutes for TAC meetings

Research Task Force Group

Semi-Annual Report, April 1, 1988 to September 30, 1988

Status of Extramural Proposals 3/20/89

STS Agenda, Summary Note

STS Meetings -- Summary Notes

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**Appendix D**  
**Financial Tables**

Table A

INTRAMURAL SUBPROJECTS

	MON MORSE 8-P ★	MAN MORSE 7B ★	MAN MORSE 8-CP ★★	MAN MORSE 8-CP ★★	MAN ALEXANDER WEEKLY ★	MAN MORSE PROVISION ★	MAN MORSE ★	MAN MORSE ★	MAN MORSE ★	MAN MORSE ★	MAN MORSE ★	TOTAL 1974/75- 1975/76	EXTENDED	TOTAL
CORE LAB DISTRIBUTED TO OTHERS:														
6030-CELL & COLLECTOR			19,277.43			13,324.13						32,601.56	6,726.44	39,328.00
6040-ANV OPER												0.00		76,332.00
6130-ANV. MIB			37,500.00	31,400.00	9,000.00	21,300.00	20,500.00					120,000.00	31,400.00	151,000.00
6140-RIA	20,789.76		31,104.04	22,522.20	10,374.00		17,320.00	13,820.00				106,029.00	37,171.04	143,200.00
6170-VISBLE CULTURE			37,410.21		10,100.00		24,100.00	12,070.00				71,720.00	20,700.00	92,420.00
6180-103 CELL-ALEXANDER					1,707.20					1,707.20		1,707.20		1,707.20
SERIAL CORE DISTRICT	20,789.76	0.00	127,302.31	34,122.21	41,717.70	0.00	62,100.00	66,670.00	0.00	1,707.20		384,606.76	122,457.24	507,064.00
TOTAL ITEMS & CORE BEFORE STS & SUPPORT STAFF SAL. 75.00C	31,644.17	7,520.20	300,332.92	331,648.16	210,371.31	1,144.23	132,400.00	77,870.00	24,907.20	20,000.00		1,094,826.76		
STS & SUPPORT STAFF SALARIES														
MORSE	103.25	103.25	103.25	103.25	103.25	103.25	103.25	9,000.00	103.25	103.25	10,710.75	1,301.25	10,712.00	
ALEXANDER	622.43	622.43	622.43	622.43	10,000.00	622.43	622.43	622.43	622.43	2,112.25	26,120.30	26,112.70	42,212.00	
MORSE	17,819.52	12,170.24	300.00	300.00	300.00	1,000.00	300.00	300.00	300.00	300.00	63,023.12	12,200.00	75,223.00	
MORSE	307.53	307.53	9,000.00	13,775.30	307.53	307.53	3,075.00	307.53	1,112.00	307.53	25,222.00	21,500.00	46,722.00	
MORSE	106.25	106.25	106.25	106.25	106.25	106.25	6,000.00	106.25	106.25	106.25	7,000.10	2,112.70	9,112.80	
											0.00			
MORSE	600.00	600.00	700.00	600.00	600.00	600.00	600.00	600.00	600.00	600.00	6,120.00	1,072.00	7,192.00	
MORSE	1,104.00		7,300.76	7,300.00		4,212.00	1,000.00	2,000.00			20,717.04	1,370.50	22,087.54	
MORSE	2,011.02	2,011.02	2,321.00	2,321.00	2,011.02	2,011.02	2,011.02	2,011.02	2,011.02	2,011.02	21,379.36	1,020.04	22,400.00	
MORSE	531.20	531.00	531.00	531.00	531.00	531.00	531.00	531.00	531.00	531.00	6,000.00	6,000.00	9,100.00	
MORSE	234.00	234.00	234.00	234.00	234.00	234.00	234.00	234.00	234.00	234.00	2,370.00	1,020.17	3,390.17	
MORSE	4,576.00	4,576.00				4,722.00					12,022.00	800.00	12,822.00	
MORSE			300.00	300.00						100.00	700.00	700.00	1,000.00	
MORSE			32.00	32.00	32.00		32.00		32.00	32.00	100.00	0.00	142.00	
MORSE					16,000.00		1,320.00	1,320.00		1,320.00	22,120.00	4,200.00	26,320.00	
MORSE			6,507.00	9,502.00			1,000.00		1,107.00		20,300.00	800.00	21,100.00	
MORSE			2,022.00	2,022.00	811.00		1,200.00	400.00	811.00		6,120.00	0.00	6,120.00	
MORSE					9,900.00						12,500.00	1,700.00	14,200.00	
MORSE	7,322.00	7,322.00				1,667.00				2,520.00	10,507.00	9,072.50	19,579.50	
MORSE			1,024.00	1,110.00			1,024.00				3,600.00	0.00	4,624.00	
MORSE	1,000.00		2,520.00	2,520.00			1,000.00	1,000.00			10,000.00	500.00	10,500.00	
MORSE				25.00							25.00	0.00	25.00	
MORSE			70.00	70.00	70.00		70.00	70.00			700.00	0.00	770.00	
STAFF			822.00	616.00	616.00		616.00	616.00	616.00	616.00	6,100.00	0.00	6,100.00	
TOTAL STS & SUP STAFF SALARIES	28,309.90	20,262.34	36,315.69	44,777.19	50,042.10	22,044.30	28,077.73	19,394.63	13,379.33	10,970.50	290,703.07	122,037.02	412,740.09	
FRANKE BENEFITS (10%)	3,333.37	4,236.73	3,632.20	4,264.09	7,117.01	3,006.00	3,733.40	2,703.25	1,072.11	2,000.00	11,020.32			
INDIRECT COSTS (10%)	28,137.78	22,320.82	28,037.03	32,070.63	37,349.00	14,204.03	20,630.03	14,000.00	9,030.00	10,900.00	279,520.14			

\* Clinical Research  
\*\* These Projects are combined as one.

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**Table B**  
**EXTRAMURAL ASSIGNMENTS OF TECHNICAL MONITORS**  
**Number of Projects by Quarters**  
**And by Dollars (000)**

	Fiscal Year 1987				Fiscal Year 1988				FY 89		Totals
	1	2	3	4	1	2	3	4	1	2	
Acosta Dollars (0	0 0	0 0	1 43.7	1 36.6	2 119.3	0 0	0 0	1 120.2	1 39.6	2 78.1	8 437.5
Alexander Dollars	0 0	3 186.7	1 15	2 126.8	3 554.6	1 71.2	1 14.9	4 860	0 0	2 29.9	17 1859.1
Archer Dollars	1 36.5	0 0	1 14.7	0 0	1 207.6	0 0	0 0	0 0	1 15	0 0	4 273.8
Gablenick Dollars	0 0	0 0	1 55	0 0	3 254.4	0 0	4 53.3	0 0	0 0	0 0	8 389.3
Hodgen Dollars	2 315.1	0 0	0 0	1 216	1 131	0 0	0 0	1 15	0 0	0 0	5 677.1
No. Project Dollars	3 351.6	3 186.7	4 126.4	4 379.4	10 1266.9	1 71.3	5 74.8	6 995.2	2 54.6	4 108	42 3616.8

Summary by Monitor

<u>Monitors</u>	<u>Awards</u>	<u>Dollars</u>	<u>Percent</u>
Archer	4	273.8	7.6
Gablenick	8	359.3	10.2
Acosta	8	437.5	12.1
Hodgen	5	677.1	18.7
Alexander	<u>17</u>	<u>1859.1</u>	<u>51.4</u>
	42	3616.8	102.0

*(Handwritten mark)*

Table C

CONRAD Budget - Estimated Funding  
 Period: 10/01/86-09/30/91

Run date: 11/03/88  
 Filename: CONBUD

	Year 1	Year 2	Year 3	Year 4	Year 5	Total
	10/1/86- 9/30/87	10/1/87- 9/30/88	10/1/88- 9/30/89	10/1/89- 9/30/90	10/1/90- 9/30/91	10/1/86 9/30/89
<b>EXPENDITURES:</b>						
Salaries	645,000	362,900	1,027,428	1,078,799	1,132,739	4,746,867
Fringe	90,945	121,433	143,840	151,032	158,584	565,833
Indirect	474,075	624,361	917,160	858,018	226,386	3,000,000
Supplies	70,000	75,185	85,000	85,000	85,000	401,185
Rent & Maintenance	55,000	73,190	75,000	55,000	55,000	318,190
Capital Equipment	35,000	3,712	50,000	25,000	15,000	194,712
Office Furniture	36,500	23,681	10,000	7,500	5,000	92,681
Travel	80,000	85,000	100,000	105,000	110,250	480,250
Consultant Fees (w/TAC)	30,000	40,806	65,000	65,000	65,000	265,806
Workshops & Publications	0	116,028	150,000	150,000	150,000	566,028
Intramural Subgrants	215,000	440,994	700,000	735,000	771,750	2,862,744
Intramural Core Labs	40,000	258,825	350,000	367,500	385,875	1,402,200
Extramural Projects	1,143,480	1,282,857	2,050,600	2,017,151	1,409,416	7,903,504
CD:RI	270,000	30,000	0	0	0	300,000
<b>Total:</b>	<b>3,245,000</b>	<b>4,050,972</b>	<b>5,624,028</b>	<b>5,700,000</b>	<b>4,570,000</b>	<b>23,190,000</b>
<b>ALLOCATION OF INCOME:</b>						
AID/S&T/POP/R	1,375,000	3,273,572	3,901,428	4,500,000	3,500,000	18,150,000
CD:RI	270,000	30,000	0	0	0	300,000
AID/India	0	280,000	850,000	1,200,000	1,070,000	3,400,000
AID/NIH	0	467,400	872,600	0	0	1,340,000
<b>Total:</b>	<b>1,645,000</b>	<b>4,050,972</b>	<b>5,624,028</b>	<b>5,700,000</b>	<b>4,570,000</b>	<b>23,190,000</b>
<b>INCREMENTAL FUNDING:</b>						
	FY86	FY87	FY88	FY89*	FY90*	Total
AID/S&T/POP/R	4,750,000	3,000,000	3,900,000	3,000,000	3,500,000	18,150,000
CD:RI	0	300,000	0	0	0	300,000
AID/India	0	3,400,000	0	0	0	3,400,000
AID/NIH	0	240,000	1,100,000	0	0	1,340,000
<b>Total:</b>	<b>4,750,000</b>	<b>6,940,000</b>	<b>5,000,000</b>	<b>3,000,000</b>	<b>3,500,000</b>	<b>23,190,000</b>

\* Anticipated

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Table D

CONTRACTS - EXPIRATIONAL BUDGET

Run Date: 03/20/89

Contract Number	Program Area	P.I.	Dates	Year 1	Year 2	Year 3	Year 4	Year 5	Total
87-001	Immuno	Carron	01/01/87-06/30/87	32,317					32,317
87-002	Immuno	Goldberg	01/01/87-02/29/88	81,444	8,406				90,852
87-003	Immuno	Tung	01/01/87-12/31/87	58,509					58,509
87-004	Steril	Meeker	10/01/86-09/30/87	36,460					36,460
87-005	Steril	Meeker	04/01/87-08/31/89	14,735	550				15,285
87-006	Gonad	Bardin	10/01/86-04/30/87	275,140					275,140
87-007	Steril	Zaneveld (SHUG)	04/01/87-03/31/89	17,829	25,874				43,703
87-008	Gonad	Cheng	10/01/86-02/28/87	40,000					40,000
87-009	Immuno	Lee	08/01/87-07/31/88	33,275	38,290	40,207			111,772
87-010	Immuno	Anderson	05/01/87-02/29/89	15,000					15,000
87-011	Barrier	Zaneveld (AGB)	06/01/87-05/31/88	41,828	13,181				55,009
87-012	Immuno	Harper	07/01/87-12/31/87	14,993					14,993
87-013	LHRH	Pavlou	07/01/87-06/30/89	99,034	116,862				215,996
87-014	Steril	deCastro	09/01/87-05/31/89	36,556					36,556
87-015	Steril	Derrick	10/01/87-09/30/88	12,625					12,625
87-016	Gonad	Pomerantz	10/01/87-03/31/89	131,023					131,023
87-017	Barrier	Kendall	10/01/87-09/30/89	207,565					207,565
88-018	Immuno	Dunbar	10/15/87-10/14/88		49,641	125,000	150,000		324,641
88-019	HIV	Marx	12/01/87-11/30/89		88,981	135,586			224,567
88-020	HIV	Anderson	12/01/87-11/30/89		128,388	121,856	125,000	125,000	500,244
88-021	DDS	Lewis	12/15/87-12/15/88		106,814				106,814
88-022	DDS	Lewis	12/15/87-07/01/88		67,554				67,554
88-023	DDS	Lewis	12/15/87-07/01/88		80,000				80,000
88-024	Male	Paulsen	12/01/87-12/31/89		45,892	46,501	14,233		106,626
88-026	Immuno	Aitken	02/01/88-08-01/89		71,208				71,208
88-027	DDS	Yesair	04/01/88-12/30/88		15,000				15,000
88-028	Barrier	Cone	04/01/88-06/30/88		15,000				15,000
88-029	HIV	Bernstein	05/01/88-04/30/89		14,938				14,938
88-030	Barrier	Voeller	05/01/88-10/31/88		14,999				14,999
88-031	Barrier	Voeller	05/01/88-10/31/88		14,867				14,867
88-032	Gonad	Soules	04/01/88-12/31/88		15,000				15,000
88-033	Immuno	Blaquier	07/01/88-01/31/89		15,000				15,000
88-034	HIV	Resnick	08/01/88-07/31/91		75,396	78,411	81,549		235,356
88-035	Barrier	Chantler	08/01/88-07/31/90		46,746	50,114			96,860
88-036	Barrier	Cone	08/01/88-07/31/90		120,010	198,872			318,882
88-037	HIV	Phillips	08/01/88-07/31/91		93,158	96,884	100,759		290,801
89-038	Basic	Rogers	11/01/88-04/30/89			14,982			14,982
89-039	DDS	Bhasin	11/01/88-07/31/89			39,601			39,601
89-040	Immuno	DeIoannes	01/01/89-12/31/89			14,580			14,580
89-041	Immuno	Brown	01/01/89-12/31/89			15,000			15,000
89-042	Male	El-Rashidy	02/01/89-01/31/90			63,174			63,174
89-043	Basic	Meizel	02/01/89-01/31/90			14,994			14,994
89-044	Basic	Lingwood	02/01/89-01/31/90			14,999			14,999
Subtotal:				1,148,333	1,282,857	1,070,761	471,541	125,000	4,098,492
Pending:	Immuno	Tesarik				15,000			15,000
	Immuno	Brown				30,000			30,000
	HIV	Isahakia				140,000	150,000	150,000	440,000
	Androgen	Bhasin				100,000	100,000	100,000	300,000
Subtotal:				0	0	285,000	250,000	250,000	785,000
Total committed/pending:				1,148,333	1,282,857	1,355,761	721,541	375,000	4,883,492

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CONRAD EXTRABUDGET

Run Date: 03/20/89

Planned Solicitations

Program Area	Topic	Year 1	Year 2	Year 3	Year 4	Year 5	Total
AIDS	Animal Model			100,000	200,000	200,000	500,000
AIDS	Mechanisms			100,000	100,000	100,000	300,000
Barrier	Spermicides/Barrier			100,000	300,000	300,000	700,000
Barrier	ASB Clinical Studies			100,000	125,000	250,000	475,000
Immuno	FSH - Male			0	0	100,000	100,000
Immuno	New Antigens			100,000	150,000	150,000	400,000
DDS	NET-30 Microspheres: Clinic			50,000	100,000	100,000	250,000
DDS	Prog. Microspheres: Clinic			50,000	100,000	150,000	300,000
DDS	Test. Microspheres: Clinic			50,000	150,000	150,000	350,000
DDS	Estrogen Microspheres			50,000	100,000	100,000	250,000
DDS	ST-1435 Microspheres			100,000	150,000	150,000	400,000
DDS	Vaccine Delivery System			100,000	150,000	150,000	400,000
Male	Clinical Studies (LHRH Antag)			0	150,000	150,000	300,000
Steril	Male Sterilization			100,000	150,000	150,000	400,000
Steril	Female Sterilization			0	100,000	150,000	250,000
<b>Subtotal:</b>				<b>1,000,000</b>	<b>2,025,000</b>	<b>2,350,000</b>	<b>5,375,000</b>
Reserve for new leads and unsolicited proposals:				0	0	0	0
<b>Grand Total:</b>		<b>1,148,333</b>	<b>1,282,857</b>	<b>2,355,761</b>	<b>2,746,541</b>	<b>2,725,000</b>	<b>10,258,492</b>
<b>Funds Available:</b>		<b>1,148,333</b>	<b>1,282,857</b>	<b>2,050,600</b>	<b>2,017,151</b>	<b>1,409,416</b>	<b>7,908,357</b>
<b>Surplus (deficit):</b>		<b>0</b>	<b>0</b>	<b>(305,161)</b>	<b>(729,390)</b>	<b>(1,315,584)</b>	<b>(2,350,135)</b>

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## **Appendix E**

**New Clinical Studies Expected between  
April 1, 1989 and April 1, 1990**

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## Appendix E

### New Clinical Studies Expected between April 1, 1989 and April 1, 1990

Future CONRAD supported studies anticipated beginning within the next 12 months include:

<u>Study</u>	<u>Phase</u>
1. Progesterone Microcapsule	I
2. Norethindrone 90 Day Injectable Plus Estrogen	I
3. Oral Progesterone	I
4. Oral Testosterone	I
5. Norethindrone Metabolite Identification	I
6. Acetaminophen 4- Guanidinobenzoate	I
7. Antiprogestins to Block Ovulation	I
8. GnRH Antagonist in Women and Men	I
9. Norethindrone 30 Day Injectable	I
10. VSB	II

Future FHI supported studies anticipated beginning within  
the next 12 months include:

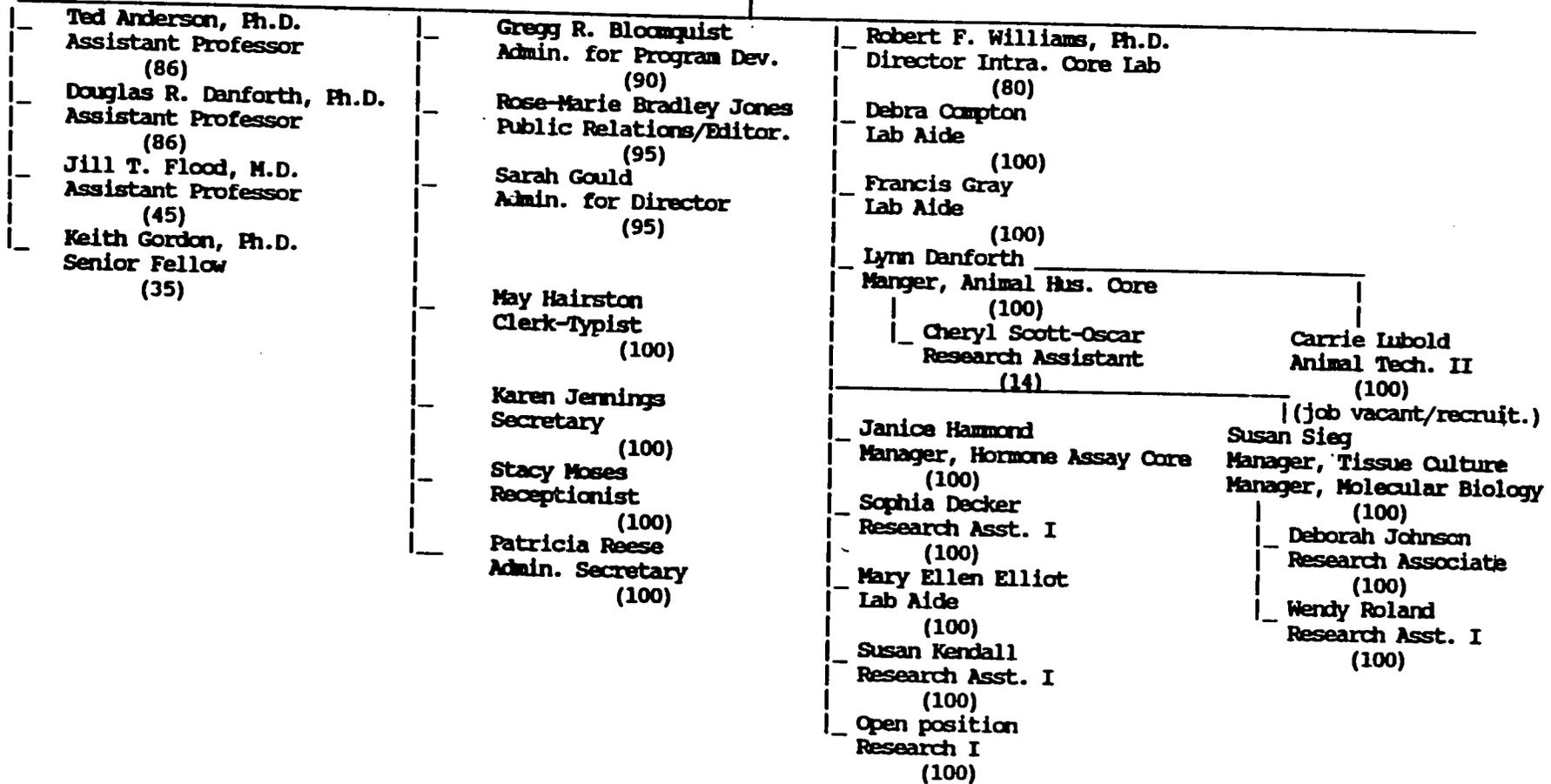
<u>Study</u>	<u>Phase</u>
1. Norethindrone Pellet	III

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**Appendix F**  
**Organization Charts**

CONRAD Program  
March 1989

Gary D. Hodgen, Ph.D.  
Program Director  
(90)



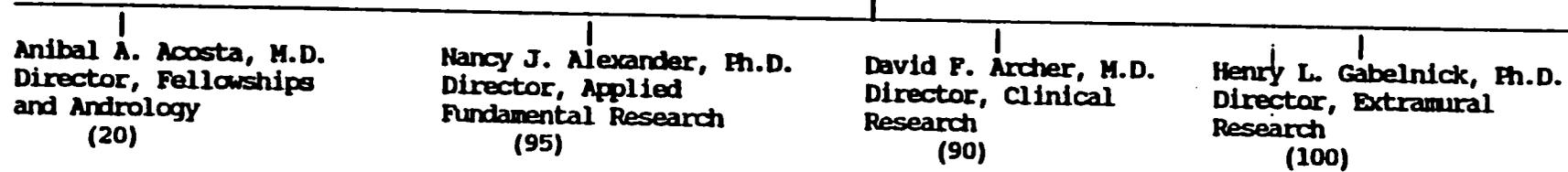
Organization Charts

Appendix F

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CONRAD Program Senior Technical Staff  
March 1989

Gary D. Hodgen, Ph.D.  
Program Director  
(90)



Numbers in parenthesis are % of full-time effort on CONRAD Program.

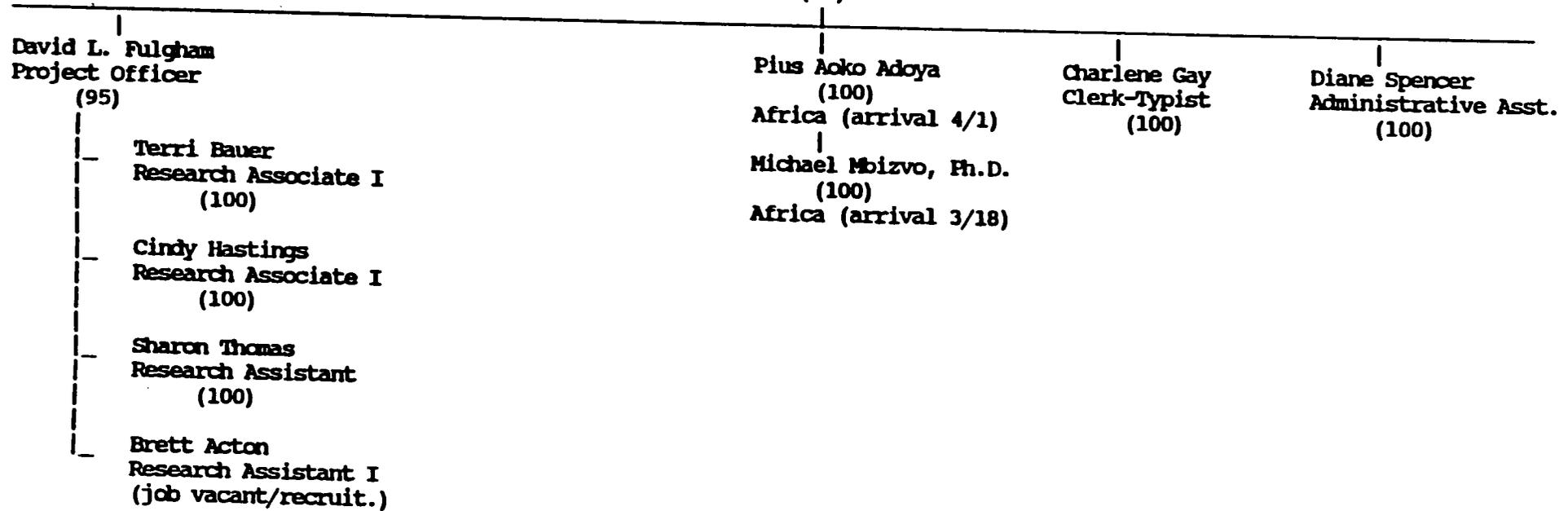
These flowcharts reflect employees receiving full or partial salary from CONRAD.

Other employees not salaried through CONRAD funds are not listed.

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CONRAD Applied Fundamental Research  
March 1989

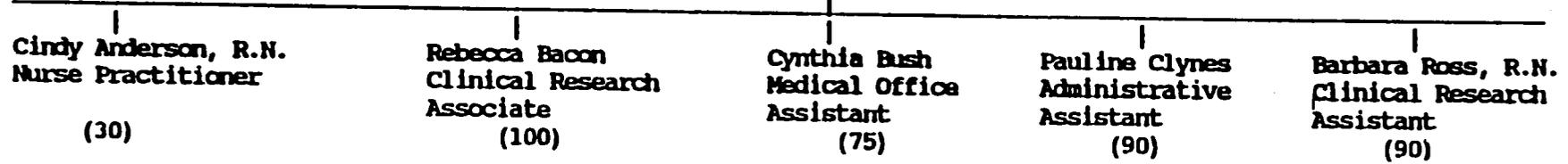
Nancy J. Alexander, Ph.D.  
Director  
(95)



Numbers in parenthesis are % of full-time effort on CONRAD Program

CONRAD Clinical Research  
March 1989

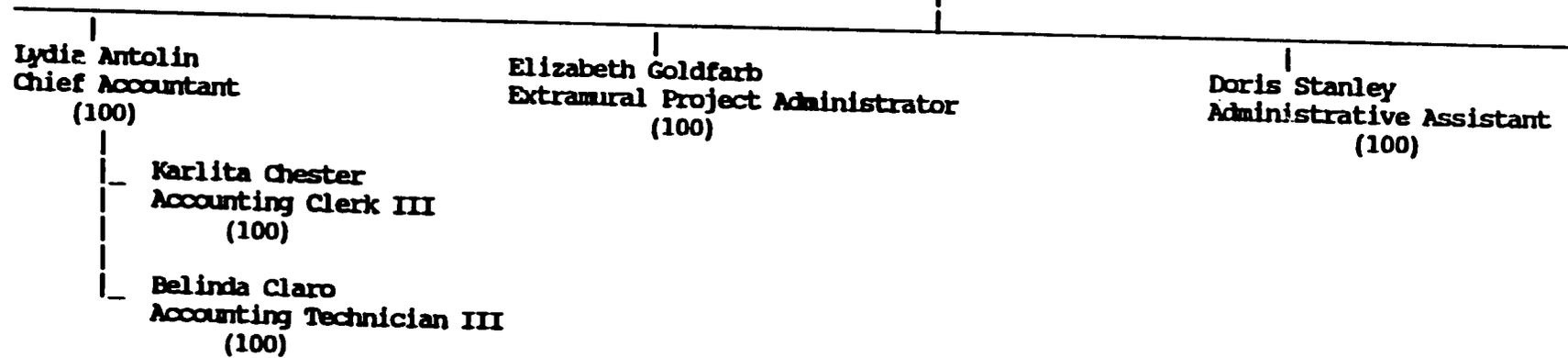
David F. Archer, M.D.  
Director  
(90)



Numbers in parenthesis are % of full-time effort on CONRAD Program

CONRAD Extramural Research  
March 1989

Henry L. Gabelnick, Ph.D.  
Director  
(100)



CONRAD Fellowships and Andrology  
March 1989

Anibal A. Acosta, M.D.  
Director  
(20)

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Brenda Clayton  
Secretary to the Director  
(19)

Numbers in parenthesis are % of full-time effort on CONRAD Program

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## **Appendix G**

### **CONRAD Labor Distribution Form**

APPENDIX G

CONRAD LABOR DISTRIBUTION

EMPLOYEE NUMBER: 00995

NAME: LYDIA T. ANTOLIN

ASSIGNED  
DIV./DEPT.

R 12

PERIOD ENDING:

DAY	DATE	TOTAL HOURS	C O N R A D					OTHER	VACATION	SICK LEAVE
			INTRA- MURAL	EXTRA- MURAL	CD:RI	INDIA BUY-IN	AIDS			
S										
S										
M										
T										
W										
T										
F										
TOTAL HOURS										

TOTAL CONRAD HOURS

PERCENTAGE OF TIME WORKED FOR CONRAD

EMPLOYEE SIGNATURE

DATE

SUPERVISOR SIGNATURE

DATE

\_\_\_\_\_

I CERTIFY THE HOURS WORKED ABOVE ARE CORRECT.

**Appendix H**  
**Recommendations**

## Appendix H

### RECOMMENDATIONS

1. Continued support should be provided to the following subprojects: GnRH antagonist, reproductive immunology, FSH suppression in male primates (although very little progress has been made to date), and the GnSIF component of the inhibin/GnSIF subproject.
2. **The level of resources allocated to intramural subprojects should be reevaluated. One suggestion is that the inhibin subproject might be contracted out as an extramural activity.<sup>1</sup> Another alternative might be to phase out this area of research entirely in view of the existence elsewhere of this line of research.**
3. Pilot research studies, such as those to purify and characterize bioactive molecular proteins, which are carried out in the core laboratories, should be treated as separate subprojects; budgets for each should be developed and approved in accordance with the procedure for all intramural subprojects. This would involve submitting each subproject to the CTO, in accordance with the terms of the Cooperative Agreement.
4. **An in-depth review should be undertaken to establish the real costs as well as the staffing levels necessary to operate the core labs and the intramural research subprojects. Such a review should help inform the program decision-makers as to which of these in-house activities are cost-effective and deserve continued support and which are less cost-effective and might be abandoned.**
5. Consideration should be given to centralizing the administrative aspect of the core labs under CONRAD's central administration.
6. **The Clinical Division staff and extramural program staff should increase its efforts to solicit extramural project that are at Phase I or Phase II trial stage. Two suggestions on how to proceed are:**
  - **CONRAD may wish to utilize consultants to encourage the submission or development of proposals.** For instance, the private sector frequently employs individuals who are responsible for product licensing; scientists are utilized to evaluate proposals presented by the Product Licensing Team. A similar approach could be taken by CONRAD, with the Clinical Division evaluating proposals from a clinical standpoint concerning their merit for study.
  - **The Technical Advisory Committee (TAC, See Section 2.3) has clinicians with expertise in contraceptive clinical research who could be utilized effectively to bring in new proposals.** This would require increased contacts with appropriate TAC committee members. A subcommittee of TAC might be an appropriate mechanism (see also Recommendation 19).
7. Time line or Program Evaluation Review Technique (PERT) charts of planned clinical trials should be drawn up to allow for the appropriate staffing level for each trial. These should be developed as the basis of the careful evaluation of protocols and realistic identification of tasks to be performed with each trial.
8. Physician involvement in clinical trials should be increased, including trials of non-invasive methods.
9. Efforts directed toward LDC clinical centers should focus on development of relationships with clinical centers at which appropriate clinical trials may be performed. As such centers are enlisted, they should be encouraged, when possible, to adhere to common protocols, case record forms and

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<sup>1</sup>Recommendation or parts of recommendations in bold face are considered major recommendations.



- should be monitored appropriately by CONRAD personnel to attempt to obtain data for FDA approval and in as many countries as feasible.
10. Efforts to establish any new LDC centers should be discouraged. The program should utilize already existing LDC centers of excellence, and should collaborate with other agencies that have supported the development of such centers.
  11. CONRAD should develop a roster of potential clinical investigators within the United States and abroad and communicate with such people frequently.
  12. Clinical protocols and collaborating centers should be developed now for the Phase I and II studies anticipated to begin within the next 12 months.
  13. **Efforts need to be increased to solicit extramural proposals, particularly those that are near-term.**
  14. The mechanism of solicitation of proposals needs to be strengthened and to be more proactive. The following means are suggested.
    - All of the STS need to be more actively involved in the process.
    - The extramural program (Rosslyn office) would benefit if the Project Administrator were replaced with a technical person (rather than another administrator). This would free the Extramural Program Director to do more active solicitation of proposals.
    - The TAC as a committee and as individual members could also play a more active role. Consultants might also be enlisted to assist with solicitation (see also Recommendation 19).
  15. The process of technical project monitoring, including site visits, could be strengthened by more inputs from the STS, utilization of the services of TAC members, and recruitment of consultants as necessary.
  16. In future appointments to TAC, an active effort should be made to include among members with the required experience, more women and members with developing country experience.
  17. Consideration should be given either to increasing the duration of the TAC meetings or to supplementing the meetings with smaller group meetings (with other members coopted as needed for the subject) to allow the Committee to address more effectively its other functions related to establishment of priorities, development of research strategies, and particularly for development of such projects for which proposals can be solicited.
  18. More attention should be devoted to soliciting projects from LDC investigators and otherwise to increasing the contribution of developing country scientists and institutions.
  19. **CONRAD management and A.I.D. should reexamine the portfolio of intramural and extramural subprojects in light of their objectives for near-term versus longer-term payoffs. It may not be either appropriate or possible to achieve the 2-1 ratio (extramural, two-thirds and intramural, one third) set forth in the Project Agreement, but efforts are clearly needed to increase the level of extramural funding, and clinical trials of near- and medium-term needs. At the same time, it is important to ensure that intramural spending does not encroach on funding for extramural subprojects.**
  20. **A thorough review is needed of the proper staffing level for intramural projects that takes into consideration the program levels desired, the funds available, the cost-effectiveness of the core labs and the productivity and morale of the staff.**

21. Opportunities for collaboration with other agencies should continue to be explored and exploited, particularly in areas that might be relevant to the extramural and clinical research programs. Possibilities might include 1) collaborating with agencies such as WHO for joint funding of projects of mutual interest; 2) participating in multicenter clinical trials sponsored by other collaborating agencies on leads of mutual interest, and 3) supporting studies in the networks of clinical research centers in developing countries that collaborate with other international agencies.
22. The workshop mechanism should be utilized to a greater degree for the generation and solicitation of research projects. This could be accomplished if the number of participants were limited and more focus given to soliciting proposals from included potential investigators. In addition, when proceedings of international workshops are distributed, a brochure about CONRAD should be included together with an invitation to submit research proposals in the area of the topic of the workshop or other areas as described in the brochure.
23. The need to convene an annual international workshop should be abandoned if it is directly interfering with progress in other program areas.
24. The Communique should continue as a medium for dissemination of information.
25. All publications acknowledging CONRAD support should be cleared with the CTO before publication in accordance with A.I.D. regulations.
26. The management of CONRAD should be reformulated with special attention to ways in which the Director can be assisted in discharging his functions. The vacant position of Director of Administration should be filled by an individual versed in administration and financial planning. The position would involve overseeing the financial functions of accounting, fiscal control, cash flow projections and budgeting. It would be advisable to move the financial management function from Rosslyn to Norfolk and to assign it to the Director of Administration in conjunction with supervision of the accounting, fiscal control and program tracking systems. This will be particularly important if the budgeting and reporting systems are to be integrated into program and subproject management system (see Recommendations 33 and 38).
27. A subproject and program management system should be developed that groups efforts and roles around objectives. Each unit needs to be organized to permit inputs by staff from various areas according to the desired end result.
28. If recommended efforts to expand the extramural program are implemented (e.g., through shifting some of the workload to other STS and use of consultants--see Recommendations 13 and 14), different forms of coordination between Rosslyn and Norfolk staff may need to be tried.
29. The management reformulation should proceed in close coordination with the other system changes recommended, particularly the planning and financial management changes (see Recommendations 33 and 35). Team building and supervisory development should be part of the process to assist in reducing frictions and integrating staff efforts.
30. The Program Director should continue the practice of determining the relevance of activities to overall CONRAD goals and establishing some mechanism for comparing desired time allocation with actual time spent. The preliminary list developed is one method that could be used. If there were consensus on such a list, various staff members could periodically keep their own record--perhaps for a week or two--and then compare actual time spent with desired allocation. When this is done with a supervisor, it can serve as a planning tool in rearranging priorities. It is important that any

such time supervision should be done with due deference to professional independence while seeking a balance between personal preferences and program needs.

31. **The present labor distribution report should be revised to show each of the intramural subprojects. This would help determine where most of the effort is going and also help the Accounting Unit in its cost analysis. It should be utilized by STS and the Program Director for determining how best to use staff time. Periodic sample reviews should be made of the accuracy of the report and employees oriented on the purpose and use to be made of the instrument. This change would appear feasible from the perspective of the Accounting Unit.**
32. **A.I.D. and the CONRAD staff should jointly develop progress indicators, based on the Cooperative Agreement. These should be used for periodic score-keeping and appraisal of the progress to be followed by corrective action, if necessary. Staff should also periodically review the indicators themselves and revise them, if appropriate. In addition, A.I.D. and CONRAD should develop, if possible, some targets to be used in the periodic workplan reviews and approvals.**
33. **Management assistance should be provided to CONRAD (and A.I.D.) in formulating a program planning process that links objective setting, strategy formulation, workplans, budgeting and reporting into a coherent system that facilitates carrying out the responsibilities of each party. The development of the planning system requires the involvement of both parties so that the process is understood, accepted and utilized by the key A.I.D. and CONRAD personnel carrying out the Cooperative Agreement.**
34. **CONRAD should review and revise its subproject management procedures to link with the overall program planning described in Recommendations 28, 30, and 31. The review should encompass all aspects of the extramural and intramural programs, the need for technical direction, financial planning and control, and the possibilities of adopting a management method that would help reduce the workload on senior staff.**
35. **Financial reports and budgets should reflect costs by program and by cost categories. The formats for these management instruments should be developed with professional assistance in close coordination with the senior staff of CONRAD and the A.I.D. CTO to assist in management decisions. In turn, the budget and financial reports should be an integral part of the program planning system (see Recommendation 33).**

The format for a program budget could vary somewhat from that shown in Table 8. For example, the cost for activities such as workshops and conferences could be shown as a separate program element. Likewise, the central management of CONRAD could be shown as a separate element, although it would be preferable if it were divided among other program areas, particularly extramural and intramural.

In addition to changes in format, financial reporting along program lines should be made to the CTO quarterly and incorporated into the semi-annual plans. The exact structure of the program budget should be carefully designed to assist management to track and decide on key aspects such as the amount of investment in central and supporting staff, the balance of intra- and extramural programs, and the relative cost-effectiveness of investment in the balance of the two program areas.

36. **A detailed study is needed to examine whether intramural subproject costs could be reduced further without harming quality or the current level of subprojects. This study could also determine what balance of investment in the two kinds of portfolios would best advance the objectives of the program as a whole (see also Recommendation 19).**

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37. **Budgets and financial reports should deal separately with obligations and expenditures and project these separately. It may also be necessary to clarify with A.I.D. the concepts and definitions of obligations, commitments and encumbrances.**
38. **The current budgeting and reporting systems at the subproject level should be integrated to facilitate management. Consideration should be given to developing a tracking system that integrates substantive progress measures with resource utilization (personnel and funds) along with a variance analysis method (departure from expected levels of resource use) that will permit management to focus upon the departures from expected progress.**

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