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**MIDTERM EVALUATION OF
CONTRACEPTIVE DEVELOPMENT AND
RESEARCH IN IMMUNOLOGY PROJECT
(CD&RI)
(USAID/INDIA PROJECT 386-0500)**

by

John B. Tomaro
Laneta Dorflinger
Lakshmi Kumari
Somnath Roy

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Population Technical Assistance Project
DUAL & Associates, Inc. and International Science
and Technology Institute, Inc.
1601 North Kent Street, Suite 1014
Arlington, Virginia 22209
Phone: (703) 243-8666
Telex: 271837 ISTI UR
FAX: (703) 358-9271

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Glossary

CD&RI	Contraceptive Development and Research in Immunology (project)
CD:RI	Contraceptive Development: Reproductive Immunology (project)
CONRAD	Contraceptive Research and Development Program
CDRI	Central Drug Research Institute
DBT	Department of Biotechnology
MST	Ministry of Science and Technology
FPCM	Family Planning Communications and Marketing (project)
GOI	Government of India
HHS	U.S. Department of Health and Human Services
IIS	Indian Institute of Science
IPR	Intellectual Property Rights
JWG	Joint Working Group
MHFW	Ministry of Health and Family Welfare
NIAID	National Institute of Allergies and Infectious Diseases
NICHD	National Institute of Child Health and Human Development
NII	National Institute of Immunology
OIH	Office of International Health
PACD	Project Assistance Completion Date
PARFR	Program for Applied Research in Fertility Regulation
PASA	Participating Agency Services Agreement
PGIMER	Post Graduate Institute of Medical Education and Research
R&D	research and development
SOW	scope of work
TAC	Technical and Scientific Advisory Committee

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Summary

Project Purpose. The Contraceptive Development and Research in Immunology Project (CD&RI) was authorized in 1988 as a three-year continuation and expansion of the Contraceptive Development: Reproductive Immunology (CD:RI), initiated in 1985. The CD&RI Project was designed to support Indo-U.S. collaborative research project in contraceptive development and disease-related immunology at participating Indian institutions (four to six), and to finance Young Investigators Awards (including Re-entry and Re-visitation Grants), Science Management Training Awards, and Core Support Awards.

Evaluation Purpose and Methodology. The three-week midterm evaluation was conducted in late June and early July 1991 to assess the current status of the project and to explore implications for the future. The four-person team reviewed pertinent documents, interviewed researchers and administrators as well as USAID and Government of India (GOI) personnel, and visited three of the four participating Indian institutions.

Findings. The evaluation found that (1) six of the eleven collaborative research proposals submitted by investigators from the four participating institutes had been jointly approved and funded, (2) seven new collaborative research relationships had been established, (3) eight research fellowships had been awarded and three fellows had traveled to the U.S., (4) one participating institute, National Institute of Immunology (NII), had procured scientific equipment, and (5) several scientific publications had been prepared.

The evaluation noted that (1) the collaborative research projects submitted for funding were conceptually very good and scientifically significant, (2) the researchers involved in the CD&RI Project were qualified and motivated and were carrying out the proposed research, and (3) the four participating Indian research institutes had good infrastructure and research capabilities.

Perceptions of the purpose of the CD&RI project were not different, since both USAID and GOI want to have collaborative links established and the research groups strengthened. The differences are mainly due to the way these are implemented. There was, for example, a fundamental difference of opinion on the definition of a "research center." The team also found that the U.S. and Indian secretariates may have inadequately communicated to participating institutions the decisions of the Joint Working Group (JWG). This delayed the development of the center plans and research proposals and affected the quality of what was submitted.

The project has had major implementation problems. A number of activities took a long time to complete: (1) defining the structure for managing the day-to-day activities of the project; (2) submitting center plans and grants; (3) peer reviewing the collaborative research proposals, especially in immunology, and (4) executing the Participating Agency Services Agreement (PASA) with the Office of International Health/National Institute of Allergies and Infectious Diseases (OIH/NIAID). Others remain obstacles to implementation: (1) the definition of intellectual property rights (IPR); (2) the procurement of U.S. scientific equipment; (3) the transfer of funds to the GOI by USAID/India. These difficulties have significantly delayed the initiation and completion of the activities proposed under the project. Three years after project launch, Indo-U.S. collaborative research is just beginning.

For unclear reasons, the CD&RI Secretariat did not systematically implement the instructions of the JWG and give the project continuous, focused attention at critical points. It took a less than active role in promoting the project among the participating Indian institutions and expeditiously addressing critical managerial and procedural issues. The JWG gave explicit instructions but did not designate the party responsible for implementing the instructions.

Recommendations. It is recommended that

(1) the project coordinators from USAID/India and the Department of Biotechnology (DBT) meet to develop in written form a draft of the management procedures and communication strategies applicable to the implementation of the CD&RI Project, prior to the next meeting of the JWG. The draft of this document should be widely circulated among those involved in the project and approved at the next JWG meeting, scheduled for November 1991.

(2) the JWG meet at least annually during the remaining period of the project.

(3) the project be given a no-cost extension; September 30, 1994, is proposed as the new project assistance completion date (PACD). In the time remaining, however, no new collaborative research proposals should be entertained.

(4) two of the outstanding implementation issues -- procurement of U.S. scientific equipment and the transfer of U.S. funds to the GOI -- be discussed and resolved at a workshop that should take place within 60 days of the completion of the evaluation.

(5) unless language on intellectual property rights that is mutually agreeable to the U.S. and the GOI can be developed prior to the next JWG Meeting, the Central Drug Research Institute (CDRI) (Lucknow) collaborative research proposal should be dropped and the funds re-allocated among the other participating institutes.

Lessons Learned. Significant lessons have been learned in the course of implementing the CD&RI Project.

(1) A program design that has dual scientific foci (in CD&RI, contraception and disease-related immunology) complicates the management structure, divides scarce resources and reduces the prospects for achieving significant results in either area.

(2) Project designs should be consistent with the time frame of the project and the funds available.

(3) When multiple agencies are involved in project implementation, e.g., USAID/India, DBT, A.I.D. Contraceptive Research and Development (CONRAD) Program, NIAID, the National Institute of Child Health and Human Development (NICHD), etc., the roles and responsibilities of each must be clearly defined and systems for communicating information and coordinating activities must be fully elaborated and closely followed.

(4) Projects sponsoring collaborative research require that procedures and timelines for peer review, approval and funding should be defined at the start of the project and strictly followed.

(5) Access to a flexible, centrally funded project like CONRAD provides a bilateral project with the assistance required to facilitate implementation and enhance project impact.

(6) If intellectual property rights issues cannot be resolved satisfactorily during the definition of a project, USAID must re-think the focus of collaborative applied research projects. Instead, these projects might focus on training young investigators and strengthening the research capabilities of selected institutions throughout the course of implementation.

1. Midterm Evaluation: Purpose, Team Composition, and Evaluation Methodology

1.1 Purpose

The purpose of the midterm evaluation of the Contraceptive Development and Research in Immunology Project (CD&RI - Project 386-0500) was two-fold: "first to assess the current status of the project and second to explore implications for the future."

Specifically, the purposes [were] (a) to assess progress towards achievement of project purpose and identify project achievements to date; (b) examine project implementation to identify mid-course corrections and critical areas where additional inputs are required over the next two years; (c) review the project within the context of current priorities and interests of A.I.D. and the Government of India (GOI) and suggest appropriate revisions in project orientation/purpose, strategies, tasks and time frames; (d) suggest the form in which activities initiated under this project should continue beyond its PACD to ensure the sustainability of the program as a whole (Appendix A - Scope of Work).

The evaluation was conducted in accordance with the Scope of Work (SOW). In addition, USAID/India asked the team (1) to suggest the options available to USAID/India for future collaborative Indo-U.S. scientific research and (2) to identify problems and obstacles to project implementation.

1.2 Composition of the Evaluation Team and Evaluation Methodology

A four-person team conducted the midterm evaluation of the CD&RI Project. The team was composed of Dr. John B. Tomaro (team leader) of the Office of Health (A.I.D./Washington), Dr. Lakshmi Kumari of the National Institute of Health and Family Welfare (Delhi), Dr. Somnath Roy of the Family Planning Foundation of India (Delhi), and Dr. Laneta Dorflinger, former biomedical scientist in the Office of Population (A.I.D./Washington).

Drs. Dorflinger and Tomaro initiated evaluation activities in the United States in June 1991. Project documents were reviewed and persons from A.I.D./Washington, the Contraceptive Research and Development (CONRAD) Program, OID/NIAID and NICHD familiar with and involved in the project were interviewed. The full evaluation team was assembled and field work began in India on June 23, 1991.

In India the team visited the National Institute of Immunology (NII) in Delhi, the Indian Institute of Science (IIS) in Bangalore, and the Central Drug Research Institute (CDRI) in Lucknow -- three of the four institutes involved in the CD&RI Project. Since it was not possible to visit Chandigarh, researchers from the Post Graduate Institute of Medical Education and Research (PGIMER) involved in the project traveled to Delhi to meet with the team (Appendix B - Locations of Indian Institutions Participating in the CD&RI Project).

At each Indian institution the team reviewed project files and visited the laboratories and facilities of researchers involved in the project. The team also interviewed researchers, fellows and administrators responsible for conducting research or supporting the research and institution-strengthening endeavors financed under the project. USAID/India and DBT staff were also interviewed (Appendix C - Persons Interviewed).

A draft of the evaluation report was submitted to USAID/India on July 10, 1991, before the U.S. team members left India.

2. Project Background and Status to Date

2. Project Background and Status to Date

2.1 History of the Contraceptive Development and Research in Immunology Project¹

In FY 1983 the USAID/India-financed Family Planning Communications and Marketing Project (FPCM) approved a US \$1 million component (\$900,000 of population funds and \$100,000 of health funds) to support biomedical research on reproductive immunology. The Government of India endorsed this program but, for administrative reasons, asked USAID/India to implement this activity as a separate project. While the FPCM Project was under the jurisdiction of the Ministry of Health and Family Welfare (MHFW), the Department of Biotechnology (DBT) under the Ministry of Science and Technology took over the responsibility of CD:RI project.

The funds available through the project were to enable India to continue the search for and development of better and more appropriate methods for regulating fertility. Resources were to cover the costs incurred in the U.S. for equipment, materials, workshops, and studies. As proposed, the project was to investigate "immunological approaches to human fertility regulation . . . [and to involve collaboration between] leading Indian and U.S. institutions based on the mutual interests of Indian and U.S. institutions and of individual scientists, particularly in the field of immunology of reproduction." An Indo-U.S. task force was to be convened to focus and manage activities involving investigators from five Indian and U.S. research centers working in five subject areas.

This project, the Contraceptive Development: Reproductive Immunology Project (CD:RI), was initially designed to involve several different Indian and U.S. institutions. The Limited Scope Grant Agreement, which authorized the project and was signed on June 26, 1985, only mentions the National Institute of Immunology in Delhi.² In addition, the agreement stipulated that U.S. funds (\$1 million) would be "used [to obtain] the services of the Program for Applied Research in Fertility Regulation (PARFR), . . . under the direction of the coordinators of the Indian and U.S. Technical and Scientific Advisory Committees (TSACs)."

The Program for Applied Research in Fertility Regulation (PARFR), a centrally financed and managed project supported by the Office of Population (A.I.D./Washington), received the funds authorized under the agreement and was instructed inter alia to

- arrange visits of Indian scientists to the United States and of U.S. scientists to India as identified by the coordinators of the TSACs,
- procure and supply laboratory equipment and supplies for the National Institute of Immunology, and

¹Contraceptive Development: Reproductive Immunology - Project Paper, USAID/India, March 1985.

²The agreement noted that "other institutions could also be used, with the mutual agreement of the parties." No additional Indian institutions were added during the course of the project. See Limited Scope Grant Agreement, p. 1.

- arrange for training, workshops and seminars in the United States.³

The CD:RI Project explicitly prohibited funding individual laboratory projects in the U.S. and India.

The CD:RI Project (PACD - May 31, 1988) was evaluated in February 1988. The project was found to have

- purchased supplies and equipment for NII, largely through the swift and effective action of PARFR, and
- facilitated short-term (two- to seven-month) scientific exchanges/training of eight NII investigators, a one-year sabbatical visit to nine laboratories in the U.S., management training of the NII administrator in the U.S., two Indo-U.S. workshops, and the publication of numerous scientific articles.

The evaluation also identified significant management and implementation problems. "Implementation on the Indian side of the project was limited to only one institution . . . project funds were not sufficient, [and] the Project Agreement [was not] flexible enough to support sufficiently the U.S. side of the collaborative research efforts."⁴

2.2 Purpose of the CD&RI Project

As a result of the evaluation of CD:RI, the project content was amended, USAID/India was authorized an additional \$2.2 million, and participating institutions were given authority to work in "all areas of contraceptive development consistent with the U.S. Foreign Assistance Act and in disease-related immunology." The title of the project was amended from Contraceptive Development: Reproductive Immunology (CD:RI) to Contraceptive Development and Research in Immunology (CD&RI).

Despite the evaluation finding that CD:RI had been underfunded, the new project had a far more ambitious design than its predecessor, yet it was funded at just over twice the level of the earlier effort. The new design called for involvement with four to six institutions, compared with only one in CD:RI. It also called for work in two distinctly different research areas. As before, the project life was to be three years.

A project logframe was not developed when the CD:RI Project was amended in July 1988. At inception, the purpose of the project had not been clearly defined. During the course of project implementation, the project purpose has evolved as follows:

- A draft of the Project Paper Amendment, dated March 4, 1987, proposes that the project focus on collaborative research between Indian and U.S.-based investigators in reproductive immunology and disease-related immunology. Although not clearly

³Ibid., p. 3.

⁴Project Paper Amendment #1, July 26, 1988.

stated, the amendment implies that the results, i.e., products and concepts, achieved through collaborative research would be the primary objective of the project.

- The minutes of the First JWG Working Group, held in Delhi in November 1989, state that the purpose of the project was "to expand Indo-U.S. collaborative efforts in contraceptive development and reproductive biology, research in immunology, and to expand Indian institutional capabilities in these areas." The same document stressed the importance of establishing "centers" within the three [later four] participating institutions to carry out collaborative research. Center grants, composed of Collaborative Research Grants, Young Investigator Awards, Research Management Awards, and Core Support Awards, were to be awarded following the receipt and approval by the JWG of center plans and budgets.⁵
- In 1990, in preparation for the midterm evaluation of CD&RI, two attempts were made to prepare a logframe for the project.⁶
- The CD&RI Status Report, dated May 24, 1991, notes that the "purpose of the project is to support Indo-U.S. collaborative scientific work in contraceptive development and [disease-related] immunology." An enhanced capability of the four Indian research centers funded under CD&RI "to develop and adapt new technologies in contraception and to strengthen immunological research in India" is mentioned as "an expected output of the program."

Over time, the concept of establishing a center to function as a mechanism for focusing collaborative research in selected areas was coupled with the conviction that institutions would benefit (i.e., be strengthened) as a result of their participation in the CD&RI Project. The current consensus is that collaborative research in contraception and disease-related immunology and institutional development are the twin foci of the project. USAID/India emphasizes the research-related aspects of the project, while the GOI stresses institutional development. To date, however, none of the project documents clearly defines the linkages between these objectives or, beyond stipulating the project components, specifies the criteria that should be used to gauge institutional strengthening or the results of collaborative research.

⁵As originally conceived, but never fully articulated in the CD&RI Project, the center was to serve as the locus for focused collaborative research carried out by groups or individuals from multiple disciplines or departments. The center concept appears to have been viewed by designers of the CD&RI Project as a fundamental strategy to increase knowledge in the areas of contraception and disease-related immunology.

⁶The first, prepared in August 1990, linked collaborative research and institutional development. According to this logframe, the purpose of the CD&RI Project was to support collaborative research in contraceptive development, reproductive immunology, and other areas of "disease-related" immunology and, relatedly, to strengthen India's institutional capabilities in immunologic research. According to a second logframe, prepared in December 1990, the project was to foster strong supportive links between individual U.S. and Indian scientists, especially young Indian scientists; develop broad linkages between U.S. and GOI institutions involved in medical biotechnology research; strengthen four Indian institutional capabilities to do contraceptive and immunological research; and ensure technology transfer in fertility regulation and disease-related immunology.

2.3 CD&RI Budget and Project Components

2.3.1 Budget

The CD&RI Project has an illustrative total budget of \$2.94 million: \$2.2 million from USAID/India and \$0.74 million from the GOI. This and the following pages contain six tables on the budget, with explanatory notes.

Table 1 presents a breakdown of the budget line items by source of funds.

Table 1

**CD&RI Illustrative Budget
(July 26, 1988)**

**Line Item Categories by Source of Funds
(000s)**

Line Items	USAID/India	GOI	Total
Technical Assistance	814	210	1,024
Training	1,178	510	1,688
Other	208	20	228
Total	2,200	740	2,940

Table 2 presents the most recent CD&RI budget allocations by project component. This budget was approved by USAID/India in Project Implementation Letter (PIL) No 19, issued on February 20, 1991, and remains illustrative.

The project specified that a program of "center grants" should be given to three to six Indian institutions, selected by DBT with the concurrence of USAID/India. These grants were to finance the following components:

- Indo-U.S. Collaborative Research Awards at participating Indian institutions;
- long-term (one to two year) Young Investigator Awards, including funds for Re-entry Grants and Re-visitation;
- Science Management Training Awards for mid-career scientists going into science administration; and
- Core Support Awards for general institutional strengthening.

Table 2
CD&RI Revised Illustrative Budget
(February 20, 1991)
Source of Funds
(\$000s)

Project Components	USAID/India	GOI	Total
1. Collaborative Research	1,030	680	1,710
2. Fellowships/Re-entry ¹	675	060	735
3. Science Management Award ²	0	0	0
4. Core Support	305	0	305
5. Monitoring/Evaluation Administration	190	0	190
Total ³	2,200	740	2,940

¹A few of those associated with the project understand that funds could be made available for Re-entry Grants to support the research activities of project-trained and expatriate Indian scientists on their return to India. Funds were to be used to establish laboratories and begin research. With the exception of a reference in the Guidelines for Preparing Centre Grant Application (November 1988), the evaluators found no written reference to the eligibility of expatriate Indian scientists. None of the investigators interviewed were familiar with this provision of the CD&RI Project. Article 2.2 of the Guidelines states: "Recently trained staff and new expatriate hires from the U.S. are also eligible for Young Investigator Re-entry Grants."

²None of the centers presented applications for Science Management Awards when PIL 19 was issued.

³This budget does not include the \$3.4 million made available to the CONRAD Program (see Section 2.5). The CONRAD funds are used exclusively for contraceptive development-related activities. However, this budget does include the \$389,587 provided to the National Institute of Allergies and Infectious Diseases (NIAID) through a Participating Agencies Service Agreement (PASA) to support the U.S. component of collaborative research in immunology.

On the recommendation of DBT, with the concurrence of USAID/India, and as stipulated in the Project Paper Amendment, the Joint Working Group (JWG), the project management unit, chose four Indian institutes to participate in the CD&RI Project. Three were selected in 1988; the fourth was chosen at the second JWG Meeting, held in Washington in July 1989. As noted in Table 3, each institute chosen was allocated an amount to pursue activities approved under the project.⁷

Table 3

**CD&RI Project
USAID/India Resources Allocated to Participating Indian Research Institutes**

Institute	Amount Allocated
National Institute of Immunology (Delhi)	\$1,000,000
Post Graduate Institute of Medical Education and Research (Chandigarh)	\$300,000
Indian Institute of Science (Bangalore)	\$500,000
Central Drug Research Institute (Lucknow)	\$400,000
Total	\$2,200,000

Before funds could be released, however, each institute was required to prepare a Center Grant Application with a one-page budget. To date, only NII has submitted a complete Center Plan in the format initially requested by the JWG. The other participating institutions have submitted documents that outline the general activities each proposes to fund with the resources allocated. The proposed budgets are presented in Table 4.

Table 4

**CD&RI Illustrative Center Budgets
(February - March 1991)
(\$000s)**

Project Components	NII		IIS		PGIMER		CDRI	
	US	GOI	US	GOI	US	GOI	US	GOI
Collaborative Research	507	114	207	116	308	167	144	232
Fellowship	335	38	45	100	45	9	0	0
Core Support	108	0	0	0	45	0	0	0
Total	950	152	252	216	398	175	144	232

⁷The Project Paper Amendment stipulated that "over a two-year period no more than 45 percent nor less than 15 percent of the bilateral project funds [should go] to any one of the selected institutions under the Center Grants Program." The PACD of the CD&RI Project was extended from July 21, 1988, to May 31, 1990 (currently May 31, 1993).

The participating institutions have requested \$1.744 million from USAID/India and \$.775 from the GOI. Since only the NII program of activities has received official approval from the GOI and USAID/India, however, the budgets presented in Table 4 can only be regarded as illustrative. In addition, since the amounts requested by the three remaining institutes either use more than the resources allocated (PGIMER) or do not use all the resources allocated to an individual center (CDRI), the budgets will have to be adjusted before final approval can be given.⁸

Table 5 is a summary of the amounts requested for each component of the CD&RI Project by the participating Indian institutions. The table presents only the amounts requested from USAID/India; the amounts to be provided by the GOI or the CONRAD Program, assuming the activity proposed is related to contraceptive development, are not included.

Table 5
CD&RI Project
Summary of Proposed Activities and Budget Amounts
(June 30, 1991)

Institutions	Collab. Research Awards	Fellowships Visits - Re-Entry		Science Management Awards	Core Support (\$000)
National Institute of Immunology-NII (New Delhi) \$1,000,000	4 awards \$507,000	6 awards \$189,000	3 awards \$120,000	no awards	\$107,000
Indian Institute of Science-IIS (Bangalore) \$500,000	3 awards \$207,000	1 award \$45,000	no awards	no awards	\$0
Post Graduate Inst. of Medical Education and Research-PGIMER (Chandigarh) \$300,000	3 awards \$308,000	1 award \$45,000	1 award \$40,000	no awards	\$45,000
Central Drug Research Institute-CDRI (Lucknow) \$400,000	1 award \$144,000	no awards	no awards	no awards	\$0

⁸CDRI (Lucknow) has only requested \$144,000 from USAID/India, although this institute has been allocated \$400,000. IIS (Bangalore) has only requested funds for three Collaborative Research proposals and one Fellowship. PGIMER's proposed activities require more funds than its \$300,000 USAID/India grant permits. The Core Support amount allocated to any given institute is equal to the amounts spent on Fellowships and Science Management Awards; however, the total center budget may not exceed the amount allocated.

Table 6 is the CD&RI Revised Illustrative Budget by Focus of Activity: Contraceptive Development or Research in Disease-related Immunology.

The amount given for Contraceptive Development does not include the US \$2.35 million that CONRAD has programmed for both Collaborative Research and Fellowships. If the amount spent by CONRAD is included, the amount available for Contraceptive Development is \$3.45 million or 79 percent of funds available for project activities.⁹

Table 6
Analysis of CD&RI Revised Illustrative Budget
by Focus of Activity
(\$000)

	Contraceptive Development	Research in Immunology
Collaborative Research	930	670
Fellowships	215	210
Total	1,145 (56%)	880 (44%)

NII is the only institution that has submitted a "true" center plan. NII's long association with the project (this center was supported under the original CD&RI program) and/or its geographical proximity to USAID/India and DBT (it is the only participating institution based in Delhi) may be the explanation. IIS in Bangalore, which has supported one Fellowship, and PGIMER in Chandigarh, which recently received approval for a Fellowship, currently qualify for Core Support Awards. Each institute needs to clarify the means for accessing these funds.

2.3.2 Project Components

Collaborative Research Activities

Collaborative research activities were both an objective and a component of the CD&RI Project. A summary of each of the 11 collaborative research projects submitted under CD&RI appears in Appendix E. These summaries mention the potential short- and long-term outcomes of each project. As noted, collaborative research projects were funded in the areas of contraceptive development and disease-related immunology.

The contraceptive development projects focus on developing one or more contraceptive vaccines, a hope for the next generation of new contraceptives. Research focuses on the development of contraceptive vaccines against sperm antigens, zona pellucida antigens, and against gonadotropins (Follicle Stimulating Hormone - FSH). In terms of the priority areas for contraceptive development, long-term reversible methods including contraceptive vaccines are one of four priority areas of the Office of Population. For a decade or longer, this office has supported

⁹When taking the CONRAD funds into account, it is important to note that to date only about 25 percent of the funds programmed annually have been spent for CD&RI project-related activities, i.e., Collaborative Research Awards and Fellowships. The majority of the funds have been spent on "related activities" that can benefit the Indian program.

research in this area through a variety of mechanisms; CD&RI's predecessor project, CD:RI, was one.

Despite the years of effort in this area, a contraceptive vaccine is still many years away. However, the areas under investigation are among the most important and on the leading edge of research in the field. For example, the sperm specific antigen identified by NII investigators is currently being sequenced and will be cloned in collaboration with the Population Council. This could be the first sperm antigen vaccine. The Indian and U.S. counterpart teams are leading researchers in this field.

Although both research tracks, reproductive and disease-related immunology, use the same research tools, the approaches being taken are conceptually distinct. For example, in the reproductive immunology area, the long-term goal is to develop a vaccine against sperm, zona pellucida, and FSH. To achieve this long-term goal, it is necessary to

- identify the appropriate immunogen;
- establish methods for producing large amounts of the specific antigens or alternatively to identify small immunologically active fragments that would be equally effective in producing an immune response;
- study ways of boosting the immune system to ensure that all individuals receiving the vaccine will have reliable immune response;
- study the means of enhancing cell-mediated immunity to increase the local vaginal secretion of antibodies to potentially enhance effectiveness; and
- develop improved delivery systems for any antigen.

The disease-related immunology projects focus almost exclusively on the development of immunodiagnosics for specific diseases. These projects appear to be activities that could not be funded under other mechanisms.

The projects funded include one that will identify antigens that could be used to develop a kit for early diagnosis of tuberculosis; one that aims to develop a sensitive and specific non-microscopic diagnostic assay for malaria surveillance; one that seeks to identify antigens and develop a kit based on these antigens which would help screen for individuals susceptible to rheumatic heart disease; and one that is focused on providing information related to the basis of allergenic diseases. With the exception of the last project, the proposals financed under this component of CD&RI would, if successful, facilitate the early diagnosis of diseases that are significant public health problems in India.

At project inception, there was some expectation that knowledge gained from the implementation of research activities in the distinct research areas would be applicable across disciplines. This is not an unreasonable expectation. Mechanisms have not been explicitly delineated within the CD&RI Project, however, to ensure that this information exchange occurs.

Fellowships/Young Investigator Awards

The CD&RI Project provides funds for young Indian scientists to work in laboratories of U.S. scientists for the purpose of acquiring knowledge or skills in new technologies. Guidelines for these awards were originally set down during the first JWG Meeting. These awards were to fund individuals for a period of one to two years to work in NIH and NIH-collaborating laboratories in the U.S., subject to the approval of the JWG. Awards were to include travel and living stipends, and Re-entry Grants (see below for discussion of Re-entry Grants). Only individuals holding *permanent* positions at CD&RI-supported institutions were eligible for these awards.

During the second JWG, when several of the components of the CD&RI were modified, the Young Investigator Awards were retitled CD&RI Fellowships. (The rationale for this change in title appears to have been cosmetic.) Candidates were to be proposed by the centers; the secretariats/technical coordinators were authorized to approve applications.

The fellowship awards had several components, including the possibility of funding local cost components (such as chemicals and supplies) for host institutions, as well as travel to meetings and workshops in the U.S. In principle, these awards were to support young scientists (under 36 years of age) who had completed their training within the previous five years. The duration of the awards was six months to two years with the stipulation that awards of less than one year "might not qualify" for a Re-entry Grant. In selecting candidates, primary consideration was to be given to fellows whose work fell within the overall direction of the center, as opposed to those whose work was not related to the focus of the center and the CD&RI Project.

Since the center grant plans were not originally completed by all of the institutes participating in the CD&RI Project, it is not possible to ensure with certainty that this "guideline" was followed other than informally by those responsible for proposing and approving fellowships. It does appear that each of the fellows proposed was either directly or indirectly involved with the collaborative research activities proposed for funding under the project.

Six applicants from NII, and one each from IIS and PGIMER, have been approved to date under the fellowship component of the CD&RI Project. The purpose of each fellowship, U.S. host laboratories, and the status of the activities are summarized in Appendices D and F.

Given the requirement that applicants for fellowships had to hold *permanent* positions at a participating institute, it is not clear why the applicant from PGIMER, who did not hold a tenured position, was chosen.

At present the GOI has a ban on international travel and insists that each trip be specifically cleared. While USAID/India has expressed a willingness to finance all international fellowship travel and living expenses, the GOI has not given a blanket approval for travel. As a consequence, some Indian scientists have had to reschedule visits to the U.S. and request their U.S. collaborators to alter arrangements.

There is a conceptually strong rationale for the fellowship component. Each of the fellows interviewed indicated that his or her U.S. host laboratory had certain technical expertise that needed to be learned and that could be applied in India. In addition, with the one exception noted, the fellows chosen have permanent staff positions and independent laboratories at their home

institutions. Therefore, any newly acquired laboratory skills should be readily applicable, particularly if Re-entry Grants that provide some support for equipment and supplies are accessed (see below).

At the same time, the requirement that fellows have permanent positions and laboratories constrains the fellowship program to some degree. Holding permanent positions, directing laboratories and supervising numerous graduate students, technicians, and post-doctoral fellows make it very difficult for many professionals to leave their institutions for an extended period of time. In general, the CD&RI Project has evolved a flexible policy to deal with this issue. Several of the fellows have structured their visits as multiple two-month visits, or a six-month visit followed by revisits of about two months.

Overall, the fellowship activities reviewed seemed to be well planned. Moreover, the training received by the fellows and their interactions with U.S. investigators are likely to benefit future activities undertaken at the participating institutions.

Re-entry Grants

Re-entry Grants were to be made available to certain qualifying individuals under terms set down by the JWG at its first meeting. Re-entry Grants were to be prepared in collaboration with the host and home institution advisors and cleared through the technical coordinators. The budget could include funds to purchase major pieces of equipment related to the investigator's research needs as well as funds to enable the fellow to return to the U.S. collaborating laboratory for some months each year (re-visitation). The minutes of the JWG meeting indicate that recently trained staff (not defined) and Indian scientists living abroad were also eligible for Re-entry Grants.¹⁰

At the second JWG Meeting it was determined that only those young investigators visiting U.S. laboratories as CD&RI Fellows for a period of greater than six months were eligible for Re-entry Grants. Although not explicitly stated in the minutes of the meeting, it was later determined that a Re-entry Grant would have an upper limit of \$40,000. In practice, however, this guideline has not been explicitly communicated, nor has it been followed. This is another example of a situation in which understandings and general operating procedures have evolved in the course of implementation but have never been documented.

In the context of institution-strengthening, these Re-entry Grants serve a useful and important function. Scientists who go to the U.S. to learn specific techniques have on their return to India the means to apply them. In addition, the re-visitation provisions of the Re-entry Grants allow collaborative relationships to be forged between U.S. and Indian scientists. The collaborative relationships that have been established and strengthened through the combined Fellowship and Re-entry Grant provisions of the CD&RI Project should lead to the development of a pool of investigators who might well continue to work together in future years.

¹⁰It is interesting to note that the minutes of the first JWG meeting mention that Indian scientists living abroad were eligible for Re-entry Grants. The general understanding and working definition of Re-entry Grants that has evolved within A.I.D. (both USAID/India and A.I.D./W) and DBT suggest that these funds were to be used to support expatriate Indians living abroad and wishing to return to India. In practice, none of the Re-entry Grants has been used for this purpose. Funds have been spent under this project category to purchase a FACS flow cytometer for NII.

Science Management Awards

Science Management Awards were designed to support mid-career scientists who wished to make career transitions to science administration. These short- and long-term fellowships in the U.S. were available to individuals from the institutes supported under CD&RI, as well as to qualifying DBT personal. These fellowships were to provide recipients with the opportunity to expand and enhance their skills in the administrative, managerial, and technical aspects of administering a research program or institution.

At the first JWG Meeting, the technical coordinators were authorized to approve Science Management Awards, according to guidelines established by the JWG. To date, no institute has utilized this component of the CD&RI Project. In early June 1991, DBT sent a letter to each of the four participating institutions asking for nominations for this award. It is anticipated that prior to the completion of the project some individuals will be supported for travel to the U.S.

It is of some concern that none of the individuals interviewed (mostly scientists) from any of the institutes fully understood the rationale or utility of the Science Management Awards.¹¹ At the same time, it is very rare in India for a mid-career scientist to opt to move to an administrative position. Such positions are generally offered to already established scientists in the later stages of their careers. Therefore, it might be difficult for an institution to select and send someone suitable.

There are other ways, however, in which these awards could be used, and it was anticipated that the JWG would delineate guidelines describing a spectrum of possible uses. It remains for the GOI members on the JWG to determine how their awards are relevant to institutional development in India and to establish and communicate guidelines that facilitate access to and use of Science Management Awards.¹²

Core Support Awards

The Core Support Awards were designed to enhance the productivity of a given center. Core Support Awards were to support the purchase of general supplies, spare parts and equipment and the development of information retrieval systems and management information systems. Funds could also be used to obtain the services of consultants or technicians, attend national and international conferences, and convene workshops and seminars.

The total amount of support available to any institution was linked dollar for dollar to the amount the institution (center) spent on Fellowships, Science Management Awards and Re-entry Grants and could not exceed the total amount allocated. The Core Support Awards were reportedly designed to compensate, partially, the institutes for allowing young staff to participate in overseas training activities supported under Fellowship and Science Management Awards. To access funds, each center had to submit a Center Grant Plan and Budget for review and approval by the JWG. As described elsewhere, these plans would provide the JWG with an overall understanding

¹¹Many may not have seen the Center Grant Guidelines or have been familiar with all the components of the CD&RI Project.

¹²Under the predecessor CD:RI Project, the administrator of NII attended a management training course at the University of Connecticut. This might be an example of the type of activity that could be funded under this component of the CD&RI Project.

of the thrust of the center and the linkage among the program elements. The plans were to be management tools used by the JWG and the secretariats to approve subactivities, monitor progress, and evaluate the CD&RI Project.

Center Development and Institutional Strengthening

In both the U.S. and India, a "center" is understood as a program of research and other activities conducted by a group or groups of individuals from multiple disciplines and/or departments operating with a common focus. The researchers may have varied approaches, but they share research facilities and hold common ultimate goals.

As noted above (Section 2.2), the project purpose has evolved over time. The terms "center development" and "institutional strengthening" are understood to be interchangeable. Although the purpose of the two may be similar, their application and scope are different, however. Institutional strengthening is a process that flows from an analysis of the needs of an institution. Center development is a focused effort to draw researchers together to address priority problems. Center development does strengthen an institution but as a by-product of carrying out a specific task; its objective, however, is to address research priorities in a rapid and focused manner.

During the first years of the CD&RI Project, the JWG instructed the participating institutions to develop center grant applications. Although the content of the application was defined by the JWG, it is not certain that this material was distributed to the Indian institutions. In addition, it is not clear why developing center grants was given such emphasis since the center concept is well known in India and is currently operating at two of the Indian institutions participating in the project -- NII and CDRI. Even at IIS in Bangalore, there is one Center for Reproductive Biology and Molecular Endocrinology.

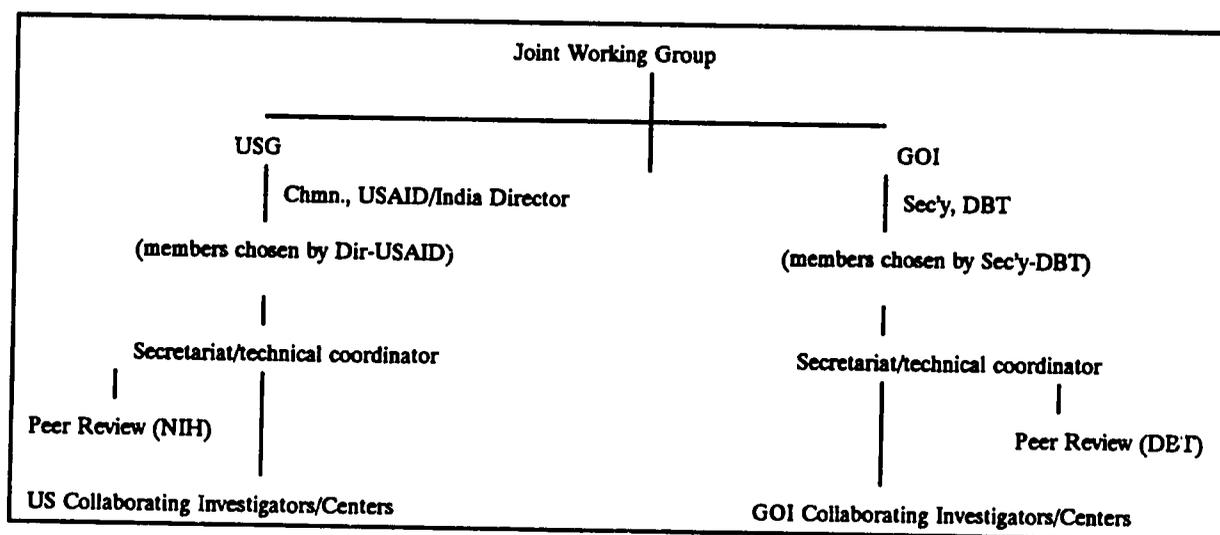
During the second JWG Meeting, two years into the project, a center was "now defined as the specific programme and projects supported within the collaborating institutions in India with CD&RI funds." The statement implies a difference of opinion on the definition of a center and indicates that some other definition of center concept was held prior to the July 1989 meeting of the JWG; however, it is not possible to document the different views on this concept. It is clear that under the CD&RI Project, the center concept was never properly articulated, communicated, or understood and acted upon. It is also clear that the statement of July 1989 renders the traditional center concept meaningless except for the purpose of tracking budgets and activities approved under the CD&RI Project.

2.4 The Management Structure of the CD&RI Project

Management of the CD&RI Project was entrusted to the Indo-U.S. Joint Working Group (JWG). The current Indian membership on the JWG, determined at the discretion of the Secretary of DBT, includes directors of the institutes involved in the project and a member of the Indian Council of Medical Research (ICMR). U.S. members, chosen by the Director of USAID/India, are the Director of the HPN Office of USAID/India, a member of the Office of Population, a scientist from the University of Texas, and members of NICHD, NIAID, and the CONRAD Program (See Chart 1).

Chart 1

CD&RI Project Management Structure



The JWG was encouraged to "(1) meet annually or more often as required, (2) set policies and procedures, (3) approve Center Grants, (4) and monitor and evaluate the overall program." The JWG was to appoint the technical coordinators and, working with and through them, "manage the project" [emphasis added].

Among its principal responsibilities, the JWG was to "ensure that a Peer Review [was] followed prior to the approval of all Collaborative Research Proposals." For peer review purposes, the U.S. side was to use the services of the National Institutes of Health (NIH); the GOI side, represented by DBT, was "to establish its own mechanism."

Two secretariats, one for the U.S. and one for the GOI, were assigned responsibility for managing day-to-day activities and overseeing project implementation.¹³ Management was to ensure that a "peer review process was followed prior to the approval of all collaborative research projects to be funded under the project."

While both U.S. and Indian members of the JWG have a fundamental interest in ensuring that good scientific research is carried out, they differ somewhat on orientations and objectives. U.S. JWG members represent U.S. institutions involved in providing technical, administrative and financial support to the project. Their institutions do not receive project funds. The majority of Indian members represent the Indian centers that receive grants out of project funds. Thus, institutional interests sometimes prevail over broader program interests.

Interviews with several JWG members suggest that each has a particular view of what the project should do and/or how his specific institution would (or would not) benefit from participating in the project. At present, no member of the JWG has, as a primary consideration, the overall management of project activities. Indeed, no JWG member on either side was specifically

¹³The U.S. JWG member from the Office of Population is on the U.S. secretariat; his GOI counterpart is not a member of the Indian JWG.

designated to supervise the activities managed by the secretariats. This is not to say that the JWG is (or has been) less than committed to the swift and effective implementation of the project. It does suggest that the issue of managing the implementation process was inadvertently overlooked.

Both the project designers and the JWG seem to have assumed that the imprecisely defined secretariats/technical coordinators (see below) would "handle" procedural matters. At the first JWG meeting the secretariats/technical coordinators were made responsible for the day-to-day implementation of the project and given technical and managerial responsibilities. The composition of the secretariat and the authority of its members, however, are nowhere clearly defined. Broadly, these professionals were to

- communicate directly with institutions or centers selected and U.S. collaborators;
- develop and facilitate research projects and arrange for peer review and appropriate funding of proposals;
- submit reports to the JWG;
- request revision of proposals to accommodate critical comments;
- prepare and execute grant documents for approved projects;
- authorize or otherwise provide for the disbursement of funds;
- identify new opportunities for research;
- organize occasional scientific meetings;
- promulgate guidelines for progress and final reports;
- establish with the counterpart secretariat 1) agreements on exchanging proposals, 2) dates for submitting and reviewing proposals, 3) supporting science visits for project development, and 4) procedures for disbursing funds for project activities;
- prepare documentation for JWG meetings (e.g., minutes);
- develop plans for monitoring and evaluating the CD&RI Project (with the approval of the JWG); and
- approve fellowship grants

The documentation reviewed suggests that the JWG was initially focused on ensuring that center plans and collaborative research proposals were submitted and adequately reviewed, and that some immediate actions were taken to resolve procurement problems and to transfer U.S. funds to the GOI.¹⁴ The JWG apparently failed to appreciate the necessity of clearly defining the composition and authority of the individual secretariats and technical coordinators and of ensuring

¹⁴See the minutes of the second JWG Meeting, July 1989, Attachment 6.

that specific individuals were made responsible for establishing procedures for routine communications between each other and the participating GOI institutions and collaborating U.S. investigators. In addition, the necessity of establishing common procedures for soliciting, receiving, and approving requests, and implementing activities under the project, was overlooked or, if recognized, never acted upon expeditiously -- until recently -- by USAID/India or DBT.¹⁵ Given the complexity of USAID and GOI regulations and the apparent incompatibilities between the two, implementation problems could have been expected and should have been addressed. Only at the second JWG meeting in July 1989 did the chairman of the Indian delegation stress "the need to *streamline* [emphasis added] the project procedures and provide the secretariat with adequate instructions to move the project forward rapidly."

Since inception, the project has needed to define the components, responsibilities, and authorities of the secretariats and technical coordinators and the manner in which each would communicate with the others involved in managing the project as well as the institutions participating in CD&RI. Agreed upon review and implementation procedures and a common approach to discussing and resolving issues that arise during implementation have also been needed. The necessity of establishing these management procedures has become more obvious as key staff responsible for day-to-day activities have changed. Both USAID/India and DBT have each had two "advisors" during the life of the project. Few procedures have been written down and significant understandings remain undocumented. Only recently, as new staff have become involved in the CD&RI Project, have some significant attempts been made by USAID/India and DBT to share information on a routine basis and to develop and implement common management procedures for the project.

Most of what has been managed to date has been on an *ad hoc* basis. Managing each new activity has been a voyage on uncharted seas for the participating Indian institutions, USAID/India, and DBT. In this context -- one in which procedures are not well defined and acted upon in concert by DBT and USAID/India -- the progress achieved to date is commendable, with credit due to the energetic commitment and devotion of a few individuals. The problems that remain are understandable and continue to pose serious barriers to rapid implementation of project activities.

In some respects, a rudimentary project management structure for the U.S. Secretariat has evolved over the last three years and reflects what appears to be happening under the project. Presented on the following page, this structure has not yet been formally defined and endorsed.

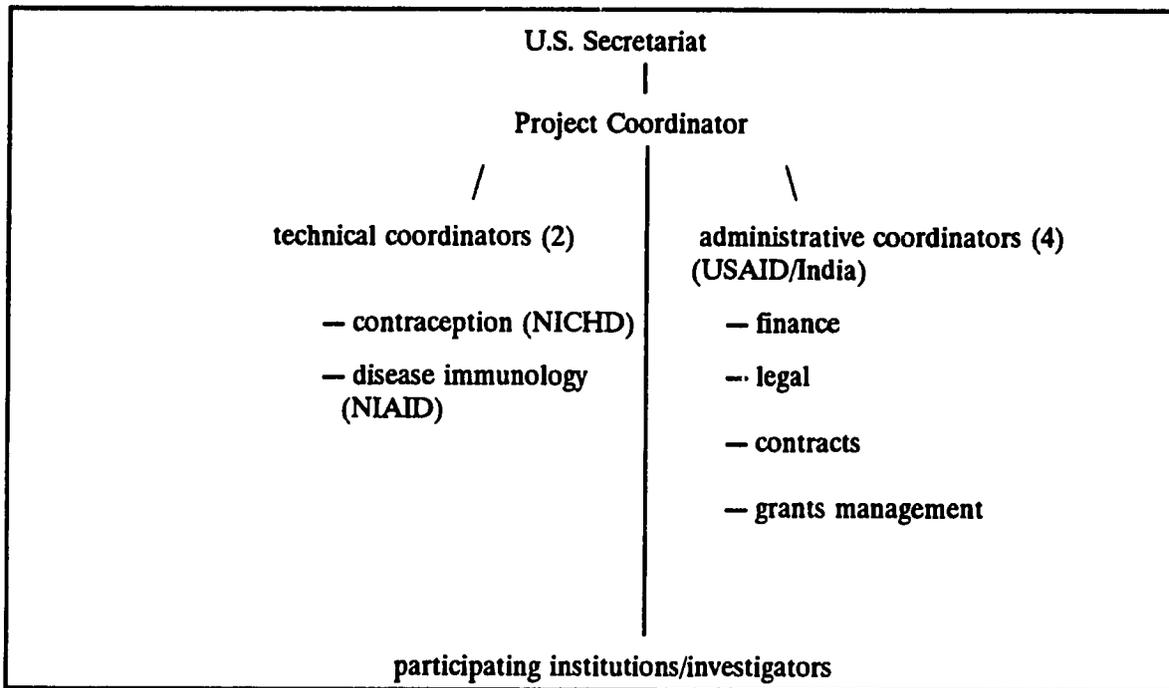
None of the structures presented in this organizational arrangement or the procedures by which they operate have been formally defined. For example, although the current project coordinators from USAID/India and DBT have come to establish a more open and routine system of communication, critical material still passes between those involved in the project without passing through the project coordinators.¹⁶ Without routine transmittal of information through the project coordinators, who are linchpins for effective and rapid action under the project, implementation is slowed, enthusiasm is lost, and some level of mistrust is engendered.

¹⁵Over the course of the project some operational understandings have emerged. For example, an amount of \$40,000 has been set as the limit for Re-entry Grants under the Young Investigator Awards. However, this position has never been documented or communicated systematically to the participating institutions.

¹⁶Recently, for example, a U.S. collaborator sent a report to CONRAD that was not forwarded to either the Indian collaborator or the project coordinator at USAID/India.

Chart 2

CD&RI Project: U.S. Secretariat Structure (proposed)



2.5 Role of the CONRAD Program

In addition to the \$2.2 million explicitly authorized by USAID/India under the project amendment, CD&RI has been able to call on the resources of the Contraceptive Research and Development (CONRAD) Program, a centrally financed program authorized by the Office of Population (A.I.D./Washington) in 1985. The CONRAD Program, a successor to the PARFR Project,¹⁷ received a \$3.4 million buy-in from USAID/India in August 1987.¹⁸

At the time the buy-in took place, the parties (CONRAD, Office of Population and USAID/India) understood that the funds would be used to benefit biomedical [contraceptive] research activities in India and to facilitate the implementation of the CD&RI Project. As noted in Attachment 1 of the Project Paper Amendment of July 26, 1988, funds were to "support research in [contraceptive development only] and related activities in India and the U.S. . . . [and] activities in the U.S. and elsewhere directly related to Indian priorities and contraceptive technology that, immediately or eventually, can be transferred to India."

¹⁷Unlike PARFR, CONRAD was not expected to act as a financial manager and procurement agent for the Indian institutions participating in the CD&RI Project. According to the CD&RI Status Report of May 24, 1991, "CONRAD funds will pay for U.S. side costs of collaborative research in contraception and of Fellows in contraception. CONRAD has, in the past, also funded scientific workshops in the NII, participation of U.S. scientists in scientific meetings held in India, and participation of Indian scientists in international scientific meetings."

¹⁸See Attachment 1 to CD&RI Project Paper Amendment entitled "Statement of Work - CONRAD buy-in" and the section below on the "Role of the CONRAD Program."

The funds provided to CONRAD were not restricted to any particular contraceptive research and development area. According to the SOW, several broad areas for collaborative research were delineated. Funds could be used to support research in contraceptive vaccines, spermicides, delivery systems, and other devices, to defray the costs of U.S. investigators working with Indian institutions, and/or to complete work that could not be done in India (e.g., animal toxicity studies required for U.S. Food and Drug Administration approval of products under development). Research ideas of special emphasis were designated "mission-oriented," "fundamental applied," or "applied basic" research.¹⁹ In addition, funds could be used for workshops, seminars and international meetings, the purchase of equipment and supplies, and technical assistance for evaluating programs, reviewing projects, developing research protocols, providing in-country training, or conducting confirmatory studies in the U.S.

Under the buy-in, CONRAD was not formally bound to use the \$3.4 million solely on activities related to the CD&RI Project. An informal agreement was established between USAID/India, CONRAD, and the Office of Population that set aside an annual dollar amount to support CD&RI activities. It was jointly understood that if CD&RI did not use the stipulated amount by approving activities in a timely fashion, CONRAD was free to use the funds for "other activities." It was further understood that "other activities" would be projects that would directly or indirectly benefit India and be related to Indian priorities in contraceptive development.

2.6 Accomplishments to Date of the CD&RI Project

The Project Paper Amendment (August 1988) describes the types of activities the CD&RI Project was designed to support but does not specify a timeline for completing any given activity. Beyond noting that collaborative research should be supported, fellowships granted, and four to six institutes should be involved in the CD&RI Project, neither the Project Paper Amendment nor the JWG defined specific project outputs.

The JWG did define five project implementation targets. Table 7 summarizes the progress achieved against the targets. As indicated, only modest progress has been made. Still, in spite of the slow pace of implementation and the absence of defined outputs, significant accomplishments have been recorded. This is noteworthy in three contraceptive development research projects which were launched before the official sanction date. Six accomplishments are noted below in Table 8; these are the direct result of the project (see Tables 7 and 8 on following pages).

¹⁹Mission-oriented, fundamental applied research and applied basic research are terms used to denote research activities that are product oriented in contrast to research that is oriented toward acquiring knowledge without a product goal in mind (basic research). Under the Office of Population's general mandate, only product-related research is supported.

Table 7

**CD&RI Project
Progress to date vs. Implementation Targets**

Target	Date Set	Achieved			Remarks
		Yes	No	Partially	
1. Three Center Plans Submitted (CDRI-Lucknow was not added until VII-89)	XI-88	X			
2. Center Budgets to be Submitted within 60 days of JWG Meeting of XI-88	XI-88		X		Center plans were submitted between October 1989 and February 1990. Budgets for individual activities were provided in most cases. No consolidated center budgets were submitted.
3. Joint Indo-U.S. management and implementation procedures developed and implemented	XI-88			X	Visits of collaborators to develop research proposals began in September 1989. Norms for paying living support to CD&RI Fellows were defined in March 1990. Procurement procedures were established in February 1991. The PASA with OIH/NIAID was completed in March 1991.
4. Peer Review of Collaborative Research Proposals to take six months to complete	VII-89		X		For over one-half of the proposals received, the peer review process took more than one year to complete. (see Appendix D)
5. All Collaborative Research Proposals Submitted for Peer Review by June 1990	VII-89		X		The two earliest fully developed proposals were submitted in early 1989. The rest of the proposals were submitted during 1990. The last two proposals were submitted in the final quarter of 1990.

Table 8

**CD&RI Project
Accomplishments to Date (July 10, 1991)**

1.	Of the eleven collaborative research proposals submitted, six have been jointly <u>approved</u> and <u>funded</u> . Two additional proposals have been <u>approved</u> but not yet funded (see Appendix D).
2.	The research proposed is significant and the Indian and U.S. institutions involved have the requisite credentials and motivation and access to the appropriate facilities.
3.	Seven new collaborative research relationships have been established between Indian and U.S. investigators as a result of the project. They are a part of the eleven collaborative research proposals. Indian and U.S. investigators have traveled to the U.S. and India to develop research projects.
4.	Eight research fellowships have been awarded and three fellows have traveled to the U.S. (see Appendix D).
5.	One participating institute, NII, has procured scientific equipment under the CD&RI Project.
6.	Several publications have been prepared by the investigators.

3. Implementation Difficulties of the CD&RI Project

3. Implementation Difficulties of the CD&RI Project

Six significant issues have delayed implementation. The first three listed below have been resolved over time; the last three have been addressed but no effective resolutions have been achieved.

3.1 Development of Center Plans

A considerable amount of project time was spent soliciting center plans from the three, later four, participating institutions. These plans were to contain scopes of work and budgets for activities proposed under the project. For the U.S. side, the development of center plans appears to have been a central objective. It is less clear how the Indian side regarded this project requirement. Project documentation does not provide a clear definition of a "center," nor state the value and objective of such a unit. The center grant application, developed and available following the first meeting of the JWG but perhaps not sent to the participating institutions, does request information on the "relationships between the proposed center and other research, academic, and administrative units of the institution." The definition of a center proposed at the second JWG Meeting suggests that the U.S. and the GOI had different views on the relevance and necessity of the concept and that these difference could not be resolved.²⁰

Still, since USAID/India was unable to approve the master plan and disburse funds until budgets were received, reviewed, and approved, and budgets could not be approved until center plans were submitted and collaborative research proposals had been peer reviewed, there have been significant delays in approving budgets and transferring funds.

3.2 Peer Review

The Project Paper Amendment states that peer review will be ensured by the JWG working through the technical coordinators. The U.S. side of the JWG would conduct peer review and use the services of the NIH, whereas the DBT side was to establish its own process, one not explicitly defined in the Project Paper Amendment. The process for reviewing the collaborative research proposals was discussed by the JWG at the first meeting in October 1988.

Collaborative research proposals were to be peer reviewed separately for scientific merit and budgetary justification. On the Indian side, DBT was to establish its own mechanism for the provision of peer review. On the U.S. side, reproductive immunology and contraceptive development-related projects were to be evaluated through the NICHD. Disease-related immunology projects were to be evaluated through the NIAID. Ultimately, the results of the separate Indian and U.S. reviews were to be brought together. The technical coordinators were to provide a common opinion on the merits of the proposals.

²⁰A center is now defined as the specific program and projects supported with the collaborating institution in India with CD&RI funds. This definition says that a center is what the JWG says it is.

At the second JWG meeting in July 1989, Dr. Ramachandran of DBT requested a change in the system for the bilateral review of projects to streamline and shorten the process. This "streamlined" review procedure, which appears to be virtually identical to one that was outlined in the first JWG, explicitly called for the simultaneous review by the Indian and U.S. sides. This process was to take no longer than six months. The Indian and U.S. technical coordinators were to share *written* review comments and resolve differences during a period of not more than one month. A summary of written reviews was also to be sent to the investigators.

In actual practice, this process has not been followed. No written reviews from the Indian side were made available to the U.S. technical coordinators, nor to the evaluation team. In addition, although approved projects were to be circulated to all JWG members for final approval, in most cases this "right" was waived by the JWG and delegated to the level of the technical coordinators/secretariat.

JWG guidelines called for a simultaneous review of technical merit by the Indian and U.S. sides. In several cases, Indian investigators prepared and submitted grants for simultaneous review by DBT and the U.S. side. In other cases, it appears that the Indian review was completed prior to submission of the proposal to the U.S. for review.

Still, as noted in Appendix D (CD&RI Project: Progress of Collaborative Research and Fellowship Activities), peer review became a lengthy procedure in the project context. Reportedly, DBT sent proposals to selected reviewers and awaited comments. Almost two years passed before the first reviews were complete. At the time of the evaluation (June 1991), reviews from Indian researchers reportedly had only recently been received on the final four proposals.

Although the Project Paper Amendment, and later DBT, insisted that U.S. peer review should be done under the auspices of NIH following any procedures NIH chose to use (e.g., *ad hoc* review, study sections, etc.), none of the reviews was conducted according to the formal NIH peer review process. Rather, an *ad hoc* process was established by NICHD to review the contraceptive development proposals and, almost two and one-half years after project launch, by NIAID for the disease-related immunology proposals.²¹

There were at least two reasons why the formal NIH peer review process was not used. First, many of the collaborative research proposals had an applied orientation and none of the standing NIH study sections were appropriate to review this type of work. Second, the proposals were submitted at different times. It was not feasible to convene an *ad hoc* committee to review all proposals together.

It is understood that NICHD sent each proposal to up to four outside reviewers. NICHD summarized and sent the reviewers' comments, through the technical coordinator, to the investigators. Proposals were revised based on the comments, as appropriate, and returned to the external reviewers for final approval.

After long delays, the proposals sent to NIAID were reviewed in-house. Two of the four CD&RI proposals involved NIH staff scientists as co-investigators, while the other two required

²¹In the context of a three-year project, normal review and approval would encompass the entire project period. No collaborative research activities could be initiated, much less completed.

NIAID to identify a suitable U.S. collaborator. Eventually, investigators with ongoing NIAID grants were identified; these grants could be supplemented without requiring additional internal review. These investigators worked with their Indian counterparts to revise and submit a final proposal that could be funded.

Although genuinely pleased with the responsiveness of NICHD, USAID/India was frustrated by OIH/NIAID's non-responsiveness and apparent lack of interest. At a meeting held on February 13, 1990, and attended by representatives of USAID/India, the Office of Population, DBT, the CONRAD Program, NICHD, NII, and DBT, alternatives to NIH, especially NIAID, were proposed. DBT felt strongly that any agency chosen as an alternative to NIAID for performing peer review should have the same credibility in scientific circles as NIAID.

In the face of this position, USAID/India turned again to NIAID and ultimately succeeded in obtaining peer reviews of the proposals in disease-related immunology. Experience to date suggests that the peer review mechanism chosen for the project has been unduly lengthy and unsuited to the time frame of this project. Moreover, it was certainly more an obstacle than an aid to the initiation of collaborative research.

3.3 PASA with OIH/NIAID

Through the buy-in to the CONRAD Program, the CD&RI Project had access to funds that could be used to support the U.S. side of collaborative research and fellowship activities related to contraception. Access to similar support for the U.S. side of collaborative research and fellowships in disease-related immunology had to be arranged through a PASA with OIH/NIAID. In putting the PASA in place, USAID/India found itself in a "Catch-22" situation. In brief, the PASA with OIH/NIAID could not be executed until budgets and scopes of work were developed. These could not be prepared until proposals had been peer reviewed. Peer review by NIAID could not start until the PASA was approved.

The Office of International Health (OIH) of the U.S. Department of Health and Human Services (HHS) offered to facilitate the execution of the PASA. In spite of the good offices of OIH, additional lengthy delays occurred before NIAID initiated peer review. The process took place following receipt of a promise that the PASA would include funds to reimburse the agency for the cost of peer reviewing the proposals. The PASA was not complete until March 1991, almost three years after project approval, in spite of the urgings and efforts of USAID/India and the Office of Population to secure NIAID involvement.

3.4 Intellectual Property Rights (IPR)²²

One proposed collaborative research project, the only activity submitted by CDRI (Lucknow), has been approved with a contingency. U.S. reviewers are concerned that the proposed activity may lead to the development of a marketable product or concept. The U.S. side has been reluctant to endorse the activity fully until both the U.S. and GOI develop a common understanding

²²The IPR issue emerged in the later stages of the project. It does not seem to have been a critical concern when the project was conceived. Had it been, projects that had an applied focus might have been eliminated.

or approach to protecting the rights to inventions that result from the research funded under this project.

On April 8, 1991, USAID/India submitted to DBT the language that A.I.D. currently includes in grants that might result in discoveries or inventions. USAID/India has suggested that both parties (the U.S. and the GOI) (1) identify the rights each is interested in protecting; (2) agree on the provisions required to protect these rights; and (3) include the agreed provisions in the approval (sanction) document. DBT is reviewing USAID/India's proposal but has not yet responded.

The IPR issue can only be resolved at higher levels of the U.S. and Indian governments. The project can have very little influence on the resolution of the matter. It remains to be determined whether an interim agreement can be reached that would allow the CDRI proposal to be funded.

3.5 Procurement

Slightly more than 40 percent of the funds made available by USAID/India under the CD&RI Project are earmarked for the purchase of U.S. scientific equipment. Access to U.S. equipment, supplies and technology is highly desired by Indian investigators and required to upgrade the research capabilities of Indian institutions. Under USAID regulations, however, all equipment purchases must follow Handbook 11 guidelines. These are complex and foreign to most of the institutes participating in the project; only NII has experience in procuring U.S. equipment. Learning and following USAID regulations have not been easy. Even in the case of NII, it took more than two years to purchase one major piece of equipment.

The delays related to following USAID procurement guidelines have been compounded by India's recent economic difficulties. At present, the GOI insists that those wishing to buy foreign currency and import products deposit 200 percent of the value of the letter of credit in rupees in a special account. Since few institutes have a cash flow position that allows them to do this, many are reluctant to open letters of credit.

In addition, the Indian investigators have found that the equipment prices quoted in the project budget, prepared in some cases as long as three years ago, have increased. Since procurement has been delayed but the project approval letters only authorize the original budget amount and, to date, make no provision for inflation, the funds made available are inadequate in most cases to complete the transaction. Submitting and requesting approval for a revised budget, based on current prices, would further delay procurement and implementation.

The Secretary of DBT has been requested and has agreed to discuss with appropriate GOI officials the steps that can be taken to eliminate the 200 percent deposit requirement for goods procured under this project. To speed equipment procurement and obviate the necessity of requesting additional budgetary approvals prior to procurement, the Secretary of DBT has also been requested to release activity approval letters ("sanction documents") that contain a provision authorizing a contingency amount to cover any "reasonable" (10-15 percent) increase in the cost of the equipment that may have occurred between the submission of the proposal and final approval.

3.6 Transfer of Funds

According to the bilateral agreement and as elaborated in PIL 19, USAID/India will satisfy allowable expenses incurred under the project on a reimbursable basis. In other words, the GOI through DBT must advance both USAID and GOI contributions to the institutions and present vouchers for expenses incurred on USAID/India's behalf when these are received from the institution. In the current economic crisis, DBT financial managers are reluctant to advance funds for the project. Since a portion of the funds will be used to procure equipment, and accommodating USAID regulations is a lengthy process, transferring U.S. funds to the GOI takes place very slowly. The longer DBT waits to disburse, the slower the rate of implementation and the more time that will pass before vouchers are satisfied by USAID/India.

In addition, the GOI faces the prospect of losing on the transaction. For example, over a two-week period (June 23-July 7, 1991), the Indian rupee was devalued by almost 20 percent against the U.S. dollar. Since USAID/India satisfies vouchers at the rate of exchange in effect on the date they are presented, the GOI runs the risk of losing on the exchange rate. This is a current concern of DBT financial managers and an obstacle to implementation.

3.7 Summary

The CD&RI Project has experienced significant implementation delays. At least five factors have been responsible for slowing the pace of implementation:

- the necessity of satisfying both GOI and USAID regulations and procedures;
- the relatively high turnover of USAID/India and GOI staff involved in managing project activities;
- the establishment of an unduly complicated and imprecisely defined project management structure;
- the failure at the start of the project to define, promulgate, and follow consistently appropriate and mutually agreed upon joint management procedures for the CD&RI Project; and
- the lengthy delay in establishing a PASA with OIH/NIAID and the less than energetic involvement of NIAID in completing peer review of the disease-related immunology proposals.

The first two factors are common to all USAID projects; the last three are not uncommon but, in the case of the CD&RI Project, have had an undue effect.

4. Assessment of and Reflections on the CD&RI Project

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4. Assessment of and Reflections on the CD&RI Project

4.1 Collaborative Research and Institutional Strengthening

As currently expressed, the objectives of the CD&RI Project are twofold: collaborative scientific research in contraceptive development and disease-related immunology and the strengthening of India's institutional capabilities to conduct research in these areas. These objectives are mutually complementary in the sense that progress in one area indirectly supports advancements in the other. With limited funds, however, the progress that can be achieved in either area is limited.

Given the history of the current bilateral activity, supporting a future biomedical research project in India requires a thorough consideration of the priorities of USAID/India and the GOI and the development of a management structure that is based on the lessons learned and the positive experiences and approaches of both. In the case of India, the development of new approaches to contraception, immunologic and non-immunologic, is a high priority. These activities are also a high priority for USAID/India and especially for the Office of Population. In addition, both the GOI and USAID/India have experience in working together to support applied research aimed at the development of new contraceptive methods. Research in disease-related immunology is also a priority in India, and USAID/India is also funding these investigations.

Combining research of both types in one project complicates the management structure, divides scarce resources, and reduces the prospects for achieving significant results in either area. The current CD&RI Project documents this observation. Considering the need for contraceptive development as well as the tools to control the spread of major diseases in India, development efforts in both the areas need continued support. The research and development efforts in the different subject areas might be better supported under separate projects, however. It is worthwhile to ask why both research foci were combined in one project. For multiple reasons, it would be wise to think twice before initiating the same dual research program under one project in the future.

4.2 Research in Contraception and Disease-Related Immunology

The unnecessarily complex management structure has impeded project implementation. Since the proposed research is just getting under way, the project has not been able to present any research results. Still, as noted in Section 2.3.2, the proposed collaborative research in the areas of reproductive immunology, contraceptive development, and disease-related immunology offers considerable promise. The Indian and U.S. researchers involved in the program are internationally recognized, have significant accomplishments to their credit, are pursuing important avenues of investigation and, in some cases, have a good collaborative track record. It is regrettable that procedural matters have significantly delayed the research activities.

4.3 Center Development/Institutional Strengthening

As noted elsewhere (Section 2.3.2), the activities initiated under the CD&RI Project have not strictly contributed to "center development." At some institutions, centers were already in place; at others, center development was given little emphasis. For unclear reasons, the center concept does not appear to have been well communicated or understood, or uniformly supported by the participating institutions. In some respects, each viewed the project as an opportunity to carry out specific tasks in an already established procedural manner.

Although center development may have been a less than useful concept, the participating institutes saw project resources contributing to overall institutional strengthening. NII has taken full advantage of all project components, and IIS and PGIMER have applied for several awards under the project. Participation in the CD&RI Project appears likely to strengthen research and development capability to some degree at each of these participating institutions, irrespective of the presence or absence of an operating "center."

Still, it is very difficult to analyze the potential impact of these activities on institutional development. Only three of the four institutes chosen have actually initiated any activities.²³ Only NII has fully accessed the range of support available through CD&RI. The director of NII has made an effort to direct project activities in a cohesive and focused manner. As a consequence of the director's direct involvement, plus NII's participation in the previous project (CD:RI), activities have been initiated more rapidly than at other sites.

Without a full analysis of the institutional strengths and needs of each institution at project launch, it is not possible to determine the manner in which CD&RI has contributed to institutional development. It is apparent that the participating institutions have noteworthy capacities in the subject areas supported by the CD&RI project. On their face, Collaborative Research Awards, Fellowship Awards and Re-entry Grants, and Core Support Awards should enhance the R&D capacity of the participating institutions. From an institutional development standpoint, it remains to be determined whether these or other activities would have been more germane to achieving this objective. It is clear that any increased institutional capacity is a by-product, not a direct result, of the research activities.

4.4 Indo-U.S. Scientific Collaboration

Collaboration is clearly seen by both U.S. and Indian investigators as a principal benefit of the project. The Indian investigators interviewed eagerly endorse the project. The project provides access to first-rate U.S. investigators, well-equipped U.S. laboratories, new technical methodologies and scientific techniques, and the latest scientific equipment.

The CD&RI Project will have funded at least eight fellowships during the life of the project. This is a major contribution to Indo-U.S. scientific collaboration, since funds are seldom

²³The CDRI project is caught in the web of the IPR issue. Even in the absence of this issue, however, CDRI has proposed to utilize only the collaborative research component of the overall CD&RI project. CDRI is already organized along the lines of what was conceived in the project as a center. The institute has ample equipment and no apparent interest in utilizing either the Fellowship, Science Management Awards, or Core Support components.

readily available to Indian investigators to travel to the U.S. for brief periods of time, particularly in the flexible manner provided through the CD&RI Project.²⁴ Fellowships have allowed younger Indian scientists to travel to U.S. institutions to learn technologies that can be applied in laboratories in India. They also offer opportunities for Indian scientists to forge new collaborative linkages with U.S. scientists as well as other individuals who work at U.S. laboratories or universities. Relationships developed during these stays should enhance the collaboration and cooperation between Indian and U.S. scientists into the twenty-first century.

Several collaborations were in effect before the start of CD&RI and others have been instituted as a result of the project. As long as the Indian and U.S. collaborators continue to hold mutual research interests, the collaboration will most likely continue. The presence of resources through the project, however, allows the activities to take place more expeditiously than they otherwise could.

The Re-entry Grant component is a unique and critical component of the project. These funds allow the young Indian investigators who travel to the U.S. to apply the techniques acquired in the U.S. in their own laboratories upon their return to India. In the long-term, providing re-entry support speeds the rate at which technologies can be transferred, enhances the rate at which investigators can proceed with their research, and should lead to additional collaborative research activities. The Re-visitation Grant is also a unique contribution to strengthening research capacity. Fashioned on the Rockefeller Foundation model, it allows young Indian investigators to maintain active research ties with U.S. institutions.

U.S. investigators are keenly interested in having access to and participating in the development and testing of new contraceptives. Given the current low level of interest in contraceptive development in the U.S., access to the skills and commitment of Indian investigators is highly desirable. Working collaboratively gives U.S. investigators information on new areas of research and access to other research facilities. Likewise U.S. investigators in the field of disease-related immunology are enthusiastic about the project: India is still afflicted with many of the traditional pandemics, and thus collaboration with Indian counterparts offers U.S. investigators an opportunity to participate in research on disease-related immunology and the development of diagnostic kits.

4.5 Role of the CONRAD Program

CONRAD has to date played a major role in the development and implementation of the CD&RI Project. A significant percentage of the funds transferred to CONRAD have been set aside to support CD&RI research activities. CONRAD has made it possible for USAID/India to satisfy the U.S. costs associated with contraceptive research, which the mission might not have otherwise been able to do, and has provided a readily available source of funds to support the travel of U.S. and Indian investigators.

CONRAD's ability to fund the travel of fellows and to support the activities of U.S. investigators involved in the contraceptive development portion of the project are examples of the

²⁴Some travel funds are available through DBT and other Indian funding sources. However, to conserve foreign currency, the GOI has banned international travel since November 1990.

support and flexibility of the CONRAD component of CD&RI. In addition, it is noteworthy that three collaborative projects on the contraceptive research side of the CD&RI Project have already been funded, largely due to the presence and involvement of CONRAD and the NICHD peer review mechanism. In contrast, only one of the disease-related immunology projects, supported through the recently authorized PASA with OIH/NIAID (March 1991), has received funding.

The continuous and unflagging support, high degree of responsiveness, and positive efforts to overcome constraints to implementation signal CONRAD's commitment to supporting CD&RI activities and the good working relationships between CONRAD staff, the Office of Population, and USAID/India.

4.6 Role of USAID²⁵

Although collaborative research and the other components of CD&RI are important activities, it is the results of collaboration that should be the ultimate objective for both the U.S. and the GOI. It is clear from the description of the original CD&RI project and the later, amended CD&RI, that "development of contraceptive vaccines," i.e., products, was viewed as a key objective. The need for new contraceptive products and vaccines to control fertility and prevent or treat diseases was clearly identified as a priority by both the U.S. and the GOI.

Still, the GOI and USAID designed a project that has been capable only of "pushing" products along a very long research stream to market. Within the project, product ideas have been defined by the investigators and slowly developed as different research questions are raised and resolved. As in the case of Saheli, the new Indian non-steroidal contraceptive that was developed apart from the CD&RI Project, investigators largely determine when products are ready for market. Public sector enterprises, like Hindustan Latex, are then charged with producing and distributing the product. This is one approach to product development, though not necessarily the strategy employed by most private sector pharmaceutical companies in the West.

In most private sector commercial firms, the product idea, development budget, and pricing structure are set by the marketing department. Products are "pulled" from the research and development (R&D) division. Marketing develops a product profile based on research defining the need for the product, its ideal characteristics, and the overall market size. R&D is then asked to develop a product that meets the profile. In addition, the firms routinely canvass universities and research centers looking for concepts or product prototypes that respond to or could be adapted to meet market demand.

It is the "pull" component, about which U.S. industry has considerable expertise, that may be missing from the CD&RI Project. As currently configured, the pace of development -- necessarily lengthy because of the products under development -- is driven by the work plans of the investigators and the resources available through the project. Researchers are under no pressure to show results within a given period of time. In addition, it is unclear when or whether, and for what reasons, product ideas are embraced or discarded under the CD&RI Project.

²⁵See "Assessment of Indian Technologies for Reproductive and Other Health Applications," PIACT/PATH, January 1988.

It is readily recognized that developing contraceptives and vaccines is a lengthy process fraught with uncertainties, frustrations and, oftentimes, failures. Still, these R&D activities might move along more rapidly if they were carried out in the atmosphere of urgency that characterizes the operations of many private sector firms and responds to the fertility regulation and disease control objectives and priorities of both the GOI and the U.S. Private commercial firms have the expertise needed to overcome obstacles to product development, such as the issue of intellectual property rights, and have the ability to recognize the market potential for a given idea.

If a new project is developed to follow the current CD&RI Project, USAID/India should be certain that private sector management and marketing principles are used and that private sector firms are involved. Thought should also be given to involving Indo-U.S. firms that have experience in bringing contraceptive products and vaccines to the marketplace. The activities supported under CD&RI, i.e., Indo-U.S. collaborative research and fellows study and travel, should be continued, but new options for managing these activities, different from the cumbersome mechanisms currently employed by USAID and the GOI, should be identified and used.

**5. Principal Conclusions, Recommendations,
and Lessons Learned**

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5. Principal Conclusions, Recommendations, and Lessons Learned

5.1 Conclusions

5.1.1 Management Structure

Failure to develop, follow and/or promulgate policies and procedures relevant to the management and implementation of the project has seriously impeded the pace of implementation.

The overall structure of the project, set forth in the Project Paper Amendment and reviewed in the first meeting of the JWG, offered an unnecessarily complex approach to implementing the project. Management structure needs to be based on the needs of the project and not be overly cumbersome.

The responsibility of managing the day-to-day activities of the project was assigned to the secretariats/technical coordinators, primarily resident in India, but the composition of the secretariats and the authority of its membership was left undefined. In addition, until recently, no single individual resident in India with recognizable authority had been assigned or had assumed overall responsibility for the project on either the U.S. or GOI side. Some procedural and managerial definitions have evolved during the course of the project, but many implementation issues remain to be addressed, e.g., a system for exchanging information between USAID/India and GOI/DBT, mechanisms for communicating with Indian and U.S. investigators, etc.

The JWG, the policy-making body of the project, has met only twice since the CD&RI Project was initiated.²⁶ A serious commitment to defining and achieving the objectives of the project and resolving the implementation issues warrants more frequent and productive meetings.

5.1.2 Implementation

Difficulties in six principal areas have impeded implementation: (1) the development of center grants, (2) peer review of the collaborative research proposals, (3) the execution of a PASA with OIH/NIAID, (4) the definition of intellectual property rights, (5) the procurement of U.S. scientific equipment according to USAID procedures, and (6) the transfer of U.S. funds to the GOI by USAID/India.

The first three have been resolved over time; the last three have been addressed but no effective resolutions have been achieved (see Chapter 3 for details).

5.1.3 Scientific Focus

Unlike the predecessor CD&RI Project, this project has a dual scientific focus. Without systems in place to ensure linkages between the two research areas, proposals for research

²⁶A third meeting was scheduled for early 1991 but had to be canceled due to the Gulf War.

in one area are not reviewed with an eye toward the other. Consequently, advances in one area do not automatically benefit the other.

The CD&RI Project was initiated to support research in contraceptive development, reproductive immunology and disease-related immunology. To date, eleven proposals have been submitted in the collaborative research category of the project. Six are in the area of reproductive immunology, one is in the area of non-immunological contraception (spermicides), and four are in disease-related immunology. The contraceptive proposals are focused on developing contraceptive vaccines. The four projects in disease-related immunology involve developing diagnostic tests.

Four of the six collaborative relationships in reproductive immunology existed prior to the project; the researchers had received funding from other Indo-U.S. sources. Still, funding under the CD&RI Project has been critical to completing some promising research and obtaining the information needed to proceed toward the development of potential new contraceptive products. Several collaborations in disease-related immunology were formed through the project.

Although it was hoped that knowledge gained from these research activities would be shared across the disciplines, no formal mechanism exists to encourage this dialogue. It is difficult to understand how the two distinctly separate research foci -- contraceptive development and research in disease-related immunology -- could be joined in one center or institution without a strong coordination mechanism. Since the directors of the participating Indian institutions were named to the JWG, it may have been presumed that each would ensure adequate coordination in his respective institution. With one exception, this has not taken place.

Finally, irrespective of the focus of research, since the collaborative research projects were for a three-year duration, the activities proposed and in many cases only recently approved are unlikely to be completed prior to the current PACD (May 31, 1993).

5.1.4 Center Development and Institutional Strengthening

The U.S. side presumed that the development of a "center" was fundamental to the implementation of the activities supported under the project. The definition of a "center" was not clearly articulated and communicated to the participating institutions at the start of the project; only the activities of a center were noted (e.g., collaborative research, etc.). The definition of the center concept evolved during the life of the project; there is evidence to suggest that the concepts of center development and institutional strengthening were used interchangeably.

Fellowships

Preliminary findings suggest that fellowship activities have been well planned. Fellows have or are scheduled to acquire specific skills that will benefit their institutions and have or are likely to establish collaborative relationships with U.S. investigators.

Science Management Awards

No institute has availed itself of the science management awards, designed to identify and groom the next generation of department chairmen and institute directors. In part, this is because the purpose was not clearly communicated to participating institutions and in part, because in India, a mid-career laboratory-based researcher is unlikely to accept an administrative position.

Core Support

Conceptually, the Core Support component supports institutional strengthening. Since the center concept (see above) was imprecisely understood by the Indian institutions involved in the project, it is questionable whether the formula proposed was the best approach to determining Core Support.

5.1.5 The Role of USAID

USAID has played a critical role in expanding the research capabilities of the four Indian institutions involved in the project and in the definition and implementation of the CD&RI Project.

USAID support has been used to bring Indian and U.S. researchers together to develop collaborative proposals in contraceptive development and disease-related immunology. USAID has provided substantial support to purchase scientific equipment that will facilitate the implementation of the proposed research and increase the overall research capabilities of the four institutions in the CD&RI Project. The fellowships supported under the project represent a significant enhancement of trained manpower and offer, through re-visitation, the prospect of establishing ongoing collaborative relationships between young Indian investigators and U.S. researchers.

The staff of USAID/India's Office of Health, Population, and Nutrition and a key individual in the Office of Population in USAID/Washington have played seminal roles in the definition and implementation of the CD&RI Project. Staff turnover on the USAID/India side has influenced the implementation process, however. In the absence of written guidelines, it is only staff continuity that can establish and maintain consistent implementation approaches.

5.2 Recommendations for the Remaining Project Period

The recommendations that follow are based on the conclusions presented above and are actionable during the remaining period of the project. In some cases, no recommendations have been formulated.

5.2.1 Management Structure

Prior to the next meeting of the JWG, scheduled to take place in November 1991, the project coordinators from USAID/India and DBT should meet to develop in *written* form a draft of management procedures and communication strategies applicable to the implementation of the CD&RI Project. This draft should be widely circulated among those involved in the project and reviewed and approved at the next JWG meeting. Also, given the management expertise available in India and the U.S., and the project's appreciation of the importance of "science management," some consideration might be given to adding this skill to the JWG membership. Thought should also be given to including persons with expertise in the commercialization of contraceptives and vaccines. Whether the JWG should have an altered composition is a question worthy of some discussion at its next meeting.

5.2.2 Implementation

Completion of the proposed research requires a no-cost extension beyond the current PACD. It is recommended that the new PACD be set for September 30, 1994. Ensuring that the project is completed in a timely and orderly fashion warrants satisfying A.I.D.'s administrative requirements. The recommendation that the PACD should be extended should be reviewed and acted upon at the next JWG meeting. To expedite project implementation and ensure that activities have fruitful outcomes, the JWG should meet at least annually during the period remaining in the project.

Intellectual Property Rights

Unless mutually agreeable language on IPR can be developed prior to the next JWG meeting and approved at the meeting, the CDRI (Lucknow) proposal should be dropped and the funds re-allocated among the three other participating institutions. Action on this matter should be completed before the next meeting of the JWG.

Procurement

USAID should convene a workshop within 60 days of the completion of the evaluation whose prime focus would be general A.I.D. procurement policies and regulations. Investigators, administrators, and procurement officers from the institutions involved in the CD&RI Project, as well as relevant staff of DBT, should be invited to attend. Those attending the workshop should also have the opportunity to review their individual procurement issues with appropriate USAID/India officials.

A portion of this workshop should be reserved to consider other implementation-related issues, e.g., reimbursement, the status of approvals, accessing core support, etc. DBT and USAID/India should jointly prepare the agenda for this meeting (see Section 5.2.3 for additional suggestions for this meeting).

Transfer of Funds

The GOI should be requested to transfer the fully authorized budget amount to the participating institution shortly following budget approval. USAID/India should agree that vouchers presented by DBT for A.I.D. authorized activities should be satisfied using the exchange rate in effect on the date that the expense occurred rather than the date on which the voucher is presented.

5.2.3 Scientific Focus

No new proposals should be entertained and currently approved activities should be implemented without further delay.

The project's tortuous experience in reviewing and approving proposals indicates that this is the only feasible course of action, even with an extended PACD.

If the CDRI (Lucknow) proposal cannot be funded, the amount allocated should be distributed among the remaining institutions to complement and/or supplement already approved activities. In the event that it becomes clear well in advance of the November 1991 JWG meeting that intellectual property rights issues cannot be resolved and that the CDRI (Lucknow) proposal

cannot be funded, the current collaborating researchers and fellows should be asked to specify and justify additional financial requirements. These would be acted upon at the next JWG meeting. In the event that the IPR issue is not resolved before the next JWG Meeting, the JWG should authorize USAID/India to determine how the US dollar funds will be allocated.

In the light of implementation delays, the target dates for completing each collaborative research proposal need to be re-examined by the investigators. Timelines should be revised and submitted to DBT and USAID/India, as well as the CONRAD Program and the Office of Population, on or before September 15, 1991.

A portion of the proposed procurement workshop should be reserved to define the content and timing of the project progress reports that must be submitted.

The annual CD&RI scientific meetings proposed in the project paper should be organized by USAID/India and DBT, take place annually, be attended by Indian CD&RI researchers and fellows and, if possible, occur immediately prior to or following the annual JWG meetings.

Those attending should present the results of their ongoing research and exchange information. If possible, and if funds are available, a scientific workshop, attended by both U.S. and Indian investigators and researchers, should be convened at the end of the project. The timing and content of these meetings should be discussed at the proposed procurement workshop.

Although research in disease-related immunology addresses important health problems, control of population growth in India and fundamental applied research directed toward the development of contraceptives should receive top priority under any future CD&RI Project, beyond FY 1994. Disease-related immunology should be funded in a separate project.

5.2.4 Center Development and Institutional Strengthening

Fellows

To the extent possible, blanket authorizations should be given by the GOI to fellows and collaborative researchers for travel approved under the project. This action should occur within 60 days of the CD&RI midterm evaluation.

Science Management Awards.

To take full advantage of the Science Management Awards component of the CD&RI Project, the JWG must set down definitions and implementation guidelines, as called for during the first JWG meeting. These should be communicated to each center within two weeks of the conclusion of the next meeting of the JWG. The JWG should give special attention to the age and career status of the candidates proposed and selected.

5.2.5 The Role of USAID

Staff from various mission offices should make themselves available for the next three months to attend the proposed workshop and to work with the staff of the Health, Population, and Nutrition Office and the CD&RI Project to develop the management and implementation procedures applicable to the project. Since the majority of project activities remain to be implemented, the

active involvement and assistance of USAID/India staff is essential. Finally, if elements of any of the current proposals require additional U.S. peer review, the GOI should be requested to allow USAID/India to choose the mechanism.

5.3 Lessons Learned

The lessons learned from the experience of developing and implementing the CD&RI Project are very basic and should be applied in developing any future projects.

A program design that has dual scientific foci (in CD & RI, contraception and disease-related immunology) complicates the management structure, divides scarce resources, and reduces the prospects for achieving significant results in either area. A good project must have a clear focus, simple organizational and management structures, and proven, established, and well-understood implementation procedures.

Project designs should be consistent with the time frame of the project and the funds available. Underfunding was identified as a major problem for CD:RI. This problem was not corrected in the follow-on; rather, CD&RI was budgeted at barely twice its predecessor (\$2.2 million) although its scope was dramatically expanded (i.e., dealing with four to six institutions and implementing four different activities). All components of this project are justifiable but funding should have been commensurate with the magnitude of the effort.

When multiple agencies are involved in project management (USAID/India, DBT, A.I.D./W, CONRAD, NIAID, NICHD), the roles and responsibilities of each and the systems for communicating must be clearly defined. Several delays occurred, e.g., with regard to procurement, fellowship travel and support, etc., because the systems needed to accommodate the rules and regulations of the GOI and A.I.D. were not defined during the design stage of the project.

Projects supporting collaborative research require that procedures and timelines for peer review, approval and funding should be defined at the start of the project and strictly followed throughout the course of implementation. In the matter of peer review, USAID and the GOI should develop their respective systems using internationally recognized experts in the areas of investigation who should be identified at project start-up. This group should be given the responsibility to review and approve all proposals and the means necessary to meet this commitment.

Access to a flexible, centrally funded project like CONRAD provides a bilateral project with the assistance required to facilitate implementation and enhance project impact.

If intellectual property rights issues cannot be resolved satisfactorily during the definition of a project, USAID must re-think the focus of collaborative applied research projects. Instead, these projects might focus on training young investigators and strengthening the research capabilities of selected institutions.

Appendices

Appendix A
Scope of Work

Appendix A

Scope of Work

Contraceptive Development and Research in Immunology (CD&RI) (386-0500) PIO/T for Mid-term Evaluation Consultants

BACKGROUND

The Contraceptive Development and Research in Immunology Activities (CD&RI) was established in 1988 by USAID/India in cooperation with the Government of India (GOI). The CD&RI is an extension of an earlier Indo-U.S. project initiated in 1985, to support research on immunological approaches to control of reproduction. The original project was called "Contraceptive Development: Reproductive Immunology." In the first phase, the project had \$1.00 million funding from USAID and \$0.33 million from the Government of India. USAID funding was in the form of an outright grant to the Program for Applied Research in Fertility and Reproduction (PARFR), and the sole Indian institution participating in the project was the National Institute of Immunology (NII), New Delhi. In August 1988, the project was restructured, renamed and extended up to May 31, 1990. The scope of the restructured project was broadened beyond contraceptive development and reproductive immunology to include research in disease related immunology.

A Project Agreement Amendment was signed with the GOI on 8 August 1988 (A.I.D. Project Number 386-0500). A.I.D. added \$2.2 million in bilateral grant funds and the GOI \$0.74 million. A.I.D. had also obligated \$3.4 million as unilateral project funds to buy into the A.I.D. centrally funded Contraceptive Research and Development Program of the Eastern Virginia Medical School (CONRAD), Norfolk, Virginia. In May 1990, the GOI agreed to permit CONRAD to support the costs of some CD&RI project activities. In early 1990, the Project Assistance Completion Date (PACD) of May 31, 1990 was again extended to May 31, 1993.

The purpose of the CD&RI project is to support laboratory studies in the areas of reproductive and disease related immunology.

In order to achieve this purpose, collaboration between the Indian institutions and U.S. centers of excellence in research in contraception and/or immunology is designed to ensure technology transfer in fertility regulation and disease related immunology. From a long term perspective, support of the Indo-U.S. scientific relationship is also important. It is hoped that the project will foster strong supportive links between individual U.S. and Indian scientists. These linkages are valued because they can ensure continued cooperation and technology transfer between the Indian and U.S. scientific communities long after the project has ended. It is also expected that the project will develop broad and

self-sustaining linkages between the agencies of the U.S. and Indian Government involved in medical biotechnology research: the U.S. Public Health Service (USPHS), the National Institutes of Health (NIH), U.S. Universities, the Indian Department of Biotechnology (DBT), the Indian Council of Medical Research (ICMR), and counterpart institutions in India. On the Indian side an important additional objective is to broaden the base of Indian scientific expertise by involving younger scientists in the program. As provided for in the agreement with the GOI, policy and oversight for the CD&RI project is provided by an INDO-U.S. Joint Working Group (JWG). The JWG is co-chaired by the Secretary, DBT, for India and by the Director, USAID/India, for the United States. The Indian JWG members include the heads of the Centers participating in the program, as well as representatives of DBT and ICMR. Both DBT and ICMR are GOI Institutions that support and administer biomedical research. The US members include representatives of all the US institutions that support the project: A.I.D., CONRAD, the National Institute of Allergy and Infectious Diseases (NIAID), and the National Institute of Child Health and Development (NICHD). The Technical Coordinators/Secretariat designated for the respective sides have day to day responsibility for implementation of the CD&RI. The Indian Technical Coordinators/Secretariat is appointed by DBT. The U.S. Technical Coordinators/Secretariat include representatives of NIAID, USAID, and USPHS.

U.S. technical and management support to the project is provided by NIAID, NICHD and CONRAD. NIAID supports the U.S. side costs of collaborative research and fellowships in immunology and provides expert services in peer review and grants management. For this purpose USAID has negotiated a Participatory Service Agreement (PASA) with NIAID. USAID's Cooperative Agreement with CONRAD and the related arrangement with the NICHD supports the contraception activities. CONRAD pays for the US side costs of collaborative research and fellowships and provides grants management services, while NICHD organises the peer review of research proposals. All these administrative mechanisms complement each other.

The Indian institutions (Centers) participating in the project were selected by the JWG on the recommendations of DBT. They are the National Institute of Immunology (NII), New Delhi; the Indian Institute of Science (IIS), Bangalore; the Post Graduate Institute of Medical Education and Research (PGIMER), Chandigarh; and the Central Drug Research Institute (CDRI), Lucknow. Each of these institutions has been awarded a grant with which to pursue activities defined under the project. The institutions collaborate with U.S. institutions of their choice and if desired, assistance is provided in identifying suitable collaborators. The grants to the Indian institutions are as follows: \$1.0 million to NII, \$0.5 million to IIS, \$0.4 million to CDRI, and \$0.3 million to PGIMER.

Project funds may be used by the Indian Centers to conduct Collaborative Research with US centers of excellence in research in contraception and immunology; develop the capacity for collaborative research of young scientists through the Fellowship Awards; attract expatriot Indian scientists back to work in Indian laboratories through the Re-entry Grant Awards; train mid-career scientists wishing to make a change from the bench to science administration through the Science Management Awards; and enhance the research facilities available at the Center with Core Support funds. Each center may choose a mix of these institution strengthening activities based on its own assessment of needs. However the availability of funds for Core Support is directly related to expenditures for Fellowships and Science Management Awards.

Current Status

The JWG has met twice since the project was restructured and its third meeting is to be re-scheduled. At the first meeting (November, 1988), center grant allocations were made to the NII, IIS and PGIMER; Center Grant Application guidelines and a format for submission of collaborative research proposals were developed; scientific exchange visits for the purpose of proposal development were endorsed; and NII's request for \$180,000 for the purchase of a flow cytometer as part of a Re-entry and Core Support grant was approved. At the second meeting (July, 1989), Centers were asked to draw up Center Plans rather than Grant Applications. The role of the Plan was defined as that of a project management tool for the approval of sub-activities, monitoring of progress and for evaluation of the program. At this meeting the JWG called upon the CDRI to participate in the project as a fourth Center and to submit a Center Grant Plan for about \$0.4 million. Collaborative research proposal applications received by the Secretariats after the first JWG meeting were discussed and approved in principle subject to satisfactory peer review. Four Fellowship applications were approved subject to identification of appropriate host laboratories and detailing of visitation schedules.

Currently, project activities at the four Centers are at different stages of development. All the Centers have submitted Center Plans, but not all have received approval for component activities. There are a total of 11 collaborative research proposals (7 in contraception and 4 in immunology) which are candidates for funding. Three proposals each in contraception and immunology have been cleared by peer review. The rest are either in the initial or second round of reviews. However, to date, not a single research proposal on the Indian side has received funding, and research has therefore not commenced. Eight fellowship applications in all have been approved. There has been no apparent interest in the Science Management Award, and most Centers have expressed a desire to avail of Core Support funds to the maximum extent possible.

ARTICLE I- TITLE

Contraceptive Development and Research in Immunology Project (386-0500)

ARTICLE II- OBJECTIVE

To provide 2 consultants in a team of 4 persons which shall evaluate the project as restructured in August 1988 and make recommendations to USAID regarding modifications in the current project design, implementation modalities, and future role in the area of collaborative Indo-U.S. scientific research.

ARTICLE III- STATEMENT OF WORK

The contractor shall conduct an evaluation which addresses the following purpose, central issues and key questions.

Purpose of Evaluation

The broad purpose of this mid-term evaluation is two fold, i.e. first to assess current status of the project and second to explore implications for the future. Specifically, the purposes are: (a) assess progress towards achievement of project purpose and identify project achievements to date, (b) examine project implementation to identify mid course corrections and critical areas where additional inputs are required over the next two years, (c) review the project within the context of current priorities and interests of A.I.D. and the Government of India (GOI) and suggest appropriate revision in project orientation/purpose, strategies, tasks and timeframes, (d) suggest the form in which activities initiated under this project should continue beyond its PACD to ensure the sustainability of the program as a whole.

A. Central Issue: Has the concept of the Center been useful and has the idea of institutional strengthening through the concept of the Center Grant been successfully implemented?

Specific Questions: (i) What specific areas of institutional capability have been strengthened as a result of this project? (ii) What are the specific areas where transfer of technology has occurred? (iii) Do the activities undertaken by each Center have a common focus? (iv) CD&RI Centers were pre-selected by a committee instead of being competed. What implications did this have for the project? (v) Given the current status of the science and the strengths and goals of each Center, have the Centers chosen potentially fruitful areas for research? (vi) Have Centers chosen the most appropriate mix of activities from the view point of institutional strengthening? (vii) What are the important areas of research in fertility regulation and disease related immunology

where capability needs to be created and or further strengthened in each Center? (viii) How well are the CD&RI Fellowship and Science Management awards being used by the Centers? (ix) How well have the Fellowship activities been planned and are they likely to produce the desired results? (x) Are infrastructural facilities and organizational systems at the Centers adequate and supportive of research?

B. Central Issue: Have collaborative linkages between U.S. and Indian scientists and institutions been effectively forged and are they sustainable beyond the PACD of the project?

Specific Questions: (i) Why is collaboration necessary for the research funded under this project? (ii) How are the Indian and U.S. scientists actually collaborating at the different stages of design and implementation of the research? (iii) What is each party contributing to the development and implementation of research? (iv) Is the collaboration mutually beneficial? (v) What has been the impact of collaboration on scientific training and experience, and its resulting "scientific manpower" enhancement in India and the United States? (vi) What do individual investigators and agencies involved in the project see as obstacles to collaborative research? (vii) In promoting scientific research has the project been successful in matching the areas of respective competence of Indian and U.S. scientists? (viii) What plans and efforts have been made to ensure sustainability of collaboration? (ix) What spin off benefits have resulted from this project?

C. Central Issue: How appropriate, effective and sustainable in India are the mechanisms instituted by this project for assuring scientific integrity and quality of biomedical research?

Specific Questions: (i) How do the mechanisms established for the CD&RI project compare with the DBT/ICMR systems that existed before? (ii) Is there evidence to suggest that the systems established for CD&RI will eventually be extended to other scientific research programs both private and public in India?

D. Central Issue: How effective is the management structure devised for the project, involving a multiplicity of supporting agencies and levels of decision making (JWG, Secretariats, etc.)?

Specific Questions: (i) What are the strengths and weaknesses of this model? (ii) Has the multiplicity of agencies involved in decision making and providing support resulted in unnecessary delay and or compromise? (iii) Has the structure given the project added flexibility in responding to the evolving interests and requirements of the

participating agencies? (iv) What role has the JWG/Secretariats/ Technical coordinators played? (v) What is the role of NIH institutions (NICHD, and NIAID) in this program and how effectively are they playing it? (vi) Has an appropriate and effective peer review mechanism been established in India and the U.S.? (vii) What are the strengths and weaknesses of the mechanism?

E. Central Issue: Has the project effectively integrated activities funded out of bilateral project money as well as unilateral project money in the CONRAD India Buy-in?

Specific Questions: (i) What is the role and contribution of CONRAD in the CD&RI project? (ii) Evaluate the effectiveness with which CONRAD has played this role.

F. Central Issue: How critical is USAID involvement, beyond the PACD, in ensuring sustainability of the program as a whole and its long term payoffs? Will any A.I.D. inputs be required after the PACD?

Specific Questions: (i) What were the expected (anticipated) short and long term outputs of the program and how realistic/feasible are they? (ii) What is the likelihood that activities planned can be successfully completed within the PACD? (iii) Is an extension of time frame necessary? (iv) What is the likelihood that research started with project funds will continue beyond the PACD? (v) What can we realistically hope to accomplish in this program before the PACD? (vi) What is the project's potential for near term success in developing a method of fertility regulation or a break through in immunology which could be applied on a wider scale to accomplish stated project purposes and goals?

Methods and Procedures

The central issues listed above relate to the sustainability of collaborative research linkages, mechanisms to ensure scientific integrity and quality, management structures to take appropriate decisions and actions, research activities in terms of their chances of completion and fruition before and after the PACD. The examination of these issues is also expected to suggest some critical inputs from USAID before and/or after the PACD in order to ensure sustainability.

Unlike other projects primarily located and implemented in the host country, this project involves scientists and institutions engaged in the collaborative research ventures both in India and the U.S. The

evaluation team, therefore, will have to meet and discuss particularly the issues "B", "D" & "E" with collaborating scientists and institutions both in India and the U.S.

Keeping the central issues and key questions in view the following methods are suggested for the use of evaluation team.

i) Available Documents such as:

- Project paper and amendments
- Minutes of Joint Working Group
- Research proposals approved
- Peer Review summaries
- NIH/CONRAD grant awards & GOI sanction documents
- Trip reports by researchers
- Papers/articles presented/published by researchers
- GOI policy-relevant papers on Biomedical technology & research

ii) Meetings and Discussions with:

- Main collaborating scientists and centres in India and the U.S.
- Key officials from A.I.D. NIH and OIH, selected US & Indian JWG members, JWG Secretariats, DBT, ICMR and CONRAD staff.

iii) Visits and interviews (personal or telephonic) with:

- Scientists/Fellows and heads of Centres in India
- Scientists and authorities directly responsible for A.I.D.-supported research projects
- U.S. collaborating scientists

ARTICLE IV- REPORTS

1. The contractor will prepare a report of the team findings on all SOW issues listed in ARTICLE III based on an outline to be cleared by HPN/BRT and PDPS/PPE of USAID/India early on in the assignment. The final report will include but is not limited to the following sections:

- Executive summary of findings, recommendations and lessons learned
- Project identification data sheet
- Table of contents
- Body of the report to be determined
- Conclusions/recommendations
- Annexures
- Evaluation summary

2. Two (2) copies of a draft report will be submitted to the Chief, PDPS/PPE at least three (3) working days prior to the consultant team's departure. In addition, one (1) original and ten (10) copies of the final report will be forwarded by the contractor to the Chief, PDPS/PPE within 10 working days of the receipt, by the contractor, of A.I.D.'s comments on the draft report.

2. The contractor will debrief the Director of HPN (or designate) and HPN/BRT staff, and the Chief, PDPS/PPE of its findings and recommendations prior to completing the draft report.

3. The contractor will conduct two exit briefings: one for appropriate USAID staff and the second for appropriate GOI officials. As determined by the Chief, PDPS/PPE and the Project Officer, HPN/BRT, such briefings will include a presentation of a matrix specifying major findings, conclusions, and recommendations of the draft report. Upon return to Washington, the contractor will brief the U.S. Secretariat on the evaluation results.

4. The contractor will, working with the Chief, PDPS/PPE and his staff, prepare in draft according to the APRE Bureau guidelines, the AID Evaluation Summary (ES), Part I ('Evaluation Abstract') and Part II ('Summary of Evaluation findings, conclusions, and recommendations').

ARTICLE V - RELATIONSHIPS AND RESPONSIBILITIES

"The contractor shall be subject to the Technical Direction of the HPN/BRT project officer. The Chief of PDPS/PPE will serve as a primary point of contact and facilitator to the evaluation team.

USAID will provide at no cost to the contractor the services of two local hire Indian experts for approximately 18 person days each during the period June 21 to July 11. The India experts' contracts will provide for their supervision by the team leader under this contract. Their contracts will provide funding for travel throughout India in accomplishment of the evaluation.

The experts have particular expertise in reproductive biomedicine.

In addition, USAID and DBT representatives will, to the extent possible, act as technical and administrative resource persons to the team."

ARTICLE VI - PERFORMANCE PERIOD

This mid-term evaluation is scheduled to begin o/a June 17, 1991, and the contractor is expected to provide a draft report and debriefing for USAID/India o/a July 11. The final date of commencement will be set in consultation with team members. The tentative time schedule will be as follows:

<u>Activity</u>	<u>Days</u>
A. <u>In the U.S.</u>	
i) Interaction with US JWG members, Secretariat, collaborating scientists and CONRAD	4
ii) Finalization of report and briefing of US Secretariat (for team leader only)	4
B. <u>In India</u>	
i) Travel to India, AID briefing, studying documents and planning work with Indian team members/visits in Delhi	6
ii) Site visits to Chandigarh, Lucknow and Bangalore	7
iii) Preliminary A.I.D. debriefing, draft report writing, final briefing of Government of India and USAID	5
iv) Travel to the U.S.	1
	--
TOTAL (A&B) for team leader	27
for US scientist	23

ARTICLE VII - WORK DAYS ORDERED

<u>Position</u>	<u>Work Days</u>
U.S. Team Leader	27
U.S. Scientist	23

ARTICLE VIII - A.I.D. ILLUSTRATIVE BUDGET

See attachment B

ARTICLE IX- SPECIAL PROVISIONS

- A. **Duty Post:** Washington D.C.and selected U.S. sites 4- 8 days
New Delhi and selected Indian sites 19 days
- B. **Language Requirements and other Required Qualifications:** None
- C. **Access to Classified Information:** The Contractor shall not require or have access to any government classified documents.
- D. **Logistical Support:** USAID/India will provide detailed background material to the consultants upon or before arrival in India. The contractor will be responsible for providing secretarial support and for making domestic and international travel arrangements.

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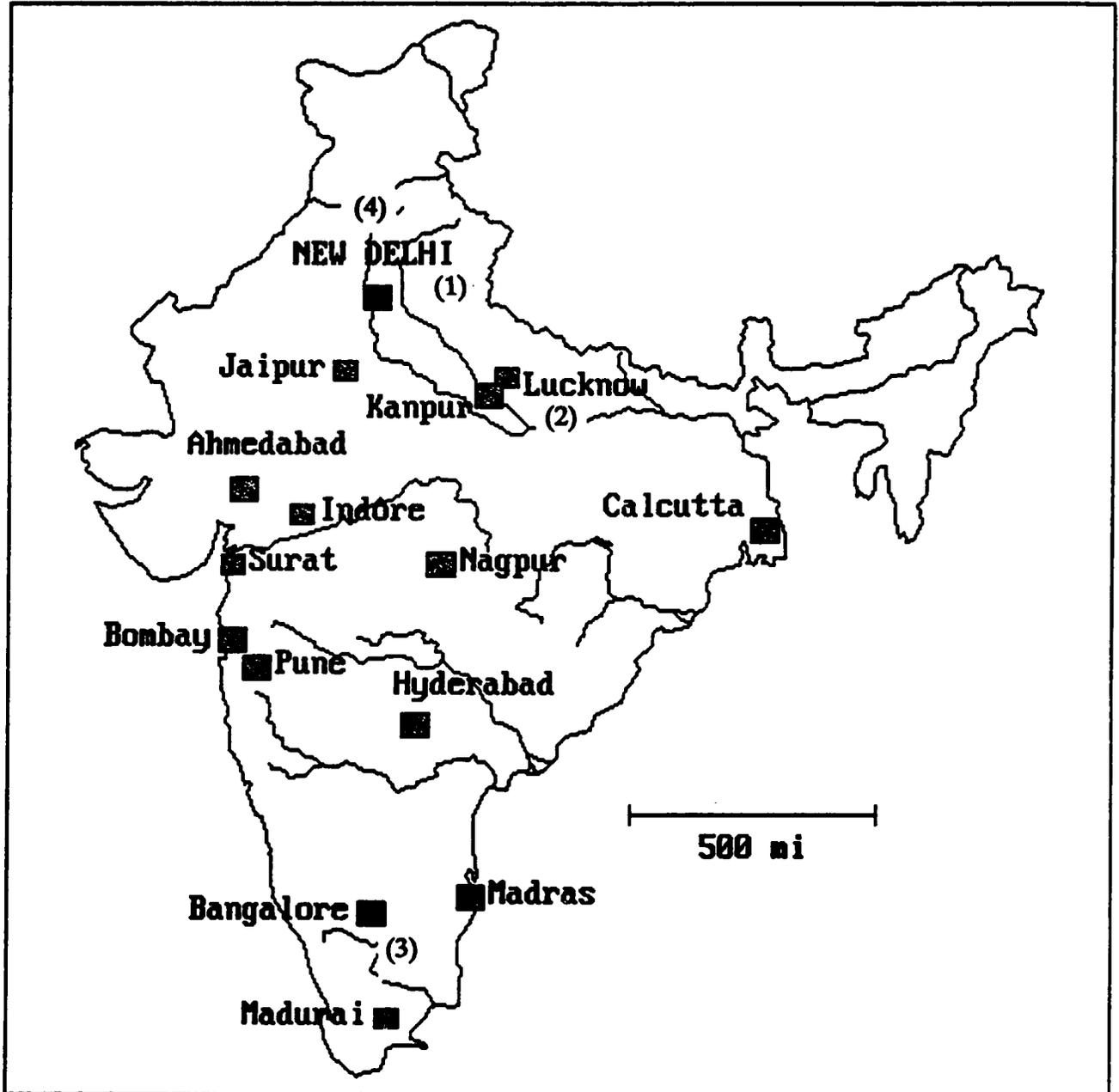
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Appendix B

Locations of Indian Institutions Participating in the CD&RI Project

Appendix B

Indian Institutions Participating in CD & RI Projects



- (1) National Institute of Immunology (Delhi)
- (2) Central Drug Research Institute (Lucknow)
- (3) Indian Institute of Science (Bangalore)
- (4) Post Graduate Institute for Medical Education & Research (Chandigarh)

Appendix C
Persons Interviewed

Appendix C

Persons Contacted

USAID/India

Walter Bollinger, Director
Steve Mintz, Deputy Director
Dr. John Farrar, HPN Office
Constance Carrino, HPN Office
Rekha Masilamani, HPN Office
Dr. B. R. Patil, PDPS/PPE Office

U. S. Embassy - New Delhi

Dr. David Madden, Science Attache
Manmohan Lal Saxena, Program Advisor (USPHS)

CONRAD Program (Washington, DC)

Dr. Henry Gabelnick, Director

Office of Population - A.I.D./Washington

Jeffrey Spieler, Biomedical Scientist

National Institutes of Health

Dr. Gabriel Bialy - NICHD
Dr. Karl Western - NIAID
Dr. Joe Albright - NIAID
Dr. Alexandra Fairfield - Fogarty International Center

Ministry of Science and Technology Department of Biotechnology (DBT)

Dr. S. Ramachandran, Secretary
Dr. Manju Sharma, Adviser
Dr. B. M. Ghandi, Principal Scientific Officer
Arvind Duggal, Administrator
S.R. Sapra, Consultant

Central Drug Research Institute - CDRI (Lucknow)

Dr. V. P. Kamboj, Deputy Director
Dr. A. P. Bhaduri, Deputy Director - Medicinal Chemistry
Dr. S. Ray, Assistant Director - Medicinal Chemistry
Dr. N. M. Khanna, Research Scientist
Dr. A. K. Roy, Scientist
Dr. B. S. Setty, Deputy Director - Endocrinology
Dr. R. C. Srivastava, Deputy Director - Toxicology
Dr. R. C. Srimal, Deputy Director - Pharmacology

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Indian Institute of Science - IIS (Bangalore)

Dr. N. R. Moudgal, Professor - Center for Reproductive Biology
Dr. R. R. Dighe, Assistant Professor - Center for Reproductive Biology
Dr. G. S. Murthy, Principal Research Scientist - Biochemistry
Dr. R. Nayak, Associate Professor - Microbiology
Dr. O. M. Prakash, St. Martha's Hospital (Bangalore)
Dr. P. V. Subba Rao, Professor, Department of Biochemistry
G. Vijayaraghavan, Financial Controller
Dr. G. Padmanaban, Chairman - Biological Sciences
Dr. R. Manjunath, Assistant Professor - Biochemistry
Dr. N. Appaji Rao, Chairman - Biochemistry
Dr. P. R. Adiga, Professor - Center for Reproductive Biology
Dr. K. P. Gopinathan, Chairman - Microbiology and Cell Biology, Center for Genetic Engineering

Post Graduate Institute of Medical Education and Research - PGIMER (Chandigarh)

Dr. Shobha Sehgal, Professor - Professor and Head of Department of Immunopathology
Dr. N. K. Ganguly, Professor and Head - Experimental Medicine
Dr. Anil Grover, Assistant Professor - Cardiology

Appendix D

Progress of Collaborative Research and Fellowship Activities

CD&RI Project Progress of Collaborative Research Activities

CD&RI Project Progress of Collaborative Research Activities																
	1988				1989				1990				1991			
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Collaborative Research																
Setty/Alexander									S	P			U	I		
SubbaRao/Metcalf										P			U	I	+	
Nayak/Ellner						S					P		U	I		+
Moudgal/Bardin										P				U	I	+
Talwar/Lal						P							U	I		+
Shaha/Catteral							S			P	U	I	+			
Upadhyaya/Anderson						P				U	I		+			
Gupta/Sacco					P					U	I		+			
Sehgal/Dunbar						S						P	U		I	+
Sehgal/Herr											P		I			+
Ganguly/Gray												P	U	I		+

Key to Collaborative Research Activities:

- S - Incomplete proposal submitted
- P - Collaborative Proposal submitted
- U - U.S. peer review complete
- I - Indian peer review complete
- + - U.S. and Indian labs funded

The gray line in the third quarter of CY 1988 indicates project start-up. The gray lines in the second and third quarters of CY 1991 reflect reports that DBT has or expects to approve proposals and fund the research.

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**CD&RI Project
Progress of Fellowship Activities**

	1988				1989				1990				1991			
	1	2	3	4	1	2	3	4	1	2	3	4	1	2	3	4
Fellowships																
Ravindranath						A			D	V						
Suri						A			D	+						
Raghupathy						A			D					+		
Das										A			D			
Salunke						A									+	
Manmohan Singh											A	D	V			
Arora									A	D	V				+	
Labhshetwar	W	I	T	H	D	R	E	W								

Key to Fellowship Activities

Fellowships

- A - Application submitted
- D - Details finalized
- V - Visit Commenced
- + - Approval Given by DBT to Travel

The gray line in the third quarter of CY 1988 indicates project start-up. The gray lines in the second and third quarters of CY 1991 reflect reports that DBT has or expects to approve fellowship applications and travel to the U.S.

Appendix E
Summary of Collaborative Research Proposals

Appendix E

Collaborative Research Project Summaries

Below is a summary of each of the 11 collaborative research projects which have been submitted under the CD&RI project. These summaries also include some mention of the potential short-term and long-term outcomes of each project.

1. *Identification of Sperm Antigens that Regulate Fertility.*

Dr. Chandrima Shaha, NII
Dr. James Catterall, the Population Council

Summary: The rationale for attempting to develop an anti-sperm vaccine for controlling human fertility is based in the fact that infertility can be induced experimentally in animals by immunization with sperm. In addition, anti-sperm antibodies are thought to be causal in some cases of human infertility. In the later case, no other side effects are noted in these patients. Therefore, a vaccine against a sperm-specific antigen has the possibility of being a safe and effective contraceptive provided the right antigen can be identified.

With support under the predecessor project of CD&RI (the CD:RI Project), Dr. Shaha used antiserum raised against whole washed human sperm to identify antigens on spermatozoa from various species which might have potential for a contraceptive vaccine. A 40 kD antigen was identified in human spermatozoa using this antisera and shown to be sperm-specific. The same antisera was also cross-reactive with a 24 kD glycoprotein of rat testicular cytosol. This rat protein was isolated, purified and used for active immunization of rats and monkeys. Both yielded encouraging results in terms of reducing fertility.

The objectives of this current collaborative research proposal include the isolation and characterization of additional specific sperm antigens which are thought to be involved in human infertility, development of monoclonal antibodies to these new antigens, extension of the work involving immunogenicity of the 24 kD antigen(s) from rat, and the purification, sequencing and cloning of this antigen(s) and any newly identified antigens to obtain large quantities for immunization studies.

Status: The research proposal was approved in February 1991 and procurement of equipment and supplies, and selection of personnel is underway. Meanwhile, the investigator has continued with her work in India on purification of the 24 kD protein. This protein (gel band) has now been shown to be nine separate proteins of which only two cross-react with her antibody. These two minor antigens have been sent to Dr. Catterall's laboratory for sequencing. Dr. Shaha has also established a cDNA library and has identified two clones which produce a protein that cross-reacts with mouse polyclonal antibodies raised to the total 24 kD gel band.

Likely Outcome: In the short term, the investigators propose to identify and characterize sperm antigens having a specific role in regulation of fertility, followed by preparation of at least one of these antigens in large quantities through recombinant DNA techniques. There is a high likelihood that this aim will be achieved by the end of the project period. In

addition, the sequencing and cloning of additional sperm antigens will most likely take place, at least in part, by the end of the project, particularly if the PACD is extended as proposed by the Evaluation Team. In the long-term, this collaborative effort offers the promise of producing an anti-sperm vaccine. In both the short-term and the long-term, there will be numerous publications that result from this research effort.

2. *Local Immune Responses to Sperm in the Female Genital Tract*

Dr. Shakti N. Upadhyay, NII
Dr. Deborah Anderson, Harvard University

Summary: Local cell-mediated immune responses have now been recognized as being potentially important to ultimately achieve 100% infertility when immunizing against reproductive antigens. The objectives of this project are to use a non-human primate model to immunize against sperm antigens in order to study humoral and local cell-mediated immunity, and their interrelationship, in order to better understand the immune mechanisms in the female reproductive tract. It will involve (i) selection of markers for the identification of immune cell populations; (ii) localization and characterization of cellular and soluble immunologic mediators in the female reproductive tract; (iii) immunization of female bonnet monkeys with purified sperm plasma membrane preparations for inducing antisperm immunity; (iv) assay of the anti-sperm cell-mediated immune responses and (v) study of the fertility status of sperm immunized monkeys.

Status: This project proposal was approved in the second quarter of 1990 and sanction was conveyed by DBT in February 1991. Dr. Upadhyay visited Dr. Anderson's laboratory for two months in August 1990 to learn bioassays for cytokines, interferons and other cell-mediated responses. He brought several of the cell lines used for these assays back to India to establish some of the techniques at NII. Dr. Upadhyay has been in France during the last two months on an Indo-French collaborative project and has not yet initiated work proposed under the project. In a change from the original proposal, a rodent model has been selected to initially conduct the route of immunization studies.

Likely Outcome: In the short term, this project should lead to an advancement in understanding cell-mediated responses versus humoral immunity in the female genital tract. In the long-term, many scientists believe that it is imperative to have a local cell-mediated immune response in order to achieve 100% effectiveness of a sperm or zona vaccine. While this hypothesis remains to be proven conclusively, this project, in combination with the data resulting from the other projects funded under the CD&RI project, will help support or disprove this hypothesis. In both the short-term and the long-term, publications should result from this research effort.

3. *Studies on Porcine Zona Pellucida Antigen ZP3 as a Candidate for an Antifertility Vaccine*

Dr. S.K. Gupta, NII
Dr. Anthony G. Sacco, Wayne State University

Summary: Research over the last decade has suggested that porcine zona pellucida antigens are good possible candidates for a contraceptive vaccine. Physicochemical characterization of porcine ZP has revealed four major glycoprotein families having apparent molecular weights of 82 kD (ZP1), 61 kD (ZP2), 55 kD (ZP3) and 21 kD (ZP4). Porcine ZP3 is comprised of two distinct components termed ZP3 alpha and ZP3 beta. Sperm receptor activity appears to be associated with the alpha subunit. In this collaborative research project, the investigators will focus on delineating smaller determinants of ZP3 having immunocontraceptive potential. Active immunization studies using these smaller determinants, as well as whole ZP3, in non-human primates will be conducted to work out an effective immunogen dosage, immunization regime, and adjuvants. In the final stages of this project, the investigators hope to clone porcine ZP3.

Status: This project was approved in the second quarter of 1990 and funded in the first quarter of 1991. A student in Dr. Gupta's laboratory has visited Dr. Sacco's laboratory to prepare large quantities of porcine ZP3 for immunization studies. Work related to delineating smaller determinants of ZP3 which might have immunocontraceptive potential has been initiated.

Likely Outcome: Given the experience of the investigators, and the results to date, there is a high likelihood that this project will add significant information related to the immunocontraceptive potential of porcine ZP3. In the long-term, this project may well lead to the development of a contraceptive vaccine. In both the short term and the long-term, publications should result from this research effort.

4. *Nucleic Acid Based, Non-radioactive Diagnosis of Malaria*

Professor G.P. Talwar, NII
Dr. Altaf A. Lal, CDC

Summary: The objective of this study is to develop highly sensitive, non-radioactive diagnostic probes for the detection of malaria infection using rRNA as a target and to compare this approach to the currently used DNA-based procedures. Comparisons will also be made between radioactive and non-radioactive labelling procedures.

Status: The project has just received its initial funding.

Likely Outcome: Given the experience of the investigators, during the life of the project there is a reasonable likelihood that this project will result in the development of a sensitive and specific non-microscopic diagnostic assay for surveillance of malaria. In the longer-term, this assay may also be developed as a diagnostic kit.

5. *Applied and Basic Studies Related to Development of a Male Contraceptive Vaccine*

Professor N.R. Moudgal, IISc
Dr. C. Wayne Bardin, the Population Council

Summary: Specific immunoneutralization of FSH in the primate results in the reversible arrest of spermatogenesis and consequent infertility. This fact forms the basis of a prototype contraceptive vaccine for the human male which is about to enter Phase I clinical trials in India. The antigen used in this vaccine is ovine FSH which is isolated from sheep pituitaries by conventional protein purification methods. To circumvent problems associated with the purification of this hormone from animal sources such as low yields and potential viral contamination, it is proposed to (i) produce ovine FSH and its subunits using recombinant DNA technology; (ii) identify immunodominant regions of FSH and regions responsible for biological activity, and (iii) to study the role of FSH, LH and testosterone in regulating germ cell transformation and spermatogenesis.

Status: The project has been approved by U.S. peer review, but not yet by Indian peer review. Therefore, it has not yet been funded by DBT and activities have not formally begun. However, collaborative research between these investigators has already been established through a Rockefeller Foundation Grant to Dr. R. Dhige, who is working in the Center for Reproductive Biology and Molecular Biology with Dr. Moudgal. Dr. Dhige visited the Population Council in 1990 to learn recombinant DNA techniques and establish a cDNA library.

Likely outcome: In the short-term, this project should contribute to the understanding of the role of FSH, LH and testosterone in spermatogenesis. In addition, since the α and β subunit genes are already available, there is a high likelihood that the investigators will succeed in establishing expression systems that allow production of large amounts of biologically active and immunoreactive ovine FSH during the life of the project. The identification of immunologically dominant epitopes of FSH seems to be a longer-term goal in that large quantities of FSH which will be required for this aspect of the project will only be available if cloning is successful. Overall, this project has promise of making a significant contribution toward the development of a contraceptive vaccine for male. In both the short-term and the long-term, publications should result from this research effort.

6. *Analysis of Epitopes of Recombinant Antigens of Mycobacterium T.B. Immunogenic in Humans*

Dr. R. Nayak, IISc
Dr. Jerold Ellner, Case Western Reserve University

Summary: Very few of the antigens of mycobacterium are unique to Mycobacterium tuberculosis. This proposal has its origin in an ongoing activity in which two major protein antigens have been isolated from Mycobacterium tuberculosis that appear to be unique to this strain. These antigens produce a strong immune response in patients suffering from tuberculosis. A lambda gt 11 expression library has been screened with human IgG and several clones producing antigens reactive with human anti-TB IgG have been identified. Under this project, these expressed antigens will be characterized both biochemically and immunochemically. The relevant antigen-expressing clones will be restriction mapped and the DNA fragments subcloned. Finally, the new set of clones will be screened for expression of antigenic determinants of the cloned proteins. The cross-reactiveness or the uniqueness of these epitopes to Mycobacterium tuberculosis would be determined by the use of standard biochemical and immunochemical techniques.

Status: This project has been approved by both Indian and U.S. peer review; however, it has not yet been funded.

Likely Outcome: In the short-term, unique epitopes of Mycobacterium tuberculosis antigens may be identified. In the long-term, these antigenic fragments can be utilized to develop diagnostic kits to detect the early onset of tuberculosis.

7. ***Recombinant DNA-Based Strategies to Study the Structure and Cross-Reactivity of IgE Binding Epitopes of Atopic Allergens***

Dr. P.V. Subba Rao, IISc
Dr. Dean D. Metcalfe, NIAID

Summary: Sources of allergens that provoke IgE-mediated allergic response are widely distributed in the environment. In addition to these antigens, many foods elicit an allergenic response in certain individuals. These allergens are proteins or glycoproteins, and have molecular weights in the range of 5 to 70 kD. Very little is known about the physicochemical basis of allergenicity and very few allergens have been purified and chemically characterized to study the basis of allergic reactions.

This research project proposes to study shrimp allergens by isolating and characterizing poly A+ RNA from shrimp (*Penaeus indicus*), preparing cDNA from the purified poly A+ RNA, preparing a cDNA expression library, immunoscreening the expression library and amplifying positive clones, and subcloning and doing nucleotide sequencing. The amino acid sequence of major allergen(s) will be predicted based on the nucleotide sequencing and sequence homology compared with different pollen, food and intestinal parasite allergens. Putative allergenic determinants will be identified and cloned to produce sufficient pure material for chemical and biological analysis.

Status: U.S. peer review approval is complete. Initiation of work is awaiting approval on the Indian side. The Indian investigator has had a continuing collaboration with his U.S. counterpart for the past decade in other project areas.

Likely Outcome: This research basically has the long-term goal of understanding the basis of allergic diseases which would allow improved immunotherapy for affected individuals.

8. *Contraceptive Research and Development: Development of an Anti-Zona Pellucida Vaccine*

Dr. Shobha Seghal, PGIMER, Chandigarh
Dr. Bonnie S. Dunbar, Baylor University

Summary: The potential use of zona pellucida antigens for a contraceptive vaccine has been of interest for many years. Results from numerous research studies have demonstrated that animals immunized against zona proteins can be rendered infertile. Drs. Seghal and Dunbar had previously conducted collaborative research with support from the Indo-U.S. Science and Technology Initiative. In those studies, it was observed that rhesus monkeys immunized with heat solubilized zona pellucida protein produced high titers of anti-zona antibodies, became amenorrheic and had dramatic alterations in ovarian follicular maturation. Other research has demonstrated that immunization of squirrel monkeys with the major porcine zona protein had no effect on ovarian function although the animals were rendered infertile. It was therefore thought that targeting a single specific protein might afford a greater likelihood of producing a safe contraceptive vaccine.

Dr. Dunbar and co-workers have now isolated and characterized cDNA clones expressing specific rabbit ZP proteins and have developed methods to produce large quantities of specific antigens to use for immunization. They have also immunized rabbits and mice using fusion proteins produced by these clones.

This current proposal has three specific aims. The first is to establish methods to enhance the immune response to recombinant ZP fusion proteins by conjugation to either keyhole limpet hemocyanin alone or in combination with interleukin-1. The second is to subclone the ZP cDNA into a vector which will allow production of a non-fusion protein which can be purified and used for immunization. The third is to immunize rhesus monkeys with non-fusion recombinant proteins which are conjugated to diphtheria toxoid with or without interleukin-1 as an immune enhancer. Specific aim 1 will be done essentially in Dr. Dunbar's laboratory and the other two aims represent joint endeavors.

Status: This project has been approved on the U.S. side, but is awaiting the results of Indian peer review.

Likely Outcome: Given the skills available in the U.S. collaborator's laboratory, it is highly likely that this project will lead to the successful cloning of the ZP proteins as indicated in the proposal. In addition, knowledge should be gained as to the potential use of and/or need for interleukin-1 to enhance immune response. In the long-term, this project and that of Drs. Gupta and Sacco using porcine ZP, may well result in the development of a contraceptive vaccine. If not, much should be learned during the process as it relates to the development of other contraceptive vaccines. In both the short-term and the long-term, publications should result from this research effort.

9. *Incidence of Anti-SP-10 Antibodies in Sera and Secretions of Infertile Couples*

Dr. Shobha Seghal, PGIMER, Chandigarh
Dr. John C. Herr, University of Virginia

Summary: The SP-10 antigen was identified during a Workshop convened under the auspices of WHO and Family Health International several years ago as a potential candidate for a contraceptive vaccine. The principal objective of this research proposal is to assess the incidence of natural antibodies to SP-10 protein in the sera of infertile men and women. The aim will be achieved by employing as a target two forms of the SP-10 immunogen: a highly purified SP-10 preparation isolated from sperm, and a recombinant form of SP-10 cleaved from a glutathione transferase fusion protein. The Herr laboratory will focus on biochemical purification of native SP-10 and on purification of the recombinant immunogen, while the Seghal laboratory will conduct the immunological studies. In addition, a pilot immunogenicity and immunopathological study of SP-10 in rhesus monkeys will be initiated.

Status: This project has been approved on the Indian side, but is awaiting final U.S. peer review clearance.

Likely Outcome: Given the skills of each investigator and their proposed activities under this project, there is a high likelihood that this project will result in short-term results related to determining the general incidence of antibodies to SP-10 in the Indian infertile population. In addition, there is every likelihood that the U.S. investigator will successfully purify and clone the SP-10 protein. Therefore, there is a reasonable likelihood that the pilot immunogenicity in monkeys can be initiated.

10. *Development of Monoclonal Antibodies Against an Alloantigen/Antigenic Determinant Specifically Expressed on B Lymphocytes in Indian RF/RHD Patients*

Dr. N.K. Ganguly, PGIMER
Dr. Edward L. Kaplan, University of Minnesota

Summary: Rheumatic fever (RF) is an inflammatory disease that follows infection with Group A streptococci. Carditis is one of the major manifestations of RF. Control of rheumatic fever/rheumatic heart disease (RF/RHD), specifically among young children, is an important need in India. The incidence of RF in 5-15 year olds is 6-12/1000 and about one-half of cardiac ward admissions are for the aftermath of RF. Dr. Ganguly and co-workers have developed a diagnostic technique to screen for RF. Based on a finger-prick test, slides are air-dried in the field and sent back to a central laboratory for culture and analysis. Because of the need to use a central laboratory this test has limitations. However, diagnosing RF is important because it can be cured by treating the streptococcal infection.

It is not clear what factors cause certain individuals to be susceptible to developing RHD following Streptococcal infection. One theory relates to the presence of certain alloantigens on the surface of the B cells of these individuals. It is thought that by identifying a positive reaction for the presence of B-cell alloantigen these susceptible individuals might be identified. However, two monoclonal antibodies produced against these alloantigens gave varying results in the Indian population and results that differed when compared with a U.S. population. Additional monoclonal antibodies need to be developed and tested for this purpose.

The objectives of the proposal include: (i) identification of an antigen or a group of antigens expressed on the surface of B cells of Indian subjects which increase their susceptibility to developing RF/RHD; (ii) production of monoclonal antibodies to these antigens and determination of whether any of these antibodies can identify individuals susceptible to RF/RHD; (iii) development of a diagnostic test based on the results of (i) and (ii); and (iv) cloning and characterization of the B cell alloantigen(s) recognized by the monoclonal antibodies produced in (ii).

Status: This project has been approved by peer review on both the Indian and U.S. side, however, the project has not yet been funded. Work has, therefore, not been initiated although linkages between the U.S. and Indian investigators have been established.

Likely outcome: In the medium term, it is likely that a diagnostic test for use in the field for detecting susceptible RF/RHD populations can be developed.

11. *Development of New Vaginal Contraceptives*

Dr. B.S. Setty, CDRI
Dr. Nancy Alexander, NIH

Summary: Earlier studies with molecules designed and synthesized at the CDRI, and belonging to the aminoethylacrylophenone family, have been shown to have potent spermicidal activity. Subsequently, quinine derivatives and substituted aminomethyl dienones have been synthesized which have spermicidal activity. The present proposal is a continuation of this previous work and is aimed at developing new safe and effective spermicides. Additional new compounds will be synthesized and evaluated at CDRI for *in vitro* and *in vivo* spermicidal activity using appropriate test models. Dr. Alexander will confirm the spermicidal potential and additionally have these compounds evaluated for chlamydiacidal and antiviral (anti-HIV) properties.

Both investigators will undertake pre-clinical testing with the potential compound employing a commonly agreed upon protocol and may also initiate work on a suitable carrier vehicle assuming a good candidate compound is identified before the PACD on the project. Eventually, if a good candidate spermicide can be identified, the safety evaluation in human (Phase I clinical trial) and efficacy studies (Phase II and III) would be carried out in both countries.

Status: This proposal has been approved by the U.S. side with a contingency that an understanding be reached on the rights to any products which results from this collaborative effort. Peer review on the Indian side is still pending. Funding of this project will be held up until the issue of product rights can be resolved. In the meantime, using funds available to the Institute from other sources, CDRI scientists have continued to synthesize additional compounds and identified two as potential spermicides. It is expected in 1991 that four more compounds will become available.

Likely outcome: The short-term goal of this project is to identify potential new spermicides that have anti-bacterial and anti-viral activity. If this project is eventually funded, there is a reasonably good chance that at least one compound will be identified which has the desired characteristics. With regard to the long-term goal of developing a new vaginal contraceptive, it is difficult to determine at this point whether any compound identified would make it through the tortuous pathway from toxicology through efficacy studies to actually become a contraceptive product.

Appendix F

Summary of Fellowship Proposals and Awards

Appendix F
CD&RI Project
Fellowship Awards

National Institute Of Immunology, New Delhi

Fellow	Area Of Research	To Visit	Details Of Visit Duration — Commencement	Status (As Of May 24, 1991)
1. Dr. Raj Raghupathy	Identification, characterization and isolation of cell mediated effectors of immuno-infertility in the male and in the female. Unravel the roles and mechanisms of cellular immunity, the major histocompatibility complex and cytokines in reproduction.	Dr. Deborah Anderson Dept. of Obstetrics and Gynecology Harvard Medical School Boston, MA, USA	Two months — April 1, 1991	DBT has not cleared Raghupathy's first visit
		Dr. Virginia L. Scofield Dept. of Microbiology & Immunology, UCLA School of Medicine, Los Angeles CA 90024, USA	Two months — 1992	
		Prof. Jack Strominger Dept. of Biochemistry and Molecular Biology Harvard University Cambridge, MA 02138 USA	Two months — 1993	
2. Dr. Anil Suri	Purification and characterization of sperm specific antigens and identification of corresponding genes in CDNA libraries using antibody probes and oligonucleotide probes, followed by the expression of these genes in appropriate production vectors.	John C. Herr Associate Professor Culture Center University of Virginia School of Medicine Box 439, Charlottesville, VA 22908 This initial visit will be followed by two other short term visits of two months each in 1992 & early 1993. Dr. Suri has not yet indicated where he will be going.	one year — July 1990	Dr. Suri left on July 4. He visited Delhi in December and says he is doing well. A re-entry grant form was given to Dr. Saha for Dr. Suri. Suri has asked for a 4 week extension to work in the laboratory of Dr. Roy Curtis. John Herr requested CONRAD for a two month extension for Suri at Herr's lab. Both requests have been turned down by DBT.

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Fellowship Awards

Fellow	Area Of Research	To Visit	Details Of Visit		Status (As Of May 24, 1991)
			Duration	Commencement	
5. Dr. Labhshetwar	Controlled release vaccine delivery system	Prof. Robert Langer Massachusetts Institute of Technology Cambridge, MA USA or Dr. Curt Thies	six months — two months —	o/a Dec., 1990 o/a Jan., 1992	NII has confirmed that Dr. Labhshetwar has resigned. NII will let us know if they have an alternate candidate to propose.
6. Dr. Ashish Das	Lyse blood cells infected with the malarial parasite and fix the total Cellular RNA to the solid support	Dr. Altaf A. Lal Center for Disease Control Atlanta, GA, USA	six months		Mr. Das is in Atlanta on a six-month UNDP fellowship. When this ends, he will stay on for another six months as a CD&RI fellow.

Indian Institute Of Science, Bangalore

Fellow	Area Of Research	To Visit	Details Of Visit		Status (As Of May 24, 1991)
			Duration	Commencement	
7. Dr. N. Ravindranath	IVF techniques in monkeys and studying the implantation process in monkeys including approaches on follicular maturation process and ovulation as well as micro-manipulation techniques.	Prof. Zalesnik Univ. of Pittsburgh School of Medicine Pittsburgh, PA The second and third visits are yet to be planned.	One year	May, 1990	Dr. Ravindranath did not obtain DEA clearance before he traveled to the U.S.

Fellowship Awards

Post Graduate Institute Of Medical
Education & Research, Chandigarh

Fellow	Area Of Research	To Visit	Duration — Details Of Visit Commencement	Status (As Of May 24, 1991)
8. Dr. Sunil Arora	Make immuno relevant antigens of L. donovani promastigotes using recombinant DNA technology	Dr. Peter Melby Veteran's Admn. Hospital University of Texas San Antonio, Texas	One year	Dr. Melby has sent the IAP 66 for Dr. Arora. DBT clearance is required for Arora to travel.
9. Dr. Nayak's Asst.	not known	not known		Money will probably need to be added to the PASA

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