RESEARCH FOR DEVELOPMENT

A Grants Program for the Third World

Michael P. Greene

NATIONAL RESEARCH COUNCIL

Digitized by Google

RESEARCH FOR DEVELOPMENT
A Grants Program for the Third World

by Michael P. Greene

National Academy Press
Washington, D.C. 1991

NOTICE: The project that is the subject of this report was approved by the Governing Board of the National Research Council, whose members are drawn from the councils of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine. The members of the committee responsible for the report were chosen for their special competence and with regard for appropriate balance.

This report has been reviewed by a group other than the authors according to procedures approved by a Report Review Committee consisting of members of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine.

The National Academy of Sciences is a private, nonprofit, self-perpetuating society of distinguished scholars engaged in scientific and engineering research, dedicated to the furtherance of science and technology and to their use for the general welfare. Upon the authority of the charter granted to it by the Congress in 1863, the Academy has a mandate that requires it to advise the federal government on scientific and technical matters. Frank Press is president of the National Academy of Sciences.

The National Academy of Engineering was established in 1964, under the charter of the National Academy of Sciences, as a parallel organization of outstanding engineers. It is autonomous in its administration and in the selection of its members, sharing with the National Academy of Sciences the responsibility for advising the federal government. The National Academy of Engineering also sponsors engineering programs aimed at meeting national needs, encourages education and research, and recognizes the superior achievements of engineers. Robert M. White is president of the National Academy of Engineering.

The Institute of Medicine was established in 1970 by the National Academy of Sciences to secure the services of eminent members of appropriate professions in the examination of policy matters pertaining to the health of the public. The Institute acts under the responsibility given to the National Academy of Sciences by its congressional charter to be an adviser to the federal government and, upon its own initiative, to identify issues of medical care, research, and education. Samuel O. Thier is president of the Institute of Medicine.

The National Reseach Council (NRC) was organized by the National Academy of Sciences in 1916 to associate the broad community of science and technology with the Academy's purposes of furthering knowledge and advising the federal government. Functioning in accordance with general policies determined by the Academy, the Council has become the principal operating agency of both the National Academy of Sciences and the National Academy of Engineering in providing services to the government, the public, and the scientific and engineering communities. The Council is administered jointly by both Academies and the Institute of Medicine. Frank Press and Robert M. White are chairman and vice chairman, respectively, of the National Research Council.

The Board on Science and Technology for International Development (BOSTID) of the NRC's Office of International Affairs addresses a range of issues arising from the ways in which science and technology can stimulate and complement the complex processes of social and economic development in developing countries. BOSTID oversees a broad scientific program with organizations in developing countries and conducts special studies.

Funding for this report has been provided by Carnegie Corporation of New York and The Rockefeller Foundation.

Copies of this report are available without charge from:
Board on Science and Technology for International Development
National Research Council
2101 Constitution Avenue, N.W.
Washington, D.C. 20418

Preface

The author, Michael Greene, who organized the Research Program of the Board on Science and Technology for International Development (BOSTID) and was its Director from 1981 to 1990, has a Ph.D. in physics from the University of California, San Diego. He left an academic career in 1974 to work in international development. Before joining BOSTID in 1981, he was deputy director of the science and technology program at the Organization of American States, with responsibility for a research grants and technical assistance program.

The staff brought to the program wide experience in research and development. At its peak, the professional staff included the program director, three scientists, a half-time scientific consultant, three administrative professionals, including a full-time equipment and supplies procurement officer, a half-time procurement consultant, and a visiting scientist on sabbatical from a university. The support staff consisted of three program assistants, and an editorial assistant.

Preparation of this report was motivated by the desire to summarize the experience of the staff who managed on a day-to-day basis this competitive research grants program for developing country scientists. Clearly, then, the opinions expressed here are not comprehensive or totally disinterested, but are presented in the hope that these recollections and suggestions would be useful for others involved in international development and research program support.

The following present and former BOSTID staff members made significant contributions to this report: Judith Bale, Tresa Bass, Karen Bell, Yvonne Forsbergh, Maurice Fried, John Hurley, Constance Reges, Joann Roskoski, and Jennifer Shupp. Several scientists from developing countries who received research grants have made comments on the program, and are named

where the comments appear. Joanna Dobereiner, a grantee from Brazil, has written a more extensive note on her view of the program, and John Torrey, of Harvard University, has provided the perspective of a member of the program's oversight committee.

The BOSTID staff is grateful to the Office of the Science Advisor of the Agency for International Development for supporting the BOSTID Research Program, and to the Rockefeller Foundation and the Carnegie Corporation of New York for support for the preparation and publication of this manuscript.

The views expressed here do not necessarily represent those of the National Research Council or its Board on Science and Technology for International Development.

Contents

OVERVIEW ix

INTRODUCTION 1

START-UP 8
Selection of Areas, 8
Computerized Data Base, 12
Organizational Meetings, 15
Eligible Countries, 16

PROCEDURES 18
Proposal Evaluation, 18
Pregrant Visits, 20
Human Studies, 22
Grant Agreements and Financial Management, 23
Scientific Support, 24
Evaluation and Monitoring, 26
Publications, 28
Closeout, 29
Program Evaluation, 29

GRAIN AMARANTH 32
Organizational Meeting, 34
Coordination Meetings, 35
Advisory Meetings, 36
Grain Amaranth in Peru, 38
Research Results, 40

Nutrition and Food Use, 41
Agronomy and Plant Improvement: Latin America, 41
Agronomy and Plant Improvement: Asia and Africa, 42
The Future of Amaranth, 43

BIOLOGICAL NITROGEN FIXATION 46
Organizational Meeting, 47
BNF Advisory Group, 48
Coordination Meetings, 49
Workshop on Molecular Genetic Techniques for BNF Field Research, 52
Research Results, 53

TROPICAL TREES 57
Organizational Meeting, 57
First Coordination Meeting, 60
Procedural Manual, 61
Other Coordination Meetings, 62
Advisory Meetings, 62
Research Results, 63
Species Inventory and Trials, 64
Nitrogen Fixation, 66

MOSQUITO VECTOR FIELD STUDIES 69
Organizational Meeting, 72
Advisory Group, 73
Coordination Meetings, 75
Human Bait Policy,77
Research Results, 79

RAPID EPIDEMIOLOGICAL ASSESSMENT 85
Organizational Meeting, 87
Advisory Group on Rapid Epidemiologic Assessment Methods, 88
Coordination Meetings, 90
Research Results, 92

DIAGNOSIS AND EPIDEMIOLOGY OF ACUTE RESPIRATORY INFECTIONS IN CHILDREN 98
Organizational Meeting, 99
First Coordination Meeting, 102
Laboratory Manuals and Procedures, 103
Data Management, 104

Pathogenesis of ARIs, 105
Later Coordination Meetings, 105
Site Visits and Training, 106
Symposium on Etiology and Epidemiology of Acute Respiratory Infections in Young Children, 106
Research Results, 107
Future of the ARI Program, 109

CONCLUSIONS 112
Research Capability, 113
Capacity Building, 118
Comments from Grantees, 120
Termination of the Program, 123
Lessons Learned, 124

APPENDIXES
A Committee on Research Grants 127
B The CRG Program: A Member's Perspective 130
C BOSTID Project on BNF in Gramineae in Brazil 133
D Proposal Evaluation Criteria 136
E Research Grants Program Publications List 139

Overview

Beginning in 1981, the Board on Science and Technology for International Development (BOSTID) of the National Research Council (NRC) operated a small research grants program for developing country scientists. The last grants were awarded in 1987, and the program is scheduled to end in January 1992. Funds were provided by the Office of the Science Advisor of the Agency for International Development (AID) as part of a new U.S. initiative to strengthen the capability of Third World scientists to do research on important development-related problems.

The National Research Council is a nongovernmental scientific institution, the operating arm of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine, that produces more than 300 studies a year on scientific and technological topics, most of which are on contract for U.S. government agencies. BOSTID is the unit of the NRC concerned with scientific and technical problems related to development, and it is well known for a series of publications on little-known, underexploited resources of potential economic value and for its collaborative programs with developing countries.

The research program was not a traditional type of program for the NRC. It was unusual in that it actually commissioned new research and required BOSTID to assume the role of an international donor organization, with all the attendant management responsibilities. Because no similar program had existed previously in the NRC, it was necessary to design the form and structure to meet the technical and financial requirements of research projects in distant developing countries.

Research grants were offered in six technical areas:

- Grain amaranth, a highly nutritious and vigorous crop inherited from the Aztecs;

- Biological nitrogen fixation, with emphasis on the quantitative measurement of the nitrogen fixed;
- Tropical trees, for comparative research on fast-growing, multipurpose species;
- Mosquito vector research, to determine the identity, behavior, and effective control measures for the major vectors of disease;
- Rapid epidemiologic assessment, to develop a new subfield of epidemiology focused on developing country problems; and
- Acute respiratory infections in children, a coordinated research program on the etiology and epidemiology of these infections, featuring viral and bacterial diagnoses of pathogens and identification of risk factors, with emphasis on confirmation and quality control.

The BOSTID program was characterized by several features:

- Grantees were selected on a competitive basis, with peer review of proposals and staff visits to applicants, to evaluate capability and assist with response to reviewers' comments on proposals.
- Staff were heavily involved in technical assistance, equipment procurement, financial management, and publication assistance.
- U.S. researchers participated as advisors, site visitors, and reviewers, and were also utilized for short-term training.
- Annual coordination meetings of grantees and advisors were held to report on research progress, discuss problems, and learn new techniques in hands-on workshops.

Between 1981 and 1988, 564 proposals were received from developing country researchers; 109 grants were awarded, with a total research budget of nearly $16 million. The average grant was about $150,000 for three or four years. Forty-five percent of the grants went to Latin American institutions, 37 percent to Asians, and 18 percent to Africans. The research grants resulted in the publication of more than 300 journal articles or book chapters. In four of the six areas, grantees published some of their results together in special refereed editions of international journals dedicated to the BOSTID work (a refereed journal is one in which outside peer reviews have been performed).

GRAIN AMARANTH

Researchers studied the performance of selected varieties of grain amaranth under different climatic and soil conditions. Germ plasm collections and selection and breeding produced new lines with favorable properties so that recommended varieties are available for planting in many parts of the world. Nutritional and processing conditions have been studied, and the properties of grain amaranth are now well understood. An amaranth news-

letter is published quarterly with BOSTID support. As a result of the BOSTID project, amaranth has been recognized and promoted in Peru at the highest political level; commercial farmers and agroindustries have become interested; and the market for amaranth products is expanding rapidly.

BIOLOGICAL NITROGEN FIXATION

In biological nitrogen-fixing systems, fixation is by bacteria that live in symbiotic association with leguminous plants and by free-living bacteria. In the BOSTID program, new knowledge of the quantity and fate of fixed nitrogen was generated by analysis of plant uptake of fertilizer dosed with the isotope ^{15}N and other quantitative techniques. This enabled researchers to design multicropping systems that use nitrogen-fixing legumes to nourish row crops like maize. It has also enabled the selection of rhizobia, the nitrogen-fixing bacteria that infect leguminous crops, for survival under stressed conditions. Molecular genetics was applied to the study of competition among rhizobial strains and to the manipulation of nitrogen-fixing genes to enhance the efficiency of the symbiosis. Fixation by free-living bacteria in association with grasses has been documented and quantified in sugarcane, and a salt-tolerant fodder grass has been found to "fix" nitrogen in highly saline environments.

TROPICAL TREES

Researchers in the tropical trees program field-tested some little-known multipurpose tree species (mostly nitrogen-fixers) for their growth properties and productivity. The data enables the selection of species and varieties for particular environments and purposes. Management and cultural methods for optimal production for each variety were established. Two projects developed and tested agroforestry schemes for use of nitrogen-fixing trees to nourish row and other tree crops. Other projects investigated tissue culture techniques for rapid selection and mass propagation of high productivity clones.

MOSQUITO VECTOR FIELD STUDIES

The mosquito vector program studied vectors of malaria, arboviruses, and other parasites. Many of the projects sought to identify the principal vectors in a region and study their life cycles. Others studied biological control agents, mostly of botanical origin, to isolate the active factors and formulate control applications. Three projects examined the influence of environmental changes related to human activities on vector-borne disease transmission, and found clear evidence of a causal relationship. With the advice and assistance of researchers from the Walter Reed Army Institute of

Research and the National Institutes of Health, grantees incorporated newly developed emzyme-linked immunosorbent assay (ELISA)-based technology for analyzing blood meals and detecting infected mosquitoes for more precise studies of malaria vectors.

RAPID EPIDEMIOLOGIC ASSESSMENT

Rapid epidemiological assessment refers to epidemiological survey techniques for gathering public health information that are characterized by low sample sizes, rapid surveys, low cost, and simplicity for adaptation to conditions in the Third World. Researchers worked in four broad areas: small number survey and sampling methods, screening and individual risk assessment, community indicators of risk or health status, and case-control methods for evaluation; all validated their results against other larger, traditional surveys. This allows use of rapid methods to quickly assess population-based problems for health-care planning and decision making.

ACUTE RESPIRATORY INFECTIONS IN CHILDREN

Acute respiratory infections are among the greatest causes of childhood mortality in the Third World. The BOSTID program aimed to identify the principal pathogens and the major risk factors through coordinated research in several population settings. Research groups in twelve countries trained together and adopted similar protocols. Manuals for bacterial and viral diagnoses and for epidemiologic design were prepared by advisors and grantees working together, and laboratory diagnoses were checked by reference laboratories in the United States and Sweden. Knowledge gained of the role of viruses and bacteria will be incorporated into development of vaccines and of case-management protocols to reduce mortality due to ARIs.

CONCLUSION

The research grantees in the program have had many outstanding accomplishments and in some cases have contributed substantially not only to the better understanding or solution of local problems, but to international science as well. Yet many factors were found to impede successful research in the developing world. Some are similar to problems shared by scientists in industrialized countries, such as access to equipment and bibliographic resources. Others arise from the weak career structure for researchers in the developing societies, with few incentives to publish original scientific work and the lack of strong scientific communities. As a result, it takes special determination and entrepreneurial skills to be successful as a research scientist in a developing country. The BOSTID Research Program placed greatest emphasis on quality of research and on publication of results in

international journals. The annual meetings of grantee researchers, which included international experts, were calculated to encourage and reward those with the capability to perform on the international scientific stage. This gave them enhanced stature, both internationally and locally, and, by example, built capability, recognition, and interest among their colleagues. The equipment and supplies provided, the research experience and training gained, and the international links forged were enduring benefits of the program to the participating institutions. In turn, the participating scientists and institutions produced a substantial body of important research.

Introduction

Between 1981 and 1991, the Board on Science and Technology for International Development (BOSTID), a major division of the National Academy of Sciences complex, organized and managed a program for support of research projects in developing countries. Selecting grantees and awarding grants is not a customary role for the Academy complex, and the program was managed in a manner that was uncommon among research support agencies. This report is an attempt to analyze the goals and achievements of the BOSTID Research Program and the extent to which it may be a model for future programs.

The conceptual forerunner of the BOSTID Research Program was the so-called Institute for Scientific and Technological Cooperation (ISTC).[1] Proposed by the Carter Administration, ISTC was to be funded as a new, small, semi-autonomous agency within the framework of the basic policies and overall budget of the International Development Cooperation Agency (IDCA) and in parallel with the Agency for International Development (AID). ISTC was to foster and support science and technology cooperation between U.S. scientists and developing country counterparts. Activities were to be directed at a limited number of selected problems, and funds would be available to support research in the United States and developing countries, including the middle-income or advanced developing countries. Its position outside of the normal AID framework would allow it some flexibility in dealing with developing countries, and to some extent insulate the scientific initiatives from political considerations. The new institute was the centerpiece of the U.S. presentation at the 1979 United Nations Conference on Science and Technology for Development (UNCSTD) in Vienna. Because it did not want to create a new government agency, however, Congress failed to appropriate funds for the institute, and thus it never came into being.

Nevertheless, it was increasingly clear to Congress and others that some further mechanism was needed to support scientific research in the developing countries. Science and technology were emerging as a central focus of the AID program. Many of the problems having a significant impact on development programs were scientific in character, and much of the field work was site specific and had to be conducted in the developing countries—not only for scientific reasons but for political reasons as well. It was also a central tenet of AID policy to build technical infrastructure and develop human resources in client countries. Scientific cooperation that mobilized the U.S. scientific community was perceived as necessary to help the developing world gain the skills and resources to confront the technical problems of development.

Although Congress did not support the ISTC as a new entity, it did support many of the ISTC principles, and so directed AID to establish a focused program for scientific cooperation and research with the developing countries. A new position of Science Advisor was created, reporting directly to the Administrator of AID, and his office managed a Program in Scientific and Technological Cooperation that eventually included a research grants program similar to BOSTID's, but encompassing a wider range of research areas. Also included were funding for the BOSTID research program and a set of activities aimed at strengthening scientific and technological capacities of developing countries. In 1981, the incoming administration created a central science and technology bureau in AID and appointed a senior assistant administrator to direct it. (Other bureau heads were assistant administrators.) Creation of this bureau did indeed give prominence to science and technology in AID's structure.

Concurrently with the actions in AID, a strong feeling persisted among U.S. scientists and within AID that some effort related to the ISTC, based in an institution independent of AID or even the United States government, could still be mounted on a small scale. Scientists in the United States and even some developing countries had expended considerable effort to design the ISTC program, and its failure in the congressional appropriations process left many of them deeply disappointed. It was hoped that a program might still be mounted that would incorporate many of the ISTC principles and, if it were successful, might help to influence Congress in future to reconsider funding for the ISTC itself.

Encouraged by this convergence of interests of supporters of the ISTC and of a stronger research program in AID, during the latter part of 1980 BOSTID prepared a proposal for a large program of research grants for developing countries, not to substitute for ISTC, but to implement part of the ISTC concept. The proposal underscored BOSTID's long and wide experience in working with a variety of scientific institutions in developing countries, plus the extraordinary access it had to all parts of the scientific

and engineering communities as part of the NRC. Preparation and negotiation of the proposal went forward under the leadership of Victor Rabinowitch, BOSTID's first director, with substantial assistance from his deputy, John Hurley, who succeeded him in 1982 when Rabinowitch became head of the Office of International Affairs at the NRC.

An important test of Rabinowitch's negotiating skills was persuading the Governing Board of the NRC, then chaired by NAS president Philip Handler, to approve the entire concept. A grants program was very different from the usual NRC advisory studies, and the Governing Board carefully weighed the idea at two different meetings before finally giving its endorsement. When the proposal was submitted to AID, it was reviewed by an independent panel, which endorsed the basic concept.

In January 1981, a grant agreement was signed between AID and BOSTID envisioning a five-year $36 million program officially called Application of Science and Technology to Development. As a unit of the National Research Council, the operating arm of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine, BOSTID has a mandate to advise the government in matters of scientific interest by carrying out funded studies on request, and in fact part of the new program would support analytical studies on scientific topics related to development. The largest part of the grant, however, was dedicated to the creation of a new mechanism for fostering and supporting research in the developing countries—the BOSTID Research Program. A total of $16.3 million was to be used for research grants to developing country institutions, with an additional $7.7 million for ancillary activities and administrative costs. Other funds in the grant were to be used for the studies and for informational activities.

AID was to approve the technical areas in which research grants were awarded, but the decision on the actual grant awards and payment was left to BOSTID.[2] It was an unusual arrangement, enabling flexibility in financial transactions, which subsequently paid off in the ability to provide researchers with funds and equipment in a timely manner.

One of the most significant features of the program was the ability of BOSTID to award grants to institutions in non-AID countries, specifically the so-called advanced developing countries, when the research would benefit developing countries in general. Thus, grants were made in countries such as Mexico, Brazil, Argentina, Chile, Malaysia, and Colombia, which receive little development assistance from the United States. Since many of these countries are in Latin America, it enabled BOSTID to maintain links with a region that had been relatively isolated scientifically from the United States for a decade or more.

Within AID, the funds for the grant to BOSTID were drawn from the budget administered by the newly formed Office of the Science Advisor,

which was soon to create and administer a similar and complementary research grants program of its own. Howard Minners, a Public Health Service officer who was AID Science Advisor during the lifetime of the BOSTID research activity, took a lively interest in the program from the outset. Day-to-day management of AID's support for the program was exercised by John Daly. Although the Office of the Science Advisor was very busy running its own grants program and differences with BOSTID over priorities or operational philosophy inevitably arose from time to time, the Science Advisor and his staff were strong proponents of research in developing countries and supported the BOSTID effort, particularly in making the case for maintaining research funds that often were coveted by other parts of AID.

Initially, the BOSTID Research Program was funded for five years, but after a series of no-cost extensions, it will ultimately have operated for eleven years. There were 107 research grants awarded, and grantees published more than 300 scientific papers. Many aspects of the management of the program were unique, and much was learned about opportunities and constraints for carrying out high-quality research projects in the Third World.

Since 1969, BOSTID has been the primary unit within the National Research Council concerned with the science and technology problems of developing countries. It has carried out a well-known series of studies on underexploited resources of promising economic value, such as fast-growing trees, tropical legumes, and rural technologies. In addition, bilateral activities were held in Brazil, Indonesia, Sri Lanka, India, Korea, and, altogether, more than fifty countries. Special conferences and workshops advised AID on technologies relevant to development programs. However, the research program was to be the first experience of BOSTID as a donor, and an uncommon one for the NRC, apart from the institution's established fellowship programs.

There were four objectives of the BOSTID Research Program:

- To help developing countries strengthen their capability to deal with important development-related problems and move toward greater scientific and technological self-reliance;
- To stimulate and support research and development in developing countries on problems of high priority for development and human welfare;
- To provide developing countries with greater access to the scientific and technological knowledge and expertise that exists in the United States and other countries; and
- To provide a focus within the U.S. scientific and technical communities for assistance to the developing countries, and to encourage greater interaction with colleagues in the Third World.

One of the assumptions underlying AID's award of the research grants

program to BOSTID was that BOSTID's long experience with underutilized resources and its collaboration with developing country scientists would be advantageous for the selection of research topics and of grantee scientists and institutions. The first task was the selection of research areas. Developing country scientists working outside the United States were consulted by mail. In addition, three meetings were held in different cities in the United States[3] to allow U.S. scientists and developing country scientists working in the United States an opportunity to suggest research areas for the program.

A Committee on Research Grants (CRG) was formed to choose the areas and select grantees. The chairman was Frederick Seitz, president-emeritus of Rockefeller University and a former president of the National Academy of Sciences. The membership included distinguished U.S. scientists and engineers and officials from developing countries. One scientist each from Canada and Sweden were also included. Organizationally, CRG was a subcommittee of BOSTID, and the chairman of CRG was an ex officio member of BOSTID.

The role of CRG was to establish policy, maintain a balance among the research areas, and assure that the objectives of each program and the program as a whole were achieved. It was intended to be a committee of highly distinguished scientists, but not necessarily with specialties in the selected research areas. It would rely on reviews of proposals by expert referees and ad hoc specialized working groups, rather than incorporate all the expertise required for the several research areas in the committee itself. Thus, CRG members were not necessarily actively engaged in research on one of the topics under consideration, but were selected for their broad scientific experience.

In later years, as the number of proposals increased, the committee divided into "agriculture" and "health" working groups to save time in initial discussion before bringing their recommendations to the full committee for decision. In most of the cases, decisions were based largely on the written reviews, with CRG providing a synthesis or overview. In this way, the BOSTID system differed from the "study-section" model, used by the National Science Foundation and the National Institutes of Health, in which proposals in each research area were selected by a different committee of experts. The CRG model created one program working in several fields, rather than several independent disciplinary programs sharing the same budget.

Funding was sufficient to eliminate the need for competition among proposals in the different technical areas; no project that CRG wished to support was ever rejected for lack of funds. (Only in 1988, when the program was abruptly suspended after Congress mandated a budget cut, were some CRG-approved proposals not funded. This is described in the last chapter.)

An executive secretary of CRG, Michael Greene, was hired in July 1981

to direct the BOSTID Research Program.[4] Greene had been a professor at the University of Maryland and had directed a research grants program at the Organization of American States. At its peak, the professional staff would later include the program director, three Ph.D.-level scientists, a half-time scientific consultant, an administrative professional staff of three, including a full-time equipment and supplies procurement officer; a half-time procurement consultant, and a visiting scientist on sabbatical from a university. The support staff consisted of three program assistants and an editorial assistant. In 1985, the BOSTID Research Program staff received the National Research Council Group Achievement Award.

An important complement to the work of the regular staff for the research program was the input of a number of "resident" or visiting staff members, who spent varied amounts of time with BOSTID—typically one year—through sabbatical, borrowed-personnel, or consulting arrangements. These resident experts brought specialized knowledge and experience to the program, providing substantial help in such endeavors as defining the directions for particular research areas, monitoring projects and providing technical help to grantees, conducting workshops and seminars on specialized techniques, or advising on the publication of grantee research papers. The resident staff members included: Dwight Baker, Battelle-Kettering Memorial Laboratory (tropical trees); Stephen Berman, University of Colorado School of Medicine (acute respiratory infections); Maurice Fried, formerly with the International Atomic Energy Agency (biological nitrogen fixation); Arnold Monto, University of Michigan (acute respiratory infections and rapid epidemiological assessment); Gilbert Otto, Johns Hopkins University (mosquito vector research and rapid epidemiological assessment); Beatrice J. Selwyn, University of Texas (acute respiratory infections and rapid epidemiological assessment); Gordon Smith, Johns Hopkins University (rapid epidemiological assessment); David Steedman, International Development Research Centre (grant-making process and administration).

Another vital contribution to the research program was made by hundreds of volunteer participants from the U.S. scientific community and occasionally other countries as well. These volunteers donated literally thousands of days of effort in numerous ways, including reviewing proposals, making site visits to grantees, reviewing publications, assisting with networking meetings, providing training, or serving on committees. In return, they received no compensation (out-of-pocket expenses such as travel costs were reimbursed) except for the interest derived from the programs with which they worked and the knowledge that they were helping colleagues in developing countries. Their efforts helped BOSTID substantially to multiply the resources available to the program.

NOTES

1. *Fiscal Year 1981 Congressional Presentation: Institute for Scientific and Technological Cooperation.* Annex IX of the Congressional Presentation of the Agency for International Development. Undated [1980].
2. Although BOSTID is a unit of the National Research Council, which carries out activities on behalf of the National Academy of Sciences, the National Academy of Engineering, and the Institute of Medicine, the corporate body empowered to enter into legal agreements is the National Academy of Sciences.
3. Regional meetings were held March 30, 1981, in San Francisco; April 13, 1981, in Washington, D.C.; and April 20, 1981, in Chicago.
4. At that time the research program staff consisted of Michael Greene, the new executive secretary or program director; Tresa Bass, the administrative officer; Betty Wells, secretary; and Karen Bell, a health professional, shared half-time with the Institute of Medicine. Victor Rabinowitch, director of BOSTID and after 1982 executive director of the Office of International Affairs of the National Research Council, John Hurley, succeeding director of BOSTID, Rose Bannigan, and other BOSTID staff had conceived and carried out the negotiations with AID to create the program, and they continued to assist.

Start-Up

AID required that an implementation plan for the new research program be submitted for approval by August 1981. Also during the last half of 1981, staff submitted draft grant agreements, including the memorandum of grant provisions, and the operational and financial procedures that would govern the BOSTID Research Program. Accounting, reporting, and evaluation systems were established, and a microcomputer was purchased for use in an information retrieval system. In creating a whole new system of operations and procedures, BOSTID staff spent considerable time studying the workings of Canada's International Development Research Centre, (IDRC), which has many characteristics that inspired the drafters of the ISTC concept. The IDRC responded with great generosity to BOSTID's requests for guidance.

The CRG held its first meeting in June 1981, when it discussed the lists of recommended topics produced by the regional meetings, and decided that the grants should neither be so small that the research could not be completed with the funds provided, nor so large that they would outfit new laboratories or institutes, but should be in the range of $50,000 to $150,000 for two or three years. This set the scale of the program in terms of number and size of grants.

A second CRG meeting was held in December 1981. On the agenda for that meeting were two seemingly disjointed goals: (1) to select the research areas for the program, and (2) to award the first research grants in those areas at the same time, because AID and BOSTID felt it was important to launch the program as rapidly as possible.

SELECTION OF AREAS

The initial agreement between NAS and AID provided that 80 or 90 percent of the research grants would be awarded in certain preselected tech-

nical areas. AID also expected that BOSTID would preselect all candidates for grants and accept no unsolicited proposals. This practice was never adopted, however, because CRG felt that better projects would result from giving equal opportunity to researchers unknown to BOSTID. But for free competition, the selected areas had to be explicitly and carefully described in published announcements. Limiting the areas would also enhance networking activities and collaboration among the grantees.

The optimum number of grant areas for the program was estimated, based on the initial five-year timetable, which required that most of the research grants be awarded within the first two or three years of the program, and dictated the number and size of grants to be awarded per area. If the average grant size was $100,000, then the program could support 160 grants, and if it was reckoned that at most a dozen grants could be given in a short time in any one area, then the optimum number of areas was fourteen. Staff sought to propose research areas to CRG so that fourteen could be selected.

For CRG to have some grant applications to consider at its December 1981 meeting, it was necessary to make an early selection of at least one or two areas. CRG staff proposed two areas that were closely related to past or ongoing BOSTID studies. A series of reports on fast-growing tree species had been published by BOSTID's Advisory Committee on Technology Innovation (ACTI) over several years, subsequently culminating in the two-volume series, *Firewood Crops*.[1] Of the species featured in those works, among the most promising for multiple uses were the leguminous trees, whose nitrogen-fixing capability makes them particularly suitable for tropical soils. Furthermore, in the fall of 1981, ACTI was planning a study on grain amaranth, a hardy grain known for its high-quality protein, which had been identified as a promising crop in the 1975 study *Underexploited Tropical Plants with Promising Economic Value*.[2] The concurrent existence of an ACTI panel on grain amaranth could assist in the organization of a grant program on that subject. Staff proposed to take advantage of BOSTID experience in these two areas to expedite the quick recruitment of the first grantees. They submitted to CRG a mail ballot for the approval of the first two research areas: fast-growing, nitrogen-fixing trees and grain amaranth. CRG approved the two areas in July 1981 and awarded grants in these areas in December 1981.

Under the terms of the grant agreement with AID, research areas were to embrace agriculture and biological resources, technology and mineral resources, and health and nutrition. BOSTID had relatively little experience with health and nutritional problems, and sought collaboration with the Institute of Medicine (IOM). The IOM seconded a professional staff member who devoted half of her time to the BOSTID Research Program, and a special BOSTID-IOM committee was created to advise CRG on health-related issues. This committee, the Advisory Committee on Health, Bio-

medical Research, and Development (ACHBRD), was chaired by Dr. D.A. Henderson of the Johns Hopkins University School of Public Health.[3]

The implementation plan for the BOSTID grant was submitted to AID in late August 1981. It provided details on activities planned and operational procedures, and it described fourteen candidate research areas. Five of the six areas that were ultimately adopted were on this initial list.

Consistent with the overall objectives of the program described earlier, five criteria were used by CRG to select research areas:

1. Importance to international development.
2. Advantage of carrying out the work in a developing country for ecological, environmental, or other reasons, and the likely presence of some capability and existing research facilities in the countries.
3. Likelihood of achieving significant progress in a short time, with technical assistance and technology transfer by U.S. scientists and engineers.
4. Absence of substantial funding available from other international donors.

A fifth criterion was also important, but did not apply in practice when some of the health-related areas were considered:

5. Prior experience of BOSTID and the role of BOSTID publications in elucidating the importance of the problem.

Taken together, these criteria characterized problem areas that represented constraints to development that might have technical solutions. Moreover, the countries had to have capability to address the problems, and the special ecological, edaphic, or environmental conditions surrounding the problem should necessitate that the work be done in developing countries. In other words, CRG wanted to fund projects in the Third World that could not be done better in the United States. On the other hand, it sought opportunities for technology transfer, where U.S. scientists could provide techniques or materials that would enable developing country researchers to solve problems that were important to the development of the countries or to the field in general. The areas finally approved all emphasized field work, in most cases combined with laboratory analysis. Supporting activities explicitly included the introduction of new research techniques through workshops and expert consultant visits. Most grant budgets provided for the purchase of microcomputers, and several workshops were held to train researchers in their use.

During the next two years, CRG continued to consider the selection of additional grant areas. Letters were sent to developing country scientists soliciting suggestions. Staff visited Washington-based agencies such as AID, the United States Geologic Survey, United States Department of Agriculture, National Science Foundation, United States Forest Service, World Bank, and National Institutes of Health. In all, thirty-four areas were formally proposed, with documentation, to CRG. These are listed in Table 1.

TABLE 1 Research Areas Proposed to the Committee on Research Grants

Agriculture and Biological Resources
Grain amaranth
Fast-growing, nitrogen-fixing trees
Integrated pest management
Exploration for legumes in Andean forests
Biological nitrogen fixation
Post-capture technologies for fish
Monitoring the effects of environmental degradation on fish stocks
Animal production
Halophytes
Aquaculture
Shrimp production
Technology and Mineral Resources
Tropical soils geochemistry for detection of ore deposits
Charcoal production from agricultural wastes
Monsoon modeling and prediction
Small hydroelectric power plants
Alcohol production from waste fruit
Farm-scale fertilizer plant
Marine hydrocarbon pollution in the Caribbean
Application of remote sensing
Ferrocement
Nondestructive evaluations (of materials)
Essential oils and resinoids
Liquid fuels from biomass
Energy from grasses
Sanitation and water supply
Health and Nutrition
Guinea worm control
New epidemiological techniques for rapid assessment and evaluation
Arthropod vector research (later approved as mosquito vector research)
Dietary energy requirements
Infant mortality in first year of life
Pharmacological research
Acute respiratory infections in children
Blindness due to trachoma
Benefits and risks of contraceptives

From the outset, CRG and staff realized that there was a problem with the timetable in the AID grant agreement. The program originally was scheduled to be completed in five years; after two years it was clear that the start-up time originally anticipated was not sufficient and so the program was extended to eight years. But the way to complete the program even within an eight-year time frame was to award four-year research grants only

during the first three years; thereafter, only shorter research grants could be allowed. There would be no possibility of renewal of a successful grant. When CRG rejected as unrealistic the notion of increasingly shorter research grants with each succeeding year, the only solution was to award a large number of research grants in the first three years, and the time devoted to selection of the technical areas was making this problem more severe. However, a meeting with AID resolved this issue.

Following the December 1982 meeting of CRG, Frederick Seitz requested a meeting with Nyle Brady, senior assistant administrator of AID, to expedite the process of AID concurrence in the newly approved research areas. The meeting took place in February 1983. Walter Rosenblith, foreign secretary of the National Academy of Sciences, and other NRC and AID staff were also present. Dr. Brady surprised the participants by proposing a new timetable for the CRG program. He referred to the implementation plan, in which CRG had proposed to award grants in fourteen areas, with a timetable allowing for completion of the last grant by late 1988. He argued that resources should be concentrated in fewer areas to give better support and get more effective research. He argued that a more rational approach would be to schedule grant awards as though the program would continue beyond 1988, thus allowing for renewals and a roughly constant number of active grants at any time. This would help also to rationalize staff utilization. The economics of this approach, which was enthusiastically embraced by the NRC participants, allowed, at most, six operational grant areas, with about twenty active grants in each at any time. By mutual agreement between NAS and AID, two of the newest areas approved by CRG at the December 1982 meeting, aquaculture and trachoma, were set aside, and the BOSTID Research Program was dedicated to just six areas. These were grain amaranth (AMA), fast-growing, nitrogen-fixing trees (FGT), biological nitrogen fixation (BNF), mosquito vector field studies (MVR), rapid epidemiologic assessment techniques (REA), and etiology and epidemiology of acute respiratory infections in children (ARI).

COMPUTERIZED DATA BASE

One of the first tasks facing the staff, and before any proposals were received, was to create a computerized data base to register contacts in the developing world, proposals received, grants awarded, and scientific reviewers. A system based on the package dBase II (later upgraded to dBase III) was developed, which recorded data in a file called CONTACTS on all developing country scientists who received announcements, whether through a professional society, say, or upon unsolicited inquiry. When the data was entered, the system would automatically prepare a letter to the applicant providing instructions for submitting a proposal. For those who responded with a proposal, the information was transferred to a new PROPOSAL file,

and a letter was automatically prepared for acknowledgment. Those awarded grants were registered in the GRANTS file. The system was designed to prepare acknowledgment letters when the data was entered. This convenient system also provided an element of control, since any acknowledgment letter that had not been done on the computer and in which, presumably, the data had not been entered, could easily be spotted in the circulating "reading file."

Information included in the files became more detailed in progression from CONTACTS to PROPOSALS to GRANTS. Apart from information related to geographical area, mailing and electronic addresses, and field of technical interest, data was compiled on educational level of the principal investigator and place where training was received, whether in the United States, Europe, or the Third World. This was part of an attempt to understand and improve the approval rate for proposals from different geographical areas and persons of different background, and this information was later used in the design of workshops on proposal preparation.

Ultimately the computerized files contained over 2,000 CONTACTS records of scientists working in one of the six areas in developing countries, as well as 524 proposals and 109 grants. Table 2 shows a distribution of proposals received by geographic area. An analysis of 137 proposals received between 1985 and 1987 indicated the educational level of the successful and unsuccessful applicants as follows:

- 12 percent of the principal investigators had an M.D. degree.
- 68 percent had a Ph.D.
- 17 percent had an M.S.
- 4 percent had a B.S.

The success rate (grants awarded) showed little difference between Ph.D. and M.S. holders, and slightly favored the M.D.s. Of the applicants receiving grants:

- 44 percent were M.D.s.
- 31 percent held Ph.D.s.
- 30 percent had an M.S.
- 40 percent held a B.S. (2 out of 5 proposals).

Of these principal investigators, the following educational levels were attained:

- 32 percent earned their highest degree from the United States, and had a success rate of 27 percent.
- 25 percent earned their highest degree from Europe, and had a success rate of 36 percent.
- 43 percent got their highest degree from a developing country, usually their own, and had a 36 percent success rate.

TABLE 2 Proposals Received and Grants Awarded, by Country

COUNTRY	PROPOSALS	GRANTS
AFRICA		
Botswana	2	
Burkina Fasso	1	
Burundi	1	
Cameroon	1	
Congo	4	1
Cyprus	1	
Egypt	14	2
Ethiopia	1	
Gambia	1	
Ghana	1	
Kenya	18	6
Lesotho	1	
Madagascar	2	
Malawi	2	
Mali	2	
Morocco	2	
Nigeria	27	2
Senegal	5	3
Sierra Leone	3	
Sudan	4	1
Tanzania	7	
Tunisia	1	
Uganda	4	2
Zaire	2	
Zambia	1	
Zimbabwe	1	1
TOTAL	109	18
LATIN AMERICA		
Argentina	7	2
Bolivia	3	
Brazil	27	6
Chile	19	6
Cayman Islands	1	
Colombia	12	3
Costa Rica	12	1
Dominican Republic	3	
Ecuador	2	1
Guatemala	20	8

Haiti	6	2
Honduras	1	1
Jamaica	7	1
Mexico	37	8
Panama	7	2
Paraguay	2	
Peru	19	5
Trinidad & Tobago	5	1
Uruguay	6	1
Venezuela	4	1
TOTAL	200	49
ASIA		
Bangladesh	14	2
Burma	2	1
India	34	2
Indonesia	14	1
Korea	4	
Malaysia	11	4
Nepal	7	
Pakistan	10	4
Papua New Guinea	1	1
Philippines	65	11
Sri Lanka	17	3
Taiwan	1	
Thailand	34	11
Vanuatu	1	
TOTAL	215	40

Among this sample of researchers applying for U.S. grants, there appeared to be no disadvantage for those educated in their own countries. In fact, those with degrees from the United States did not do as well as those trained in Europe or in their own countries.

ORGANIZATIONAL MEETINGS

For each of the six project areas approved by CRG, an organizational meeting was held to define and organize the research program before the availability of grants was announced and proposals were solicited. (In the case of REA, a preliminary meeting was held first to clarify the goals and set the terms of reference before the organizational meeting.) Each organizational meeting included both developed and developing country researchers active in the particular field, representatives of international organiza-

tions, AID officials, and at least one member of CRG. Given the general outline and goals approved by CRG for the particular area, the participants were asked to fill in some of the details: What are the most urgent research needs in this area for developing countries? Which techniques or methodologies should be emphasized? What would be appropriate mechanisms for collaboration among grantees? Which institutions in developing countries should be invited to apply?

The developing country participants were selected from among the most active researchers in each field. It was hoped that some of them might prepare successful proposals and that, having participated in the design of the research program and therefore feeling a stake in its success, they might play a leadership role among the group of grantees. A special session on proposal writing and grant management was held for them at each organizational meeting.

The product of each organizational meeting was the first draft of the program announcement or "request for proposals." This document described the research goals of the technical area, which lines of research were of interest to CRG, and what techniques were, if not required, at least favored.

After approval by CRG, the announcements were disseminated by various means. Copies were sent to scientists known to BOSTID or identified at the organizational meeting as active in the field. They were distributed to members of appropriate international professional societies, authors of relevant papers, and to U.S. scientists for circulation to their developing country colleagues or students. Announcements were published in scientific journals and newsletters. When letters from developing countries arrived in response to these notices, BOSTID sent a copy of the relevant program announcement, the proposal preparation guidelines, and, after 1985, a copy of a paper called *Elements of the Successful Scientific Proposal,* prepared by the research program director, which provided advice on proposal preparation. Copies of proposal guidelines and *Elements* are available from BOSTID.

ELIGIBLE COUNTRIES

One of the features that distinguished the BOSTID Research Program from many other AID-supported activities was the ability to award grants to advanced developing countries, the so-called AID graduates. The main criterion in awarding such grants was that the research should be important to developing countries in general; in practice, this was applied to proposals from all but the poorest countries. However, advanced developing countries often were given less assistance with proposal preparation and sometimes less "benefit of the doubt" in close decisions by CRG. The result was that there was little to distinguish the projects of the advanced developing countries from others. There were some countries whose eligibility was

uncertain. For example, inquiries were received from Turkey and from Israel. The latter was in the form of a letter from the deputy director of the Weizmann Institute to CRG, with copies to AID and the U.S. Congress, asking why grants were awarded to middle-income countries such as Brazil and Mexico but not to Israel. In response, it was explained that there were several other sources of funds available to Israeli scientists, such as the United States-Israel Science Foundation, supported with U.S. funds, and that the BOSTID Research Program was intended for those developing and advanced developing countries that have few other opportunities. (Shortly thereafter, Congress authorized and funded a Cooperative Development Research Program in the AID Science Advisor's Office with grants available only to Israeli scientists who collaborate with developing country institutions.) The eligibility criteria were expressed by CRG as "non-OECD,[4] non-Eastern Block, non-Israel and non-South Africa." In principle, this would allow for grants to the "NICs," or newly industrialized countries of Korea, Singapore, Taiwan, and Hong Kong, but since only a few proposals were ever received from them, and they were rejected for technical reasons, the issue was never faced.

The most controversial country to be excluded from eligibility for grants was the United States. The wording of the terms of the AID grant to BOSTID seemed to permit grants to U.S. institutions in exceptional cases to assist developing country researchers, but CRG decided this was not feasible. Some U.S. scientists considered the inability to fund U.S. collaborators a serious weakness of the program, but it is likely that large sums of money and considerable time of staff and CRG would have been consumed in the selection and funding of U.S. grantees, which would have greatly multiplied the number of proposals received.

NOTES

1. *Firewood Crops: Shrub and Tree Species for Energy Production*, Vol. 1, Washington D.C., National Academy of Sciences, 1980; Vol. 2, 1983.
2. *Underexploited Tropical Plants with Promising Economic Value*. Washington, D.C., National Academy of Sciences, 1975.
3. Membership of the Advisory Committee on Health, Biomedical Research, and Development: D.A. Henderson, Johns Hopkins University (chairman); Joseph Cook, The Edna McConnell Clark Foundation; Davidson Gwadkin, Overseas Development Council; Gail Harrison, University of Arizona; James Hughes, Kaiser Aluminum and Chemical Corporation; Gerald Keusch, Tufts University; Nathaniel Pierce, Johns Hopkins University; Henry Hiecken, National Library of Medicine; Gerard Rohlich, University of Texas; Allen Rosenfield, Columbia University; Karen Bell, staff officer.
4. The Organization for Economic Cooperation and Development includes the industrialized countries of North America, Europe, and Japan.

Procedures

PROPOSAL EVALUATION

In most cases, submission of a proposal was not the first contact of BOSTID staff with the applicant. Most applicants had received directly from BOSTID, or from colleagues who had communicated with BOSTID, copies of the announcements and proposal preparation guidelines. Often, applicants sent preproposals, or long detailed letters describing the proposed project. Preproposals were not part of the CRG system, but staff always responded informally to such documents, giving advice on the suitability of the topic or approach, with the caveat that staff could not speak for CRG and that faithful adoption of the advice would not guarantee approval.

Preproposals were not requested for several reasons, one of which was that BOSTID quickly learned that, based on staff site visits to applicants and their institutions, even the first version of a full proposal is very often a poor indicator of the capability of a research group, and a three-page preproposal is worse. Staff visitors found that the groups were often better prepared than their proposals would suggest, and sometimes they found, to the contrary, that the proposals exaggerated the resources available for research.

A more important reason for not employing preproposals was that CRG felt it was essential that the cycle time, that is, the time between initial submission and the first grant payment to a successful applicant, be as short as possible. Preproposals would have added at least three months to the process and required additional meetings of at least part of CRG. At its best, the CRG cycle time was about six months, including site visits; this was achieved during the early period when the number of grants already requiring management attention was low and the committee met three times per year. Later it increased to about eight months.

There was an additional, practical reason for not requiring preproposals. It is much easier to prepare a three-page preproposal than a thirty-page full proposal, and the experience of the companion Program in Science and Technology Cooperation (PSTC) small grants program, funded and administered by the Office of the Science Advisor of AID, showed that one can expect submission of many more preproposals than proposals. Each one must be analyzed, evaluated, and answered, consuming a considerable amount of staff time to do it well. CRG received a total of 524 full proposals and awarded 109 grants. As a comparison, the PSTC received about 600 preproposals and awarded 40-50 grants per year during the same period. The best use of staff time is a question of priority; on balance, research program staff dedicated much more time assisting grantees to carry out their projects than they spent processing proposals to select them. This would not have been possible with the additional demands of processing preproposals.

Each proposal received was assigned to one of the six areas and given a number; for example, the twelfth nitrogen fixation proposal received was called BNF-12. The number served as an identifier until the proposal was approved and funded. The number was assigned and the proposal was entered in the system before any evaluation was done, ensuring that all proposals were tracked, acknowledged, and received a response indicating the next steps in the evaluation.

Nearly all proposals were sent for external review. The reviewers were working scientists, mostly in the United States, who had relevant expertise in the topic. The number of reviewers for a given proposal varied between three and six, depending on the complexity and multidisciplinary aspects of the proposal. Those proposals that were not related to one of the six research areas or were not of serious quality were reviewed in writing by staff. On a few occasions the proposals were sent to active grantees, among others, for review.

Reviewers were supplied with a copy of the proposal, a copy of the announcement to which the applicant was responding, a report of the organizational meeting for that area for background, and some specific questions framed by the program staff. Toward the end of the program, these were refined into an evaluation form with five questions and space for a response.

When initial reviews were complete, the staff did a preliminary screening. Those proposals that appeared to be unpromising and that were unlikely to be funded even after revision were submitted with all reviews to the six CRG members who comprised the executive committee. The executive committee, which sometimes met by conference call, was advised to reject those proposals. (Because they did not see the more promising proposals at that time, the executive committee meetings were considered by some members to be depressing and unrewarding.) Occasionally the com-

mittee recommended further evaluation of a proposal. About 50 percent of all proposals were rejected by the executive committee; these unsuccessful applicants were sent an explanatory letter and unattributed copies of the reviews. Generally the reviews were constructive, and some of these proposals were reoriented and funded at a later date.

PREGRANT VISITS

One of the unique features of the BOSTID Research Program was the pregrant site visit. All applicants whose proposals were not rejected by the executive committee were visited by BOSTID staff or consultants. The pregrant visits had three major purposes. The first was to present the reviewers' comments to the applicants and assist in the revision of the proposal, where necessary. There was sometimes a good deal of understandable culture shock associated with the peer review process, and a sympathetic U.S. scientist could be quite helpful in interpreting the reviews and advising on an appropriate response.

The second objective was to gather additional information about the proposed research, the capability of the investigators, the facilities available for the project, and the financial management system of the host institution. For this last goal, a financial management questionnaire prepared by an independent auditor was an important tool.

The third purpose was to acquaint the prospective grantee with the scientific and administrative requirements of the BOSTID system and to gather information that would be required, if the grant were approved, to prepare the grant budget and the formal grant documents and initiate the project.

The positive results of the pregrant visits convinced CRG and staff that they should be an essential part of the evaluation of proposals from the Third World. When the expense was challenged, it was pointed out that the travel cost for all the visits was about one percent of the total value of the grants awarded, and they certainly saved many times their cost in avoiding unpromising projects and improving marginal ones.

One other important element of every pregrant visit was the consultation with the AID mission or responsible embassy officer in the country. Although the BOSTID Research Program required no administrative or logistical assistance from the local AID missions, the CRG staff briefed the missions during visits to the countries. During the pregrant visit, the CRG staff informed the AID mission of the status of the program, with emphasis on any ongoing projects in the country. AID was briefed about the nature of the new proposal, and the mission was asked to comment to CRG on whether the proposal duplicated other AID activities in the country. The AID mission had the right to veto any proposal coming from the country that was considered incompatible with U.S. interests. In fact, this right was

In one example, the site visit was decisive. CRG received a well-written proposal in the Fast Growing Trees program related to tissue culture of an important species of tropical forest hardwood. The proposal was well received by referees, and the young investigator appeared to be well trained, although he had not published in refereed journals. But a pregrant visit to his university produced a surprise. The laboratories were empty of research equipment. Nor were those basic items that were missing from the laboratory included in the proposal budget. When asked about it, the researcher admitted that he had a problem, but said he hoped to use the facilities at another laboratory in the same city. But a visit to that laboratory revealed that he was not known to the staff there, and they had no interest in helping him. The university researcher was not funded, but the other laboratory subsequently submitted a successful proposal to BOSTID. (Despite the urging of the visiting CRG staff member, however, they declined to include the young professor in their proposal, and, in truth, he had little to contribute.) CRG concluded that without the pregrant visit a grant might have been awarded to the university researcher, who would have had no chance of completing the research.

never exercised, and on the few occasions when the AID staff advised against funding a project, CRG was in agreement.

Following the pregrant visit, about two-thirds of the applicants returned revised proposals; the others, usually those whose peer reviews were favorable overall, wrote explanatory letters. These revised proposals, and sometimes the letters, were resubmitted to reviewers, generally the same ones who had reviewed the original proposals, but sometimes someone new. Again the reviewers submitted written reviews. The material then went to CRG for a funding decision.

CRG considered four options with regard to each proposal: (1) it could be accepted and approved as written (always pending staff negotiation on budget items); (2) it could be approved provided certain changes were incorporated and accepted, and it did not need to return to CRG for further review if the applicant was agreeable to the conditions; (3) it could be approved conditionally, with the requirement that specified changes be made by the applicant, sometimes with the assistance of a BOSTID consultant, before reconsideration (those revisions generally had to be approved by the executive committee, but the proposal did not have to be resubmitted to

the full CRG); and, finally, (4) a proposal could be rejected, with or without encouragement to the applicant to submit a new proposal. In every case, the decision of CRG was transmitted to the applicants with unattributed copies of any peer reviews they had not yet seen.

AID missions were informed of the funding decisions, including the reasons for approval or rejection. Where a proposal was approved for funding, it was suggested that the U.S. ambassador might like to enhance the recognition with a congratulatory letter, and a sample was enclosed. In many instances, the ambassadors did send letters; in a few cases they also held ceremonies at the embassy in honor of the grantees. In one case in particular, however, this caused some misunderstanding. John Gunther Dean, then the U.S. ambassador in Thailand, was particularly interested in science and technology; he became well known for encouragement and support of scientists. When one BOSTID grant to a Thai scientist was announced, the ambassador not only sent the congratulatory letter, but he arranged a ceremony in which he and the rector of the university formally signed a document of agreement, unknown to BOSTID. Meanwhile, the grantee had been instructed not to spend or obligate any funds until the official grant documents were signed in both countries. But what could be more official than the signatures of the rector and the U.S. ambassador? Assuming the condition fulfilled, she began to spend her own funds, thinking she would be reimbursed later by the grant. It was some time before CRG staff understood what happened and arranged for repayment.

HUMAN STUDIES

About 40 percent of the grant projects involved studies on human subjects or health risks to researchers, particularly in the areas of mosquito vectors, rapid epidemiologic assessment, and acute respiratory infection. AID required that the principal grantee institution, the National Academy of Sciences, take responsibility for the protection of human subjects and research workers. Therefore, before any approved project could begin, the proposal protocol for human studies had to be reviewed and approved by the Academy's Committee to Review Human Studies. That committee reviewed the protocol to identify risks to patients, subjects, and researchers, including violations of privacy. They examined consent forms, and, where the grantee institution itself had an institutional review board, required approval of the protocol by the local board. Frequently they requested modifications of consent forms, and occasionally they disallowed experiments they considered too invasive or of limited value for the risk involved. Grantees had to assure compliance with the requirements of the Committee to Review Human Studies before the project could start, and CRG staff were charged with monitoring compliance during site visits.

GRANT AGREEMENTS AND FINANCIAL MANAGEMENT

Formal agreement between the National Academy of Sciences and the institution receiving a research grant was embodied in a grant document signed by the heads of both organizations. The agreements included a standard memorandum of grant provisions, which specified the objectives of the research and the activities to be carried out in a section titled "purposes and objectives," based on the approved proposal. The budget was detailed by line item and year and divided according to funds that would be paid in U.S. dollars, managed by BOSTID, for items such as equipment and international travel, and funds that would be sent to the grantee for local expenses, including salaries, local travel, equipment and supplies purchased locally, and overhead. (The only items that could not be included in a grant budget were items proscribed by AID, such as pharmaceuticals, abortion equipment, and motor vehicles.) The agreement also included a list of the grantee's contributions to the research, which could include salaries, facilities, and other goods and services made available by the grantee institution. The names of the principal investigators along with the time they would dedicate to the project were listed, either in the grant budget or as a grantee contribution, depending upon who paid the salaries. A change in principal investigator or a failure to provide all or part of the grantee's contribution constituted a violation of the agreement unless there was written approval for the change by both sides.

The memorandum of grant provisions embodied the operational mechanisms for the program, including budgetary requirements, specifying that NAS obligations were limited to those items included in the budget and setting restrictions and procedures for budget adjustments. It also included payment and reporting requirements and maintenance and use of funds, supplies, and equipment. Other provisions dealt with accounting, auditing, and records, indicating the NAS right to conduct field audits; refunds of unexpended funds; the requirement that the grantee institution provide the items and services specified in the "grantee contribution"; protection of human subjects and avoidance of risk of disease to researchers; publication of results, with appropriate citation of NAS contributions; patents; international travel regulations; nonliability of NAS for legal claims; termination procedures; and jurisdiction of the laws of the District of Columbia.

A basic operating rule of the program recommended by CRG and the NAS comptroller required each grantee to open a separate, non-interest-bearing bank account to be used exclusively for grant funds. All grant expenditures were to be made directly from this account. Grantees unable or unwilling to open a separate bank account operated their projects on a cost-reimbursable basis, that is, with no advance payments. In a few difficult cases all receipts and vouchers submitted for reimbursement were sent to Washington for review before payment.

Expenditure and technical reports had to be up-to-date before grant payments were sent. Only the first payment (about a quarter of the first year's budget for local costs) was sent automatically on receipt of the signed grant document. The second payment was sent on request. The third payment was sent only when the expenditure report for the first payment had been received, and so on. Payments, roughly one-quarter of a year's budget, were sent only on request of the principal investigator to match the pace of the project and so that unspent funds would not accumulate in local accounts and risk decline in value because of inflation.

Technical reports were due every six months. At half-year intervals after the signing of the grant, brief activity reports, indicating equipment received, consultant visits, trips to the field, and other activities, were to be submitted. At each anniversary of the grant, full annual scientific reports were expected. These described the scientific progress, reported data, and discussed plans for the next year. At the conclusion of the project, a full, technical final report was required.

A *Grantee Handbook* was prepared and distributed to all grantees to explain procedures. It also provided detailed instructions for reporting, especially for expenditure reports, which tended to be complicated when exchange rates varied with time.

The audit policy and procedures were key components of financial management. "Audit" began with the questionnaire administered by the staff visitor to the institutional financial officer and principal investigator during the pregrant visit. It was designed to elicit information about internal control and reporting, administrative procedures, care and protection of equipment, and personnel practices. It also conveyed the message that BOSTID was serious about financial management. CRG's independent audit consultants reviewed the completed questionnaires and proposal materials for each approved project, and they based their recommendations for field audits, in part, on the answers to the questions. Where it was considered necessary, the BOSTID administrative officer visited a grantee institution before the first payment to assist in setting up an appropriate system for managing the grant. CRG, from the outset, left administrative matters to the staff and made funding decisions solely on scientific considerations.

SCIENTIFIC SUPPORT

Once the project began, the staff assisted the grantees in many ways:

- Selection, purchase and shipping of equipment and supplies;
- Arrangement of international travel connected with grant activities, including itinerary, air ticket, reservations, and per diem expenses;
- Selection and logistical arrangements for visits by international experts;
- Organization of periodic coordination meetings of grantees in each field;

- Critical reviews of technical reports by staff or consultants;
- Editing of manuscripts for publication; and
- Offering friendly support and collegial advice.

Program Cost Ratios

As of April 1990, the ratios of costs for different parts of the program were:

Administration	20 percent
Networking	13 percent
Research Grants	59 percent
G&A	8 percent
Total	100 percent

Administrative costs cover basic costs of selecting grantees; financial management, including auditors; equipment purchases; site visits; evaluation.

Networking includes coordination meetings and workshops, publications, and general assistance to grantees.

Research includes grants and other forms of direct assistance to individual grantees.

G&A are indirect General and Administrative charges imposed by the National Research Council on all program funds.

Procurement and shipment of equipment and supplies deserves special mention. Considerable resources, including one full-time professional and a half-time consultant, were dedicated to procurement. Many of the projects were heavily dependent on the selection and timely arrival of scientific equipment, and the effort dedicated to procurement was a necessary protection of the grant investment. In many projects, researcher salaries began with the first grant payment, but the work did not start until the equipment arrived. A long delay could be costly.

Catalogs were provided to grantees to assist in the selection of equipment. Some suppliers had catalog prices "on line" so that quotes could be obtained by computer. BOSTID negotiated generous discounts from some of the largest suppliers, and had a good working relationship with international shippers. Clearing items through customs was the responsibility of the grantee, and grant funds could not be used to pay duties. But BOSTID supplied appropriate letters of donation, and there were relatively few serious problems at the receiving end. In some of the most notoriously difficult countries, the Pan American Health Organization gave generous assistance.

On the other hand, some rather costly problems were encountered at the U.S. end. There was some equipment lost or unaccounted for by shippers, but in the ARI program, most of the trouble involved shipping of cell cultures and other biological materials. Shipping of designated "hazardous biologicals" must follow certain federal guidelines. Labile reagents or cell cultures are often shipped in dry ice, which is considered a hazardous material. These shipments must be carefully tracked, because every U.S. airline pilot has the right to review the cargo on passenger flights and reject any shipment. On several occasions, materials packed in dry ice were off-loaded and shipment was delayed, causing loss of expensive materials. In one case, a bacterial strain was donated by a researcher in Washington State to a grantee in Uruguay. Since this was not a commercial transaction, BOSTID was responsible for arranging the export licensing for hazardous biologicals and preparing the proper paperwork to accompany the shipment. The forms were submitted to the International Trade Administration of the Department of Commerce, and after several weeks a license was received. Several times the U.S. researcher attempted to ship the materials, but the airline pilot refused to load the package. Finally it was shipped in dry ice to Miami, but airline personnel in Miami who were unfamiliar with the export procedure for biohazardous and perishable materials shelved the package for three days. Before the airline was satisfied that the paperwork was in order, the dry ice had evaporated and the culture was useless.

At best, shipment of live cell cultures is tricky, and cultures sometimes arrived in poor or unusable condition. Live culture in media and frozen tissue culture had to arrive within two to four days to have any chance of survival. Whenever possible, researchers and visiting consultants carried perishable supplies to the projects. It took special effort to assure that grantees had stock cultures in their laboratories year-round, and frequently the annual meetings of all principal investigators provided the opportunity to replenish stocks. When a meeting was held at one grantee's laboratory abroad, she took the responsibility of growing and testing the cultures and distributing them to the others.

EVALUATION AND MONITORING

For each research grant, two files were created. The BOSTID program manager's files contained all information related to the technical aspects of the project, such as the proposal, pregrant visit and consultants' reports, technical reports from grantees, staff comments, and published papers. Grant agreements, payment records, expenditure reports, financial questionnaires, audit reports and follow-up, and procurement documents were kept in the administrative officer's files.

BOSTID Audit Program

The BOSTID audit program included pregrant, interim, and final financial reviews for all grants. In addition, based on assessments from these reviews, fifty-nine grants to thirty-eight institutions in twenty-five countries were audited in the field.

The main objective of the audit program was to employ audit as a way to strengthen financial management in developing country institutions. This was accomplished in part by encouraging program, finance, and administrative staff to meet together during site visits and field audits to solve financial and administrative problems as they occurred. Once each group understood the needs of the others it was easier to work as a team. Teamwork proved helpful to everyone, especially principal investigators, because in some grants there were problems in administering the separate bank account, in custom and bank clearances, in hiring of personnel, and in obtaining money locally for project use.

Accountability and internal control in grantee institutions varied from maintaining no formal records to double entry accounting systems. The goal of the auditors while in the field was to help grantees develop systems consistent with their resources. To that end, most audits included recommendations to encourage better systems of financial control, and provided training if the recommendations were accepted.

About midway through a grant project, either staff or a scientific advisor paid an interim visit to the institution. A second financial questionnaire prepared by the auditor checked on compliance with procedures and provided additional information for field audit recommendations. Staff checked progress toward completion of objectives, discussed possible changes of work plan, objectives, or budget, monitored human studies procedures, and tried to solve any problems. Often, after an interim visit, a U.S. consultant was sent to advise on a particular aspect of the project.

CRG felt strongly that each project should have U.S. or other international scientific collaborators. If a grantee did not identify or request a collaborator in the proposal, the staff helped to identify appropriate individuals and added the costs for collaborative visits to the grant budgets. Projects were visited about once a year, and the consultants' reports formed an important part of the evaluation process. In addition, all semiannual progress reports and annual reports were reviewed by staff; normally a

memo was put in the file, or a letter was written to the grantee commenting on the report.

One of the most rewarding and interesting elements of the project-monitoring system was the annual coordination meeting. All grantees working in the same program met at one of the grantee institutions, at the site of an international meeting, or in Washington. The grantees reported on their progress and received comments and criticism from peers, invited experts, and staff. Most meetings included special workshop sessions, led by grantees or invited experts, on new techniques, and sessions were dedicated to discussion of common concerns, like preparation and submission of scientific papers in English and putting research results into practice. Staff also met privately with each grantee to discuss the project, answer questions, and solve administrative problems. There was an initial period of uncertainty, when some grantees called these meetings the "third degree," but later grantees apparently began to look forward to the individual meetings and would arrive with long lists of written questions.

About twenty-seven of these meetings were held, and they soon became the hallmark of the BOSTID program. International organizations, like WHO, PAHO, and the World Bank, and bilateral aid agencies, like the International Development Research Centre of Canada, sometimes sent their representatives, and many American scientists were eager to attend. Generally, the spirit was friendly and cooperative, and some grantees felt that when their projects were finished, the end of their participation in the coordination meetings was the greater loss.

PUBLICATIONS

A major goal of the program was to ensure that the research results were published in the international scientific literature. This was a prime responsibility of each BOSTID program manager. Staff offered editorial assistance, usually through volunteer advisors who had visited the project, and payment of publication charges could be made with non-grant funds set aside for the purpose. (This publications account was set up so that papers could be published after the grants had formally expired.) In four of the six research areas, staff arranged joint publication of research papers in special editions of refereed journals. Thus, for example, papers from the amaranth project are being organized for publication in a special edition. Papers of BNF grantees appeared together in *Plant and Soil.*[1] REA papers were published in *The International Journal of Epidemiology.*[2] ARI grantees' papers appeared in *Reviews of Infectious Diseases.*[3]

Publications

A partial count of publications in refereed journals or books and advanced-degree dissertations was made in early 1990. The totals by area are:

Amaranth	65
Biological nitrogen fixation	75
Tropical trees	40
Mosquito vectors	108
Rapid epidemiologic assessment	75
Acute respiratory infections	44
Total	407

CLOSEOUT

When a research grant ends, the closeout procedure has several steps. The first is a complete file review. The administrative officer determines whether all expenditure, activity, and annual progress reports were submitted in a timely and accurate manner, and identifies outstanding problems for resolution. The program manager then reviews all technical, site visit, and consultant reports and prepares an assessment of the project results. Next, the external auditor reviews all material, prepares a list of items needing clarification, documentation, or correction, and advises whether the expenditure report reconciliation indicates that the grantee is owed additional funds by BOSTID, or whether a refund of grant funds is owed to BOSTID. Recommendation is also made for a final field audit, if necessary. Finally, if everything is in order, the equipment that was purchased with grant funds is donated to the grantee institution.

PROGRAM EVALUATION

Two formal evaluations were carried out during the life of the program. The first was by BOSTID, the parent body of the CRG, in 1984. Three members of the Board were designated to carry out the evaluation: William Krebs of Arthur D. Little Inc., Robert Burris of the University of Wisconsin, and Claudia Carr of the University of California, Berkeley. They examined administrative procedures, visited grantees, observed the auditors in action in the field, and attended a coordination meeting. Their report,[4] while admittedly describing an early stage in the program, answered in the affirmative four questions posed by BOSTID:

1. Is the program stimulating and supporting high quality research and development in LDCs on development-related problems of priority concern?
2. Is the program strengthening the capability of research institutions in developing countries?
3. Is the program encouraging participation of U.S. scientists and others from the international scientific community?
4. Are operations efficient and effective?

They then proceeded to raise a number of issues for the future. They suggested that more emphasis should be put on linking research to utilization of research results, and that applicants should be asked about implementation plans in their research proposals. Such a question was thereafter included in the instructions for applicants. They wished to expand the participation, as advisors, reviewers, and consultants, of scientists of high repute from LDCs themselves. In response, an effort was made to include existing grantees among the reviewers of proposals and to invite grantees to lead workshops at coordination meetings. The evaluators also urged strengthening the institution-building aspects by including training and networking for other members of the research groups apart from the principal investigators, an idea that was employed in the ARI program. They invited the CRG staff to reexamine their own procedures. Finally, they recommended adding some new research areas to the original six, an idea that AID opposed as premature. The evaluation, and even the interaction with the evaluation team itself, was beneficial to the program, and increased the self-confidence of the staff and committee.

A few months later, AID asked its Research Advisory Committee to carry out an evaluation of the BOSTID Research Program. Two members of the Research Advisory Committee, Emery Castle of Resources for the Future and Rita Colwell of the University of Maryland, were joined by two "invited scientists," John Sherman and David Pimentel. Pimentel was also vice-chairman of CRG and was listed as "nonvoting." Their brief report[5] assumes two objectives for the program:

1. To support good science in a limited number of areas, and
2. To enhance scientific capability in developing countries.

It then goes on to say, "It is not clear to the panel . . . that these dual objectives are well understood and accepted by those associated with the program." However, it declares:

> [T]he enhancement of scientific capability in developing countries is not the same as institution building as it is generally used in the development literature. Thus the efforts of those administering the program being reviewed to create a regional infrastructure and to establish communication among re-

> search scientists assists in creating a desirable atmosphere for scientific research even though such efforts may not be considered institutions as the term is often used.

The panel recommended increased participation of U.S. scientists, both for site visits and as collaborators in the research, and more use of the resources of the Academy complex itself. They found that the program was well designed, well managed, and that the grantees were well selected. In summation:

> [T]he panel unanimously recommends (Pimentel abstaining) the continuation of the program at NAS/BOSTID. While we are unable to judge the opportunity cost of expansion, we believe the performance and promise of the program warrants growth; in any event, we recommend strongly against curtailment, transfer, or discontinuance.

Since the achievements of the BOSTID Research Program ultimately related to the research accomplishments of the grantees, in the following chapters we will review the objectives and summarize the research results in the six research areas.

NOTES

1. Bale, J.R., E. Crasswell, M. Fried and K. Mackay, eds. "Selected Papers from the Symposium 'The Contribution of Biological Nitrogen Fixation to Plant Production,' Cisarua, Indonesia, 3-7 August, 1987." *Plant and Soil* v 108, no. 1, May,1988.
2. Selwyn, B.J., R. Frerichs, G. Smith, and J. Olson, eds. "Rapid Epidemiologic Assessment," *International Journal of Epidemiology* v 18, supp. 2, 1989.
3. Bale, J.R., ed. "Etiology and Epidemiology of Acute Respiratory Tract Infections in Children in Developing Countries, *Reviews of Infectious Diseases* v 12, suppl. 8, November-December 1990.
4. Burris, Robert, Claudia Carr, and William Krebs, *An Interim Evaluation of the BOSTID Research Grants Program.* BOSTID, May 1985.
5. *Panel Report—National Academy of Sciences/Board on Science and Technology for International Development Research Grants Program*, Research Advisory Committee, undated. [January 1986].

Grain Amaranth

Grain amaranth has been described as the plant with the highest quality protein known.[1] It is a broad-leafed plant, related to the common pigweed, which produces a high fraction of protein with a balanced amino acid content in a large number of tiny seeds. It is a C-4 plant, which means that it is an efficient converter of photosynthesis—like maize and cane. Its origin is in Mesoamerica, and legend has it that Montezuma received twenty tons of amaranth seed per year in tribute. The legend continues that the Aztecs used amaranth seeds mixed with human blood in some form of religious ceremony, and the conquering Spanish, in their effort to destroy the Aztec religion, forbade the cultivation of amaranth. In fact, direct mention of amaranth in the chronicles of the conquest is rare, but amaranth grain is still found on the streets of Mexico City in the form of a sweet confection called *alegria*. The leaves are also high in protein and are consumed in many parts of the world.

Amaranth was identified in a BOSTID publication in 1975 as an underexploited tropical plant with promising economic value,[2] and in 1981 a panel was formed to study in more detail its properties and opportunities for finding a niche in the marketplaces of the Third World. The possibility of basing one of the CRG research areas on this BOSTID study was highly attractive. It would give BOSTID the opportunity to create a linkage between the experts on the study panel and a group of developing country researchers interested in the topic. It would also put to the test the research priorities defined in the study report, and provide feedback on progress induced in the field. However, some concern was expressed that, to avoid a conflict of interest, researchers who might later submit a proposal to BOSTID not be included on the study panel. Therefore, although the study panel met the week before the amaranth organizational meeting, none of the developing country

GRAIN AMARANTH GRANTEES

Ricardo Bressani	Archivos Latinoamericanos de Nutrición, Guatemala. *Grain Amaranth Newsletter.*
Ricardo Bressani	Institute of Nutrition of Central America and Panama, Guatemala. *Development of Basic Information on Guatemalan Amaranth Germplasm.*
A. Sanchez-Marroquin	Instituto Nacional de Investigaciones Agrícolas, Mexico. *Agronomic and Industrial Studies of Grain Amaranth.*
V. K. Gupta	University of Nairobi, Kenya. *Selection and Introduction of Grain Amaranth for Dryland and Semi-arid Climates.*
Luis Sumar Kalinowski	Centro de Investigaciones de Cultivos Andinos, Peru. *Grain Amaranth: Selection, Nutritional Analysis, and Agronomic Comparison of Andean Varieties.*
Enrique Morales	Institute for Nutritional Research, Peru. *Human Digestibility and Utilization of Grain Amaranth Protein and Carbohydrates.*
Chuckree Senthong	Chiang Mai University, Thailand. *Yield Improvement, Agronomy, and Local Use of Amaranth.*
S. Duriyaprapan	Thailand Institute of Scientific and Technological Research. *Species Selection and Potential Uses of Grain Amaranth as an Introduced Crop.*
L. Herrera-Estrella	Center for Research and Advanced Studies, National Polytechnic Institute, Mexico. *Development of Transformation Systems and Cloning of Storage Protein Genes of Grain Amaranth.*

experts brought to the organizational meeting participated directly in the study. Overlap and continuity, however, was provided by the U.S. participants who communicated the panel's research priority recommendations into the CRG program.

The CRG purpose in selecting a "new crop" like grain amaranth for one of the research areas was twofold. First, amaranth had been cultivated, presumably with success, in the past. But it had become feral and neglected and had never received the benefit of agronomic, nutritional, and plant improvement research; it did not look like a modern crop. Most varieties were multiple-branched and hard to harvest, were tall and subject to lodging (falling over), spilled their seeds on the ground (shattering), had very small seeds, and were not high yielding. The first objective, therefore, was to select and culture the plant to develop a crop that might prove economically viable. Second, amaranth was used as a backyard crop in only a few places, and was found in the marketplace only in Mexico and northern India. (How it arrived in northern India has been the subject of several scholarly investigations.) By supporting some socioeconomic studies and some projects outside the amaranth-consuming areas, CRG also hoped to learn something about the dynamics of marketing of new crops.

ORGANIZATIONAL MEETING

The Organizational Meeting was held in Washington, D. C., September 23-25, 1981. It was the first organizational meeting of the BOSTID Research Program, and all subsequent meetings would follow a similar pattern. The participants were amaranth researchers from the United States, Guatemala, Peru, India, and Kenya. Most of the Americans were members of the panel that was preparing the BOSTID study.

CRG had set the following goals for the grain amaranth program:

- Determine the conditions—soil, climate, altitude—under which amaranth may provide more nutritious food or additional income in developing countries.
- Determine and develop the best varieties of amaranth and most effective growing strategies for each region.
- Develop methods for harvest and use of the amaranth plant, taking into account local conditions, customs, and traditions.
- Develop an information base to facilitate expanded production and use of amaranth.

The question was posed at the beginning of the meeting: If amaranth was used so widely in the past, why is it so little used today? The participants felt that the story of the Spanish conquistadors did not explain the present situation, and that there must be another reason why amaranth could

not compete economically. They suggested that BOSTID researchers seek to determine the limiting factors and attempt to develop a plant and cultural system to overcome them. They listed the conditions that would likely define the "special niche" where amaranth could substitute for or supplement traditional foods: low rainfall, medium to high elevation, hilly terrain, marginal tropical soils, and economic areas where imported wheat is important or traditional grains are low in protein.

The following areas were selected for priority consideration:

- Growing and harvesting (particularly determination of soil requirements), determining the parameters of extreme tolerance in terms of factors such as rainfall and soil, and development of a small hand-operated thresher and winnower for the grain;
- Breeding, particularly for reduced lodging and shattering, high grain yield, early maturity, white seeds, food quality, and drought tolerance;
- Processing, including survey of current uses, cooking and milling, feed quality assessment, use as extender, and determining physical characteristics; and
- Economic and social analysis to determine the conditions under which amaranth will be adopted as a food.

The participants also agreed on certain modes of cooperation among grantees, among which was a newsletter to enhance communication among amaranth researchers. The Rodale Research Center volunteered to coordinate seed distribution and exchange and evaluation of germ plasm, and it was suggested that one laboratory be designated to carry out the chemical analysis.

Another significant recommendation was made but ultimately was rejected by CRG. Participants suggested that BOSTID play an active role in promoting use of amaranth through meetings between farmers and scientists, and through extension, training of producers, and manuals for growing amaranth. However, CRG never supported these activities, neither with amaranth nor in any other research area. They said that the purpose of the BOSTID Research Program was to make reliable data available to decision makers, producers, and consumers, not to prejudge the ultimate value of any crop by promoting its use before the research was complete.

COORDINATION MEETINGS

The first coordination meeting of the amaranth program was also the first for the BOSTID Research Program. It was held November 8-10, 1982, partly in Washington and partly in Kutztown, Pennsylvania, site of the Rodale Research Center, focal point for U.S. amaranth research. The purpose of the meeting was to discuss and compare research results obtained

thus far among the grantees, and to review future plans. The grantees agreed on common methodologies for agronomic trials and nutritional testing of amaranth products, and established mechanisms for germ plasm collection, maintenance, replication, distribution, and exchange. Initial emphasis was to be on screening and observation of the performance of different varieties in different settings. A standard experimental design was proposed and a protocol adopted for nutritional testing. The Institute for Nutrition of Central America and Panama (INCAP) offered to measure protein efficiency ratios (PER) for all grantees at a substantial discount. All grantees would do the collecting, and the most favored characteristics would be selected by consensus. The Rodale Research Center agreed to receive samples from all collections and accessions (sent via USDA as required by U.S. law), to evaluate them, and to make them available to all grantees. This service played a major role in sorting out the information that was generated in the various locations. This also presented an opportunity for the grantees to meet with the staff of Rodale to learn from their experience in adapting amaranth to a new environment. Several of the grantees stayed on for a few days for specific training. Subsequently, Rodale received a grant from the Office of the Science Advisor of AID, through the PSTC program, to support their work with the BOSTID amaranth grantees.

A successful proposal to publish the amaranth newsletter was submitted by Ricardo Bressani, editor of the Latin American Archives of Nutrition and the principal investigator of the INCAP project. It was to be published three or four times per year in Spanish and English. The first issue was to contain the agreed protocols so that other amaranth researchers could follow them.

Finally, staff and grantees discussed administrative procedures for transfer of funds, expenditure reports, international travel, equipment purchases, and so forth. Later, staff met privately with each grantee to discuss individual problems and future plans.

Subsequent coordination meetings followed a similar pattern. In later years, the reports of the grantees took on added importance as research data accumulated. The second meeting was held in conjunction with the Third Amaranth Conference at the Rodale Research Center in September 1984. The third meeting was held in Cuzco, Peru, at the laboratory of Luis Sumar, the Center for Andean Crops Research, to give the grantees an opportunity to see one of the most remarkably successful projects. The fourth meeting was held in Nashville, Tennessee, where the American Association of Cereal Chemists was holding a symposium on amaranth during its annual meeting.

ADVISORY MEETINGS

On two occasions, CRG sought the advice of a group of experts on policy questions related to the amaranth program. Amaranth was unique in

the research program because it dealt with a single crop—a crop whose worth was questionable. Some people feel that research on any new crop is of limited interest scientifically and of doubtful value for development. (Few doubted, however, that of the so-called new or underexploited crops, it held the most promise.)

On September 19, 1983, a group of amaranth researchers[3] met in Washington, D.C., to coordinate the services provided by the Rodale Research Center, supported directly by AID. In addition, CRG noted that after a year in which few amaranth proposals were received, the appearance of the *Amaranth Newsletter* had generated a new batch of proposals. But few were interesting, and CRG wished to bring more focus and direction to the area. The editor of the newsletter also attended the meeting.

The group recommended a multifaceted strategy. In Latin America, they agreed, the emphasis should be on agronomic testing of many different varieties, including some collected locally. In South Asia, where the crop is also established and known, trials of introduced varieties should be encouraged. In Southeast Asia, introduction of different varieties and experimentation with production practices is most important. In Sahelian Africa, a series of spot trials should be organized, coordinated by an institution in West Africa. The group also identified certain problems associated with germ plasm collection, harvesting and cleaning of the grain, nutrition, and food processing, and suggested that grantees be sought to address them. They also emphasized the importance of economic analysis in all amaranth projects.

Eighteen months later CRG was still uneasy about the amaranth program. During its meeting of February 25, 1985, it reviewed the progress of the program and discussed recommendations contained in three commissioned papers by amaranth experts.[4] CRG decided to narrow the focus of research on amaranth to a limited number of problem areas, and at the same time to explore the possibility of including research on other selected new crops in the program. They asked the staff to convene an advisory group to make recommendations on these two issues.

In response, the advisory group meeting took place on April 19, 1985, in Washington, D.C.[5] The chairman was Ronnie Coffman, plant breeder and CRG member from Cornell University. The experts pointed out that the most important factor limiting amaranth's success in the marketplace is the high cost of the grain—up to ten times the cost of other comparable grains. This restricts the market for amaranth and discourages investment. The best way to lower the price is to breed and select for high yield. It was noted, however, that an increase in the harvest index—for example, through breeding—would mainly benefit the commercial farmer (and in fact, most grantees were orienting their research toward the commercial farmer). The

best way to assist the subsistence grower was much less clear, and this topic was recommended for discussion at a future coordination meeting of grantees.

The current BOSTID-supported research was showing that amaranth is, at the least, not inferior to other major grains, and the group recommended that emphasis be moved away from nutritional research and toward socioeconomic studies carried out by economists. Meanwhile, a simple economic analysis, including estimates of costs of inputs and value of harvests, should be required of all researchers.

The group thought it worthwhile to investigate other underexploited crops with which amaranth might be compared. Among the possibilities discussed were perennial grains, crops for intensive urban agriculture, and eel grass (a marine cereal).

These recommendations were accepted by CRG at its meeting of June 1985. However, AID did not accept the suggestion of adding other crops to the amaranth research program; it was felt that more could be gained by continued concentration on one crop, following the model of the International Rice Research Institute. CRG subsequently dropped the idea and maintained a reduced amaranth program, approving thereafter only two grants focussed on selection and one on genetic engineering.

GRAIN AMARANTH IN PERU

Two of the grants in the amaranth program were made to Peruvian institutions, and both were remarkable in different ways. Luis Sumar Kalinowski, of the Center for Andean Crops Research of the National University of Cuzco, received one of the first five grants awarded in December 1981. He was unknown to BOSTID before he wrote to Noel Vietmeyer, staff director of the amaranth study, in early 1981. He included a full proposal with his letter and inquired about possible sources of funds, totally unaware of the BOSTID Research Program that had just been negotiated between BOSTID and AID. On the strength of his proposal, he was included in the organizational meeting.

Shortly after he received the BOSTID grant, his organizational abilities and unusual energy became apparent. He collected and tested dozens of amaranth lines, and, in collaboration with the Rodale Research Center, began to develop high-yielding varieties. In a companion effort, his staff developed a line of nutritious amaranth-based food products. He adapted or invented machinery suited for planting, harvesting, and cleaning seed in the Peruvian altiplano environment.

In 1985, Sumar was "discovered" by his own country. The president of Peru, Alan Garcia, became interested in amaranth as a native Peruvian folk crop with great worldwide potential. He began to serve amaranth at diplomatic dinners, and mentioned the crop in his national and international

speeches. Sumar, as the nation's leading amaranth researcher, was awarded the Gold Medal of the Order of the Sun, Peru's highest award, which had never before gone to a civilian. Garcia mentioned the support and recognition of NAS in the award ceremony. Instantly, Sumar became a celebrity. The demand for amaranth soared, and farmers scrambled to obtain seed.

Amaranth obtained a toehold in the market in Peru. Some small enterprises were formed to produce and market amaranth products, and the largest food company in the country announced plans to manufacture amaranth products; in fact, this company never was able to get enough seed to carry out the project. Amaranth (kiwicha) became a household word, and a popular song called "kiwicha kiwi" linked it to past glories of Peru. A presidential proclamation and award "fast-forwarded" the work of decades.[6] The question remains: Will amaranth lose its niche when the fad dims and the government changes? Or will its nutritive value and taste earn it a place in the daily diet? Much depends on the farmers. Although the price is high, the supply is limited. Furthermore, the technology for popping and toasting the seeds is very primitive and slow, and amaranth is not penetrating the large urban market of Lima to meet demand.

The second Peruvian amaranth project was at the Institute for Nutritional Research (IIN) with Enrique Morales as principal investigator. The objective was to determine directly the nutritional value of amaranth prepared in three different ways: popped, toasted, and flaked. Animal experiments carried out at INCAP by Dr. Bressani found flaked to be best, followed by popped, but all with higher protein efficiency ratios than maize. The subjects in the IIN experiments were to be small children, and this gave rise to social and ethical questions that possibly exceeded in interest the technical results of the project.

The children are referred to IIN in a state of severe malnutrition by local hospitals that are without facilities to treat them. The medical staff at IIN treat and stabilize the children (a few cannot be saved). Then, in their weight gain stage, they are used as subjects in nutritional experiments supported by a variety of international donors, including AID. These experiments, not the treatment of children, are the Institute's sole reason for being; it is a research institution.

The IIN proposal to study amaranth was supported by the referees in general, but caused consternation among members of the CRG and the NAS Committee to Review Human Studies, the Academy's institutional review board charged with reviewing all projects for conformity with ethical standards. The NAS Committee's approval of this project was based on the principle that the subjects, malnourished children, were drawn from the same societal group that stood to benefit from the results of the research. In other words, the human studies committee would probably have rejected a project to test on poor Peruvian children a food product for Americans. A

motion in that committee to require that a social worker be sent to the home of each child subject was narrowly defeated on the grounds that the funds diverted to this purpose would limit the number of malnourished children "saved" by participation in the project. (In fact the IIN had no experience in social work and would have had difficulty carrying out such a program successfully.)

CRG also had ethical reservations about the project, motivated more from frustration with the facts of life in a poor developing country than criticism of the protocol. They did impose one significant restriction on the research. To guard against the presence of antinutritional factors in the amaranth, all preparations were to be selected and prepared by Professor Sumar in Cuzco and sent to Dr. Bressani in Guatemala for testing on animals before being fed to children. This established a three-way collaboration that was beneficial to the program as a whole, and provided a sort of scientific oversight of the IIN project.

Technical uncertainties surrounding the project persist, however. The result of the series of experiments suggests that amaranth is about the same as the other major grains in nutritive value, and the most biologically efficient amaranth preparation is toasting, followed by popping and flaking. This is in direct disagreement with the INCAP animal studies, which usually mirror human response. The IIN results have been challenged on the grounds that the childrens' diets did not stress them enough to distinguish among the preparations, that is, there was too little amaranth and too much casein control in the test diets. The resolution of this dispute will have to await some future repetition of the experiments, if at all.

RESEARCH RESULTS

The amaranth grantees were asked to answer a few basic questions about the crop. Where does it grow? Which lines or varieties grow best in which places? How should it be grown? What is the nutritive value, and what are the best ways to use it?

There were many answers to these questions, and a great deal of useful data was generated and published. A special issue of *Advances in Economic Botany* is devoted to the publications of the BOSTID amaranth grantees, and many of their papers have been published separately. The *Amaranth Newsletter* also disseminated the research results. A special team of grantees went to Nepal to collect germ plasm from a region that was not well represented in the collections accessible to the project.

The projects can be grouped in three categories, with some projects falling in two of them. One important distinction is whether amaranth is known and used in the country. The Latin American countries share that experi-

ence, while Thailand and Kenya do not. Thus the projects were divided as follows:

- *Nutritional and food-use projects*: INIA (Mexico), INCAP (Guatemala), IIN (Peru), CICA (Peru);
- *Latin American agronomic and plant improvement projects:* INIA (Mexico), INCAP (Guatemala), CICA (Peru), IPN (Mexico); and
- *Asian and African agronomic and plant improvement projects*: TISTR (Thailand), Chiang Mai (Thailand), University of Nairobi (Kenya).

NUTRITION AND FOOD USE

Amaranth grain has a high fraction of protein and a good balance of amino acids. The limiting amino acid is threonine, followed by leucine. It is high in lysine, and is therefore a good supplement to wheat and corn products. The problem is that, on its own, it's hard to eat. The seeds are small; and although they pop easily, the size remains small. Lacking gluten, it can be used only in small concentrations in bread or pasta products.

Nevertheless, some innovative food products were developed by grantees, particularly CICA in Cuzco, Peru, where some small businesses produced amaranth products. Amaranth can be flaked by a drum dryer process; the flakes are flavorful and can be eaten raw for breakfast with milk or fruit. In this form they compete effectively with (imported) Quaker Oats, which must be cooked. An Ovaltine-like drink, chocolate flavored, was likewise very popular. Bread products with up to 20 percent amaranth were tested in Peru and Mexico, but the amaranth adds to the cost as it improves nutrition, and proved attractive only to the governmental school lunch program in Mexico, which was willing to pay for protein quality.

AGRONOMY AND PLANT IMPROVEMENT

Latin America

Researchers began trials with local varieties and compared with lines obtained from Rodale. Samples from all local collections were sent to Rodale for evaluation, and selected lines were tried in other projects. In most cases, the local varieties outperformed the others. Factors considered in performance were early maturity, height reduction, adaptability to mechanical harvest, food quality, and high yield. Examples of the variability seen indicate that yields were highest in Peru (3,000 kg/ha), but maturity was 180 days compared to as little as 60 for some lines in Mexico. (The normal growing season for most grains is 90-120 days.) In Guatemala, two harvests were obtained from the same planting; the yield from the second growth of seed head was up to 50 percent of the first harvest.

Major problems were weeds and viral or mycoplasma disease. The amaranth seed is small and the plant is slow to emerge. Weeds tend to flourish, and the farmer often loses heart. Herbicides are of limited use without special row geometry because nearly every herbicide is designed to attack weed species closely related to amaranth and is highly destructive to the crop. Rotation of the amaranth crop with potato was found to reduce weeds in Peru, possibly because of different cultural practices or allelopathy of the potato plant. The mycoplasmic disease, which strangely causes tiny leaves to appear instead of seeds in the inflorescence, attacked certain lines while others were resistant, but the problem was quickly eliminated by judicious selection.

A number of inventions made harvesting and utilization simpler. The amaranth seed, as noted, is very small, and special devices are needed for planting, winnowing and cleaning, and sorting by size. The Sumar project in Peru produced a number of inventions and adaptations; none of these were patented. BOSTID staff at first urged Sumar to patent them, but when they were unable to clarify the U.S. government restrictions, even with assistance from AID, the idea was abandoned.

One project was different from all the others. At the Irapuato unit of the National Polytechnic Institute of Mexico, Luis Herrera and his colleagues were attempting to improve the plant quality through genetic engineering. The project had two complementary objectives: (1) to improve the characteristics of amaranth by insertion of genes for desired qualities, and (2) to improve the nutritional quality of other crops, like beans or cassava, by transferring the genes for the storage proteins of amaranth into their genome (so they would produce higher quality amaranth protein instead of their own). At the time of writing, the experiments were incomplete.

Asia and Africa

Three grants were awarded to institutions outside of regions where amaranth is found and used. In Kenya and in the two institutions in Thailand, trials began with imported lines from Rodale and experimentation with planting dates to define the seasons. The three sites in Kenya and five in Thailand varied in altitude and rainfall and in the nature of pest problems encountered.

In Kenya, V. K. Gupta's project was to discover how amaranth might fit into the farming pattern in an area with two rainy seasons each year, the long rains and the short rains. Unfortunately, in the second year of the project there were virtually no rains, and the country suffered from a severe drought. The sorghum and maize crops failed throughout the region, but the amaranth remained green and produced a yield, which generated a lot of attention. The crop also received a lot of attention from birds, perhaps in part because the drought reduced the availability of other crops. Full-time bird chasers had to be employed to save the harvest.

In Thailand, the major pests were a borer insect and weeds. The borer was particularly destructive to some lines. Another difficulty caused by the abundant light and rainfall was the extreme height of the amaranth plant. Varieties that grow to moderate height in Mexico reached more than eight feet in the lowland site near Chiang Mai and had to be staked. The principal investigator of that project, Chuckree Senthong, had his picture published in the international edition of *Newsweek* beside an eight-foot plant, purporting to illustrate the rich growing conditions of the region. But such plants lodge (fall over) or must be staked, which is prohibitively expensive.

During the course of a visit to Thailand, "Skip" Kauffman of the Rodale Research Center noted that some members of the hill tribes living in the highlands above Chiang Mai were growing amaranth as a backyard garden crop. They used it as a "health food" and as a confection on special occasions, much as it is used in other parts of the world.

One of the most important discoveries of the amaranth program was a new variety found by Gupta in Kenya. It was apparently imported from Nepal by early European settlers, and was called Jumla variety. It had many of the desirable features in an amaranth plant: short stature, high yield, white seeds, well-formed seed head, early maturity. With this discovery, much of the effort of the Kenya project was directed at development of this line, which is already undergoing trials in other parts of the world.

Finally, the BOSTID project did not generate a great increase in amaranth consumption either in Africa or Asia. The two Thai projects identified some lines that would produce a satisfactory crop in the higher altitudes of Thailand and established optimum growing conditions. Minimal effort was devoted to promotion or introduction to the farmers or consumers. In Kenya, attention had been drawn to amaranth during the drought, and there was farmer interest in the crop. A "field day" devoted to amaranth drew a respectable crowd and was reported in the newspapers. But most of the effort was concentrated on growing, and there was little demand and hence no market. We believe amaranth may have a future in Africa, but a more sustained effort with some political support would be necessary to exploit it. In northern Thailand, as in India and Nepal, it was found that amaranth is already consumed, and the projects might have been more successful if they had begun trials with the varieties that were already known, as was done in Latin America.

FUTURE OF AMARANTH

Before the BOSTID amaranth research program began, grain amaranth was known as a vigorous, hardy crop, identified as an underexploited plant of promising economic value. It was known to have good nutritive value

with a high lysine content. There were active research programs in the United States at the Rodale Research Center and the Western Regional Center of the U. S. Department of Agriculture; there was also a plant-breeding program at the University of California, Davis, and in a few places in the developing world.

After eight of years of BOSTID-supported research, the experience base has broadened considerably. Improved varieties are available for several different climatic zones, yields are higher, and much information is published on management, postharvest technologies, and nutrition. A new line from Nepal by way of Africa has been found that apparently has genes for low stature and high harvest index that can be incorporated into new improved varieties. New food products, which have gained popular acceptance, are in the markets in Peru and Mexico.

Perhaps the most interesting observations dealt with the power of a political figure to promote consumer demand and market acceptance. The "artificially" generated demand in Peru induced interest and demand for seeds on the part of farmers, and the price and quantity of amaranth quickly rose beyond any previous expectations. In the industrialized countries, the power of advertising and testimonials by prominent persons is well understood and exploited, and that this force can also work in favor of a new crop should be no surprise. Of course, it is important that no promotional campaigns be initiated before there are well-tested cultivars that can be counted on to provide reasonable yields, acceptable food products, and an economic return. Product development and plant improvement must go hand in hand with promotion for successful introduction of a new crop. Several of these conditions were, for a time, satisfied in Peru, and it will be interesting to watch the future of amaranth production and consumption in that country.

NOTES

1. Ricardo Bressani, private communication. This interesting phrase refers solely to the amino acid balance, and not to quantity or biological benefit of the protein to humans.
2. *Underexploited Tropical Plants with Promising Economic Value.* Washington, D.C., National Academy of Sciences, 1975.
3. Ricardo Bressani, INCAP (grantee); Richard Harwood, Charles S. Kauffman, Leon Weber, Rodale Research Center.
4. The papers were by Jess Martineau of Native Plants, Inc. on plant improvement, Robin Saunders of the USDA Western Regional Laboratory on food technology, and Charles Kauffman and Leon Weber of the Rodale Research Center on agronomy.
5. The participants were: W. Ronnie Coffman, Cornell University, CRG member and chairman; James Duke, USDA; Subodh Jain, University of

California, Davis; David Pimentel, Cornell University, CRG vice chairman; Robin Saunders, USDA; Loren Schulze, AID; Tresa Bass and Michael Greene, BOSTID.

6. Presidential interest does not always have a positive effect on the fate of a crop. In Kenya, the president somehow got the idea that amaranth cures diabetes, and publicly said so. The researchers were put under severe pressure to demonstrate the truth of the president's remark.

Biological Nitrogen Fixation

In the early polls of the Committee on Research Grants, biological nitrogen fixation (BNF) was high on everyone's list. It is a technology that goes to the very heart of the problems of the less developed countries: maximizing production of high-protein food crops and other food crops that do not deplete the soil of the nutrient, nitrogen. BNF has been studied since the 1920s, and it has found limited, but important, use in the industrialized countries.

In the Third World, however, BNF plays a relatively small role—for several reasons. The crops on which most of the original research was done were temperate plants, little used in the tropics. Many legumes yield less and have lower economic value than grain crops, and tend to be regarded as backyard or poor people's crops. Techniques for producing legume inoculant in developing countries, while low cost and artisanal, are not generally available or are of low quality. Also, modern methods for maximizing BNF in cultural systems are not generally applied in developing countries. There are other nitrogen-fixing systems apart from legumes that are active in BNF but have been the subject of relatively limited research. Two examples are the aquatic fern azolla, which is used to nourish paddy rice, and fixation by free-living soil bacteria in association with roots of wheat or maize.

CRG identified five focal points for the research program:

- Develop appropriate rhizobial inoculant technology for selected local or underutilized food legumes, including small-scale inoculant production and delivery systems.
- Develop techniques for growing legumes in association with other food crops.

- Identify possibilities for using the *Azolla:Anabaena* association in rice culture systems.
- Identify other promising nonlegume nitrogen-fixing technologies for field testing to determine their potential under various conditions.
- Develop an information network for BNF in developing countries.

ORGANIZATIONAL MEETING

The organizational meeting of the BNF program was held at the Resource Systems Institute of the East West Center in Honolulu, Hawaii. This site was chosen for two reasons: (1) the Resource Systems Institute had just undertaken a major study for the National Science Foundation on a technology assessment of BNF and had amassed a good deal of information, and (2) the University of Hawaii was the host institution of the Nitrogen Fixation in Tropical Agricultural Legumes (NifTAL) project, which was funded by AID to provide training and research support to developing country institutions. Several staff members of the institute and the university participated in the discussions.

The meeting recommended research priorities in three areas: legumes, azolla, and associative nitrogen fixation by free-living bacteria. In the legume area, recommendations ranged from basic microbiology and biochemistry to improved technologies for inoculation to nutritional value of legumes. Priorities dealing with azolla likewise included the fundamental nutritional and environmental requirements of azolla to socioeconomic analysis of management technologies. Although the area of associative fixation was more speculative and controversial, the door was left open to support research on basic studies and inoculation technologies.

One concern was raised that was to have later repercussions. Several of the developing country researchers pointed out that BNF was a high priority for their countries, and that some research institutions were mandated to carry out this work. Most of it involved selection of rhizobial inoculant for the primary consumable legumes. BOSTID staff and some of the U.S. participants argued that the BOSTID program should go beyond this "routine" research to address more fundamental questions in innovative ways and leave the preparation of inoculant to be done with national funds. The others replied that the program should support the highest priority work in each country, innovative or not; otherwise, researchers might not be permitted to apply for grants.

Following the meeting, CRG approved an announcement reflecting the recommendations of the Hawaii meeting. This announcement was widely distributed through BOSTID contacts, the NifTAL network of BNF researchers, and the UNESCO-sponsored MIRCEN network. This generated a large number of proposals on selection and screening of local rhizobia for par-

ticular legumes, in line with local priorities. While this research might be necessary and important at the local level, most of these proposals were not funded. At its September 1983 meeting, CRG said that the efforts of the BOSTID Research Program should be directed toward more-challenging research with potential for wider applicability. It requested the advice of a group of experts to point out suitable opportunities and examples.

BNF ADVISORY GROUP

A small group[1] was convened to redraft the announcement to promote the most-promising areas for BNF research in developing countries. The group reviewed the 44 proposals that had been received in response to the BNF announcement. It was noted that although the announcement was meant to be a guideline, many applicants were using it as a prescription, so their proposals were not innovative. Most of the rejected proposals involved selection of rhizobial strains for particular cultivars. This was the resolution of the debate at the organizational meeting: CRG was not accepting research with objectives that it considered pedestrian.

The group pointed out that BNF research had been carried out for some time, and there have been many advances, but many of the proposals were employing approaches that were unsuccessful in previous attempts, or that would generate no new knowledge. However, there are some new techniques that can be applied in developing countries, with a little help from outsiders, that would provide new, and fundamental, information. These approaches include use of ^{15}N to quantify the amount of nitrogen fixed and the use of serologically marked strains of rhizobia to distinguish inoculant from soil rhizobia. There was new interest in studying the interaction of the mycorrhizal fungi and the rhizobia. Associated nitrogen fixation was a more controversial area. Quantification using ^{15}N is critical to establishing that nitrogen benefits in a system are definitely due to fixation and not some other factor, and also critical for convincing skeptics of the magnitude of fixation. The group recommended that only very "inspired" proposals on associative fixation should be accepted. (However, two projects on this topic were already under way.) Azolla is difficult to work with, and only one applicant was successful in convincing CRG he had the experience of maintaining a culture year-round and could study the critical stage of regermination from the spore.

Other topics were proposed. Breeding and genetic manipulation of legumes for enhanced fixation had been given low priority at the organizational meeting, presumably because of the long time required for this research, but the advisory group considered this a promising area for investigation. They also recommended support of proposals on inoculation technologies and on the infection process, but only on systems that had previously been

demonstrated to have nitrogen as a limiting factor. (This criterion was never successfully met by any applicant, and so there were no grants made in this area.)

CRG adopted the new project announcement, with its prescription of ^{15}N and serological techniques for quantitative analysis. Staff decided to offer training workshops in these methods at subsequent grantee coordination meetings.

COORDINATION MEETINGS

The first coordination meeting was held July 30-August 4, 1984, in Chiang Mai, Thailand. Twelve grantees were present, including the hosts, Benjaven and Kanok Rerkasem of Chiang Mai University. Apart from the usual reporting and discussion of research results, the meeting had an additional purpose: to promote and elucidate the use of quantitative methods for measuring the amount of nitrogen fixed and of serologic techniques for identifying and distinguishing strains of rhizobial bacteria.

David Herridge of the New South Wales Department of Agriculture, Australia, led a discussion on the uses and limitations of different methods for measuring nitrogen fixation in the field. The four most common methods were the N-difference method, the ^{15}N isotope dilution or natural abundance method, the acetylene reduction assay, and the ureide method. Most emphasis was put on the ^{15}N method, but grantees were urged to apply at least one other method, wherever possible, to confirm results. There was agreement that the acetylene reduction method, which was proposed by so many applicants from the developing countries for its ease of application, was the least reliable and should not be used alone.

Maurice Fried, who had joined BOSTID as a consultant to CRG, gave a two-day tutorial on the concept and application of the ^{15}N isotope dilution method and its use in design of field experiments for measurement of nitrogen fixation. He also spent time with each grantee reviewing research plans and responding to the specific uses of ^{15}N methods proposed by researchers in light of the workshop.

The use of serologically marked strains was covered by Edwin L. Schmidt of the University of Minnesota and Ben Bohlool of the University of Hawaii. A representative of the NifTAL project was present to offer the cooperation of that AID-funded program for training and technical assistance. Finally, Harold Keyser of the USDA Laboratory in Beltsville, Maryland, discussed field application of serologically marked rhizobium strains.

One important lesson was learned by the BOSTID staff at that meeting. The staff was experimenting with privately scheduled interviews with the grantees. The initial concept was that it could be used for a scientific review of each project after the grantee had made his presentation. Accord-

BIOLOGICAL NITROGEN FIXATION GRANTEES

S.M.T. Saito	Centro de Energia Nuclear na Agricultura, Brazil. *Biological Acquisition of Nitrogen and Phosphorus by* Phaseolus *Beans Cropped in Association with Maize.*
J. Dobereiner	Empresa Brasileira de Pesquisa Agropecuaria (EMBRAPA), Brazil. *Biological Nitrogen Fixation Associated with Grasses and Cereals.*
H. Moawad	National Research Center, Egypt. *Competitive Relationships Between Indigenous and Inoculant Rhizobia and Nodulating Soybeans and Lentils.*
Juan C. Rosas	Escuela Agricola Panamericana, Honduras. *Selection and Breeding for Enhanced Nitrogen Fixation in the* vulgaris *Common Bean.*
H. Taslim	Sukamandi Research Institute for Food Crops, Indonesia. *Improved Grain Legume Production by Enhanced Biological Nitrogen Fixation.*
R. Senaratne	University of Rahuna, Sri Lanka. *Improved Nitrogen Fixation by Cowpea, Groundnut and Mungbean Intercropped with Sorghum.*
R. Palacios	Nitrogen Fixation Research Center, National University of Mexico. *Genetic Manipulation of* Rhizobium phaseoli *for Increased Bean Production.*
F. Sanchez	Nitrogen Fixation Research Center, National University of Mexico. *Molecular Biology and Genetic Engineering of Tropical Legumes for Nitrogen Fixation Improvement.*
E. Pushparajah	Rubber Research Institute, Malaysia. *Improved Soil Fertility by Inoculation of Cover Legumes with Rhizobia and Mycorrhiza.*
G. Okereke	Anambra State University of Technology, Nigeria. *Enhancement of Biological Nitrogen Fixation in the Mixed Cropping Systems Soybean/Maize and Cowpea/Maize.*
M. Umali-Garcia	University of the Philippines at Los Banos. *Application of Biological Nitrogen Fixation and VA Mycorrhizae in the Reforestation of Marginal Uplands.* (With R. De la Cruz)
R. Hautea	University of the Philippines at Los Banos. *Varietal Improvement of Grain Legumes for Enhanced Biological Nitrogen Fixation.*
Kauser Malik	Nuclear Institute for Agriculture and Biology, Pakistan. *Biological Nitrogen Fixation in Plants Growing in a Saline Environment.*

N. Boonkerd	Department of Agriculture, Thailand. *Culture, Maintenance and Propagation of Azolla Under Tropical Conditions.*
J. Dobereiner	EMBRAPA, Brazil. *Nitrogen Fixation by Plant-Bacteria Association in Tropical Grasses and Cereals.*
Roberto de Leon	Central American Institute for Industry (ICAITI), Guatemala. *Production and Field Testing for Effective Strains of* Rhizobium phaseoli.
Jean F. Felix	State University of Haiti. *Field Assessment of Need to Inoculate Pigeon Pea and Other Legumes.*
S.O. Keya	University of Nairobi, Kenya. *Effects of Environmental Factors on Nitrogen Fixation.*
B. Hernandez	University of Panama. *Factors Limiting Biomass Production and Biological Nitrogen Fixation in* Leucaena leucocephala *in Acid Soils.*
Kauser Malik	Nuclear Institute for Agriculture and Biology, Pakistan. *Associative Biological Nitrogen Fixation in Grasses Growing in Saline Environments.*
Mamadou Gueye	National Agricultural Research Center, Senegal. *Improving the Yield and Biological Nitrogen Fixation of Bambara Groundnut.*
B. Rerkasem	Chiang Mai University. *Interactions in Legume-Nonlegume Cropping Systems.*

ingly, each grantee was scheduled for a one-hour "private" meeting, and a number of experts who were attending the meeting were included. The resulting meetings were stressful for the grantees, who felt they had to defend their work before a panel of experts, much like a graduate student oral examination. Staff therefore modified the format to include only BOSTID staff and to deal mainly with administrative matters; technical and scientific questions would be discussed at ad hoc meetings, at breakfast, or other spare moments. These scheduled private meetings eventually became very popular with the grantees.

The second coordination meeting was held in Maui, Hawaii, at the NifTAL facilities on August 9-11, 1985. The venue was chosen to permit grantees to attend the Tenth North American Rhizobium Conference scheduled for the following week in Maui and to familiarize the grantees with the resources available to them at NifTAL. The third coordination meeting took place at the Brazilian Agricultural Research Organization of EMBRAPA near Rio de Janeiro, Brazil, on August 4-8, 1986, hosted by Johanna Dobereiner.

In August 1987, BOSTID joined with the Australian Centre for Interna-

tional Agricultural Research (ACIAR), the Canadian International Development Research Centre (IDRC), and the Indonesian Agency for Agricultural Research and Development to sponsor a symposium in Cisarua, Indonesia, on the contribution of BNF to plant production. All the BOSTID BNF and Tropical Trees grantees gave oral or poster presentations. Most of the BNF papers at the symposium were accepted for publication in a special edition of *Plant and Soil*, published in The Netherlands, and dedicated to the symposium.[2]

In August 1988, another coordination meeting was held at the Nuclear Institute for Agriculture and Biology in Faisalabad, Pakistan, hosted by Kauser Malik. This was six months after the workshop on application of molecular genetics to BNF field experiments (see below), and the emphasis had definitely shifted in that direction. A day and a half was dedicated to reports of the grantees' first attempts at incorporating molecular genetic techniques into their research projects and one session addressed the role of molecular genetics of rhizobia and the host plant in increasing the contribution to BNF. Finally, there was a session on future collaboration, based on the realization that the BOSTID Research Program would not continue. A letter was sent from the group to Abdus Salam, president of the Third World Academy of Science, urging him to emulate networking aspects of the BOSTID Research Program in future collaborative programs.

WORKSHOP ON MOLECULAR GENETICS TECHNIQUES FOR BNF FIELD RESEARCH

Rafael Palacios of the Center for Biological Nitrogen Fixation of the National Autonomous University of Mexico was awarded a grant in 1984 to work on genetic manipulation of *Rhizobium phaseoli* for increased bean production. His was the first proposal approved that involved genetic engineering techniques, and CRG was quite divided on the question of whether this was appropriate for the BOSTID program. Finally, in part for the sake of a balanced program and to give the other grantees an opportunity to interact with him at meetings, his project was approved.

As it developed, that approval was particularly well founded. Palacios was an active participant at all coordination meetings, and at the meeting in Indonesia, he agreed to prepare a special course to introduce the grantees to molecular genetics techniques useful for field research. They would allow fast, accurate identification of the many strains of rhizobium, mycorrhizae, and frankia, for determination of stability of key characteristics, and for transfer of desirable traits from one strain to another. The workshop was led by Palacios and his staff. Grantees commented afterwards on how well prepared and staffed the workshop was and how hard they were made to work.

The methodologies that were performed by the grantees in the lab included identification of rhizobium plasmids by electrophoresis, purification of rhizobium DNA, digestion of DNA with restriction endonucleases and analysis of digests by electrophoresis, blotting into nitrocellulose of DNA digests and plasmid profiles, labelling of DNA with ^{32}P, and hybridization of plasmid profiles and total DNA digests with specific DNA sequences for nitrogen fixation genes. A workbook with procedures and references was prepared for each grantee. For several grantees, this workshop was the high point of their participation in the BOSTID program.

RESEARCH RESULTS

BNF involves the symbiotic relationship of a plant, with a species of bacteria or other prokaryote. The plant requires nitrogen for its metabolism but is unable to tap the most generous source—the air. The microsymbiont, on the other hand, has the capability to fix atmospheric nitrogen but requires a source of energy to do so.

Only a few plant families are known to be able to enter into this kind of symbiosis, and only a few bacteria or algae have been observed to carry nitrogen-fixing genes. The problem for the scientist is to enhance this process as it occurs in useful plants, preferably in a way in which it can be economically exploited by farmers or other producers.

This problem can be approached in several ways: improving the microsymbiont, improving the plant host, and improving the management of the system to make the best use of the nitrogen. Most of the grantees worked on the legume-rhizobia system, which is the best understood and has the greatest importance for agriculture. Four projects were devoted to associative fixation in grasses, including sugarcane and a salt-tolerant fodder grass. One grantee looked at use of azolla, the aquatic fern that fixes nitrogen in association with a blue-green alga and is used as a kind of green manure to fertilize rice.

The microbiological problem relates to selection (or creation) of rhizobia that are most effective nitrogen-fixers for each crop and that are also competitive with the rhizobia normally present in the soil in ability to infect the plant. The competitive aspects turned out to be the biggest problem; in several experimental sites and commonly in farmers' fields, inoculation with effective rhizobia has no impact because the soil rhizobia outcompete the introduced strains.

The solution can be sought in two directions. Seeking more effective and competitive rhizobia for tree crops was the objective in the project of Mercedes Umali-Garcia in the Philippines, while that of S. Keya in Kenya was for common grain legumes, and the screening produced a number of effective strains. In Indonesia, where the program of transmigration from

densely settled regions to rural areas involved growing legumes where they had not been grown before and where the soils did not contain the necessary rhizobial strains, spectacular results were obtained from inoculation.

However, the competitive aspects turned out to be a major problem. In several experimental sites, inoculation with effective rhizobia gave little or no response, even though response to applied nitrogen was significant. This was very evident in the initial experiments in Haiti and Senegal. The reason becomes clear when the rhizobia in the nodule is examined. The nodules are primarily occupied by the local soil rhizobia, which are much more competitive than the introduced rhizobia, although they are less effective nitrogen-fixers. The examination of nodule occupancy was introduced into all grants studying inoculation, which gave a clearer indication of which of the strains were the most competitive. Thus, in Egypt and Panama, plant response could definitely be shown to be associated with nodule occupancy of the inoculated strain, and lack of response to an inability of the inoculated strain to compete.

Another serious problem is the inability of most strains of rhizobia to survive and fix nitrogen under highly acidic conditions or at high temperatures, both conditions commonly present in tropical soils. Thus, in Kenya, a vast number of strains of rhizobia collected from areas where common beans were growing were tested in the laboratory for survival under harsh conditions, and some strains were isolated that survived at low pH and temperatures of 40°C. Nitrogen fixation was also shown to be enhanced by inoculation with mycorrhizal fungi, which infect the roots and assist the plant in the uptake of certain minerals, particularly phosphorus. This was demonstrated by Reynaldo de la Cruz in the Philippines, and less successfully in Malaysia, where the experimental sites were not clearly responsive to added nitrogen.

A more recent approach toward enhancement of nitrogen fixation has been direct breeding of the plant for maximizing the symbiosis. With this in mind, two projects were initiated by Juan Carlos Rosas in Honduras and Randy Hautea in the Philippines. They were attempting to develop, by breeding, plants that obtain most of their nitrogen from fixation. These projects take more time than those that concentrate mainly on microbiology, and only preliminary, although promising, results are as yet available. Two other investigators, G. Okereke from Nigeria and R. Senaratne from Sri Lanka, while not breeding for nitrogen fixation, used the ^{15}N isotope dilution procedure to test cultivar collections in order to select those that obtain most of their nitrogen from fixation. They found considerable differences among cultivars in the ability to fix nitrogen in similar field situations. The high fixers are being tested in mixed cropping systems.

Two projects at the Nitrogen Fixation Research Center of the National Autonomous University of Mexico spanned both approaches using the tech-

niques of molecular biology and genetic engineering. These researchers are pioneers in this fast-moving field. Rafael Palacios looked at the genome of the rhizobial strains that infect the common bean and discovered redundancy in the nitrogen-fixing genes that reside in a plasmid along with the genes that control nodulation of the plant. He was able to show that the number of duplications of nitrogen-fixing genes has a relation to the ability to fix nitrogen. This opened the possibility of transfer of the symbiotic plasmid from one rhizobial strain to another, more competitive, one. Federico Sanchez approached the problem from the plant side, perhaps a more difficult problem. His preliminary results showed that the protein products produced by the bacterial Nif genes in different plant hosts varied. This may, in the future, assist the problem of selection of the best-fixing plant varieties.

The other approach to the application of legumes for nitrogen fixation involved the use of legumes to fertilize other crops. This is an old idea, but the effectiveness of the interaction had not previously been quantified with a reliable technique in tropical farming systems. How much nitrogen is fixed by the legume, how much is taken up by the main crop, and what is the best way to manage the system are all important questions for the farmer. Researchers in Brazil led by Tsai Saito noted that an important constraint was that row crops normally required more nitrogen at an earlier date than could possibly be supplied by the legume, and they therefore had to be fertilized. But the application of nitrogen fertilizer even in modest quantities usually reduced the fixation process. They attempted to select legume cultivars that tolerate relatively high levels of soil nitrogen and continue to fix. The project in Piracicaba, Brazil, demonstrated the practicality of this approach and documented high levels of fixation. Another approach taken in Thailand by Benjaven Rerkasem and her associates showed that the legumes fix more nitrogen when intercropped with corn than in monoculture; these results may be related since the corn rapidly takes up soil nitrogen, which, by the inverse of the effect noted above, stimulates the legume to fix more. The elements of a scientific multicropping scheme may now be established, and further research based on these results would be fruitful.

The four projects carried out by institutions in Brazil and Pakistan on associative fixation were among the best known of the BOSTID projects. Johanna Dobereiner has received wide recognition for her work on BNF over many years; nevertheless, many considered her results controversial, and the process of responding to reviewers of her original proposal to BOSTID extended over several months before the proposal was approved. During the course of her BOSTID grant, she was able to quantify the (substantial) amount of nitrogen fixed in a bacterial association with sugarcane. She also isolated and characterized a previously undiscovered bacterial species that fixed nitrogen in association with sugarcane. These impressive results laid

most of the controversy to rest. They also provided the groundwork for improving the symbiosis by selection of plant microbe and development of inoculation technologies for future commercialization.

The work of Malik and his colleagues in Pakistan was dramatic for conversion of barren land to production of Kallar grass, a forage that grows successfully on saline-sodic soils. The research team demonstrated that one reason for this success where other plants fail is that, even in the highly saline environment, a soil bacterium associated with the Kallar grass is able to fix nitrogen. The quantitative demonstration of nitrogen fixation in this system continues to be an important challenge. Kallar grass is able to establish an extensive root system in the clogged soils and in this way improves the permeability of the soil so that salt can penetrate to much lower layers rather than accumulate at the surface. Work is now under way to identify the genes responsible for the fixation and salt tolerance.

One project dealt with the use of the aquatic fern *Azolla*, which forms a symbiotic association with the nitrogen-fixing bacteria *Anabena azollae*. The fern is used as a green manure to fertilize rice crops and other crops in Vietnam and China; it is not more widely used because it is more difficult to grow *Azolla* than to grow rice. Most of the difficulty is related to the propagation and maintenance of the material. Nantakorn Boonkerd of the Department of Agriculture in Thailand studied two methods of propagation—vegetative and by means of spores. The vegetative propagation was conducted with notable success at three locations as a function of season and water depth and in saturated soil. Spore propagation is a relatively new approach, and much progress was made in understanding the sporulation process and the effect of various environmental factors. Methods were developed for germination and propagation of one *Azolla* species, and this will be published. Work on the species most prevalent in Thailand is progressing as well.

NOTES

1. Participants at the BNF advisory meeting: Maurice Fried, Washington, D.C.; Thomas Lumpkin, Washington State University; Hugh Popenoe, University of Florida (CRG member); Joann Roskoski, University of Hawaii; Robert Miller, North Carolina State University; Norman Schenk, University of Florida; Lloyd Frederick, AID; Judith Bale, Tresa Bass, and Michael Greene, BOSTID.
2. *Plant and Soil* v. 108, no.1 (May 1988).

Tropical Trees

The tropical trees program, originally titled fast-growing, nitrogen-fixing trees, was the one that built most directly on previous BOSTID experience. The BOSTID publications list includes seven titles[1] relating to forest resources. Many of these focused on the properties of particular species, and suggested a research agenda aimed at elucidating their potential for different uses and in different agroclimatic zones. The research program offered an opportunity to organize coordinated trials to solidify the data on the multipurpose species and determine options for conservationists and development planners.

In 1981, the World Bank published a monograph[2] that estimated that the current level of multilateral and bilateral support for forestry research was less than $10 million per year. BOSTID staff estimated at that time (before the number of research areas was reduced from fourteen to six) that the total cost for the fast-growing, nitrogen-fixing trees projects over the eight-year life of the program would be about $750,000 (the final amount including networking meetings was actually close to $2 million.)

ORGANIZATIONAL MEETING

The organizational meeting took place in Washington, D.C., on October 5-7, 1981. The participants were experts from Sudan, Costa Rica, Thailand, Kenya, the U.S. Forest Service, AID, and others. CRG had approved this program with the following goals:

- To identify and demonstrate methods for using fast-growing, nitrogen-fixing trees to solve development problems;

TROPICAL TREES GRANTEES

Ulf Karlin	Universidad Nacional de Cordoba, Argentina. *Management of Arboreal Prosopis in Agroforestry Production Systems.*
P. N. Unni	Center for Water Resources Development and Management, India. *Alley Cropping Systems in Coconut and Cassava Production Systems.*
Maria Valdez	National Polytechnic Institute, Mexico. *Frankia Symbiosis with* Aldus, Casuarina, Coriaria: *Ecology and Mycorrhizal Interaction.*
N. M. Majid	Universiti Pertanian Malaysia. *Use of Fast-Growing Timber Species to Reclaim Mining Areas.*
R. Escalada	Visayas State College of Agriculture, Philippines. *Nitrogen Fixation and Multiple Uses of* Albizzia falcataria, Gliricidia sepium, Sesbania grandiflora.
Cesar Orallo	West Central Luzon Forest Research Center, Philippines. *Integrated Management of* Pinus kesiya *Forest System.*
S. Halos	University of the Philippines Science Research Foundation. *Tissue Culture of Tropical Pines.*
O. Diagne	National Forestry Research Center, Senegal. *Selection of Root Endophytes to Increase Tree Productivity in Semi-Arid Region.*
K. Yantaseth	Thailand Institute of Scientific and Technological Research. *Management and Production of Selected Nitrogen-Fixing Trees.*
D. Diangana	Centre Technique Forestier Tropical, Congo Republic. *Selection of Fast-Growing, Nitrogen-Fixing Tree Species for Large-Scale Biomass Production in Savannah Zones.*
M. E. Torres	Instituto de Investigaciones Tecnologicas, Chile. *Evaluation and Testing of Fast-Growing, Nitrogen-Fixing Tree Species for Semi-Arid Regions.*
Frederick Owino	Moi University, Kenya. *Selection and Testing of Fast-Growing Nitrogen-Fixing Trees for Use in Farm Woodlots and Agroforestry Combinations.*
Enrique Pardo Luis Delagdo	Instituto Nacional de Investigaciones Sobre Jose Recursos Bioticos (INIREB), Mexico. *Native Fast Growing Nitrogen Fixing Trees in Upland and Lowland Sites as a Source of Fodder, Fuelwood, and Soil Enrichment.*

Mahdi Beshir	University of Gezira, Sudan. *Collection and Nursery Trials of Acacia Species for Biomass in Non-Irrigated Drylands.*
Kovith Yantaseth Panas Buranasilpin	Thailand Institute of Scientific and Technological Research. *Field Trials and Testing of Selected Species of Fast-Growing, Nitrogen-Fixing Trees.* Panas Buranasilpin took over the project August 1988.
Orlando Balboa	Pontificia Universidad Catolica de Chile. *Vegetative Propagation and Improved Breeding Systems for Prosopis Species.*

- To determine tree selection and management techniques suitable for a given purpose in each region;
- To investigate the properties of the trees and their potential use for food, forage, fuel, and lumber, taking into account economic and social factors; and
- To demonstrate the use and estimate the costs of the selected technologies and encourage larger scale plantings and trials where appropriate.

Several possible themes for the program were suggested, such as concentration on one or two species only, concentration on one or two applications (for example, agroforestry or fuelwood), or creating a "revolution" in forestry by emphasizing genetic engineering to achieve dramatic results in a short time. Finally, participants agreed that a multi-phase project, beginning with an inventory and proceeding through testing and trials of the most promising species, would be the best approach. Emphasis was placed on selection of highly productive trees that can be grown on land unsuitable for agriculture and on increasing knowledge of how to use the nitrogen-fixing capabilities of trees. A detailed methodology for data collection during the inventory phase should include a rationale for collecting data. After the inventory phase, field-trial procedures should be established for all participants in the project to follow, tailored to project goals. Seeds and inoculum for all test plots should come from the same sources, and central laboratory services should be made available for protein analysis, for testing for toxicity, and for testing uses of wood such as pulp, paper, and charcoal-making qualities.

There was agreement on one other aspect. In recent years, the world has seen some spectacular performances by trees transplanted from their native habitat to other regions. One of the best known was *Leucaena leucocephala*, which was native to Mexico and Central America but was showing impressive growth rates and hardiness in southern and eastern Asia. Nevertheless, par-

ticipants at the meeting agreed that emphasis in trials should be placed on local species in trials, with perhaps a few exotics added for international comparison, the better to study the biology of species in their own environments.

Based on this recommendation, CRG staff generally encouraged applicants to concentrate on local species, but to add one or more exotics to the trials for the sake of standardization; *Leucaena leucocephala* was often used for this purpose. But this policy excited a fierce reaction in some reviewers. Some of them thought time spent on local species was wasted: these trees are only food for pests. Others resented the addition of even one exotic species to the trials because of the danger of introducing weedy pests. The forestry research community appears to have disparate views on this question.

Following the organizational meeting, a grant was negotiated with the International Council for Research in Agroforestry (ICRAF) in Nairobi for support services to aid the grantees, specifically to prepare a draft manual for the data collection in the first phase of the project and procedures for subsequent field trials. The draft was to be presented at a first coordination meeting of grantees to be held in Nairobi one year later. At that meeting, grantees would review the recommendations made by ICRAF and agree among themselves on the protocols for data collection and field trials.

Unfortunately, the grant to ICRAF was clouded by a misunderstanding that may have contributed to the lack of standardization among BOSTID field-trial projects. BOSTID intended ICRAF to produce a field manual, a "how-to" reference book that could be carried to the field easily or used in the laboratory by all grantees to encourage common data-collection methodologies and experimental designs. The first draft was to have been ready for grantees' comments and revisions at the Nairobi coordination meeting.

ICRAF's understanding, however, was very different. The final product was a six-volume encyclopedic survey of agroforestry, which was delivered in late 1984, nearly two years overdue. A copy of the six-volume edition was provided by ICRAF to every BOSTID grantee in the trees program, although it did not serve the purpose originally intended.

FIRST COORDINATION MEETING

The first coordination meeting was held January 24-27, 1983, at the offices of ICRAF in Nairobi. Ten grantees, in addition to ICRAF, participated. Among the objectives were to explore the possibility of establishing common methodologies to ensure comparability of results and discuss the need for any centralized services. To facilitate these discussions, the participants broke into two working groups—one to consider questions related to germ plasm collection and the other to deal with issues encountered during field trials. In the absence of a usable manual, the groups had to

start from scratch, relying on their own knowledge and experience, and several disputes went unresolved. Nevertheless, participants reached agreement on most aspects of collection, including selection criteria, minimum data to be taken during collection, nodule collection, single tree versus provenance collection, nomenclature, seed handling, storage and testing, and nursery production. There was also some agreement on the design of field trials, but some disagreements as well. Standards for measurements and soil and plant analysis were also set forth. In all, the procedural agreements reported from the first coordination meeting probably could have formed the basis for coordinated trials, had enforcement been more energetic.

As it was, the grantees, at their own initiative, proposed to form ongoing working groups to discuss the problem areas, including nitrogen fixation measurements and microbiological concerns, and mensuration, design, sampling, statistical design, and analysis. None of the groups ever met, but a fourth group was formed later, which produced a manual covering the concerns of all the working groups.

PROCEDURAL MANUAL

In order to elaborate and document some of the decisions on procedures made at the Nairobi coordination meeting, a small group of experts was assembled to write a procedural manual.[3] Frederick Owino of the University of Nairobi, Kenya, was chairman of the group, which met in Washington, D.C., on December 14-16, 1983, to prepare the basic manual. Additional material was provided by Harold Keyser of the Beltsville Agricultural Research Center and CRG member John Torrey of Harvard Forest. The draft manual was reviewed by grantees at the next coordination meeting in October 1984 and distributed the following year.

Topics covered include design of the research plan, tree germ plasm collection and handling, nursery operations, experimental designs and methodology, areas of suggested field study, and a bibliography. There are appendixes on isolation of rhizobia, extraction of rhizobia from nodules, authentication of rhizobia, screening of rhizobia, preparation and use of legume inoculants, propagation and screening of VA mycorrhizal fungi, isolation culture and inoculation with Frankia, and a summary of special formulae and equipment.

The manual was distributed to all grantees, and to many applicants to assist them in proposal preparation. Several hundred were also distributed in answer to requests from around the world. At best, the manual may have encouraged researchers to adopt standard methodologies to make their data more comparable. Unfortunately, it was distributed too late to have a major impact on the BOSTID grantees, and staff did not vigorously insist on adherence to the methods as was done, for example, in the ARI program.

OTHER COORDINATION MEETINGS

Coordination meetings were held in October 1984 in Jalapa, Mexico; in November 1985 in Bangkok, Hua Hin and Chumpon, Thailand; in November 1986 at Harvard Forest, Petersham, Massachusetts; and in August 1987 in Bogor, Indonesia. Much of every meeting was devoted to reports of research progress by each grantee and critical comments by other grantees and invited experts. The guest experts presented seminars on topics of interest to the grantees, and a field trip to an experimental site or managed forest was included. In addition, each meeting had a special focus.

The Jalapa meeting was dedicated largely to review of the draft Procedural Manual for Research on Nitrogen-Fixing Multiple-Use Trees and to agreement on common procedures. Visits were made to field sites in two distinct climatic zones, and to a laboratory and coffee plantation to see the use of nitrogen-fixing trees in coffee cultivation.

In Thailand, the emphasis was on socioeconomic factors in tropical forestry and the dissemination of research results. The group observed the management of the king's forests for the production of fuelwood.

The meeting in Massachusetts featured a discussion of the World Resources Institute's proposal to the World Bank for a global effort in forestry research and production. Grantees toured a forest preserve managed by the Massachusetts Forest Service, which introduced some of them for the first time to problems peculiar to temperate forests (and incidentally to six inches of snow). A hands-on workshop on soil physical and chemical analysis was led by Charles Davies of North Carolina State University and grantee Maria Valdez. W. Sylvester demonstrated the acetylene reduction technique for measuring nitrogenase activity. John Torrey, Joann Roskoski, and the staff of Harvard Forest gave lectures and laboratory demonstrations of the isolation and use of rhizobia and Frankia. And John Torrey and Michael Greene gave presentations on the preparation of scientific papers and slides.

The final meeting in Indonesia was a BOSTID cosponsored symposium on increasing agricultural production through biological nitrogen fixation. Grantees of the BOSTID BNF program and grantees of the other two cosponsors, the Canadian International Development Research Centre and the Australian Center for International Agricultural Research, also participated. Some of the grantees' papers were published in forestry-oriented journals.

ADVISORY MEETINGS

Two advisory group meetings were held in connection with the fast-growing, nitrogen-fixing trees/tropical trees program. On February 1, 1984, a group convened at Tacoma, Washington, to discuss future directions for the CRG trees program, chaired by CRG member J. Lawrence Kulp of the Weyerhaeuser Company.[4] The major question before the group was whether

the restriction to fast-growing, nitrogen-fixing tree species was too limiting, and whether the inclusion of other species might lead to important studies related to new industrial and subsistence applications for local or exotic tree species. There was an interesting divergence of views between the individuals from Weyerhaeuser and those from AID and the universities. The Weyerhaeuser participants said that greater emphasis should be placed on higher value species and on plantation growth; they felt that export of forest products could be an important source of wealth for poor countries. The others were more interested in subsistence needs of rural populations, and said that the emphasis on fast growth and nitrogen fixation should not be discarded. All agreed on the value of emphasizing applications and end-use rather than a specific technology (for example, fast-growing, nitrogen-fixing trees). The name of the program was changed to Tropical Trees, without signifying an intent to exclude nontropical countries such as Nepal, and the new announcement requested proposals on improving productivity of forests and plantations of food, fodder, fuel, and commodities, as well as germ plasm collection and reproductive biology.

The other advisory group met in Bangkok following the third coordination meeting; each participant had heard the presentations and future plans of the grantees.[5] The meeting was motivated by the realization that in nearly three years there had been only one new grant awarded in the Tropical Trees program, and many of the eleven grantees who attended the first meeting in Nairobi were nearly finished with their projects. Participants were asked whether the program suffered from lack of interest of the best developing country researchers (there were still many proposals received, and rejected), whether some complementary studies should be undertaken, whether grantees whose projects had ended should carry out renewal or follow-up projects, and what should be the goal of the program as a whole.

The group felt that the major weakness in CRG's approach was the short-term nature of the projects. They suggested that there be a mechanism to follow the projects over a longer term to see the effects of longer term rotations, and a survey of earlier (non-BOSTID) trials to get a more complete picture. Above all, publication in scientific journals was considered to be important, but should be prepared carefully to guard against unwarranted extrapolation of short-term results.

CRG agreed that these were very valuable suggestions, and supported the idea of a "harvest grant" (as opposed to "seed grant") to one of the grantees or a consultant to visit the sites of concluding projects and independently assess and record the results.

RESEARCH RESULTS

None of the grantees confined their study to only one topic or to only one species. Most examined several aspects of the biology, ecology, micro-

biology, use, or management of tropical tree species. Therefore, research results are discussed below by topic rather than by individual projects.

SPECIES INVENTORY AND TRIALS

Inventories of native species were the original goal of the program as envisioned by the participants at the organizational meeting in 1981. However, only Owino actually attempted to conduct an inventory of native species. He selected twenty-one native and six exotic species, which he evaluated for growth in two different sites. He found that, with the exception of the native cashew, exotic species demonstrated faster growth than native species in both sites.

Although Torres did not do a complete inventory of nitrogen-fixing trees in Chile, she did test 46 provenances of three species, *Prosopis chilensis*, *P. alba*, and *Acacia carven*, that were being evaluated by the Forestry Department of Chile for wider use in reforestation projects. Mahdi Beshir did a similar study in Sudan using eleven provenances of *A. seyal* and *A. mellifera*. These two thorny desert species were selected, however, largely because of the lack of existing scientific knowledge about them rather than for any hope that they would be found useful.

Comparative trials constituted the most common type of research project. The normal procedure was to compare a number of native and exotic species for a desired characteristic such as site adaptability, wood yield, fodder yield, growth rate, and green manure. Although statistical comparisons among the projects are not possible because of the differences in characteristics tested for, species evaluated, and the evaluation methodology employed, certain limited comparisons are possible.

The five researchers who studied arid zone species concentrated on native species; thus, they had few species in common. Their data does not suggest a "miracle" tree for the arid tropics analogous to leucaena in the humid tropics. Large within-species variation was noted by all researchers and viewed as a positive starting point for selection or breeding programs to find faster growing and/or higher yielding germ plasm. Only Orlando Balboa and M. E. Torres, both from Chile, had species in common, *Prosopis chilensis* and *P. alba*. Torres examined the adaptability of a number of provenances of these species to grow in several sites, while Balboa studied their basic floral biology and susceptibility to vegetative propagation. Torres found that the native species were far superior to the Australian acacias she was also testing, but unfortunately, rabbit damage appears to have led to atypically suboptimal growth for all species, with the best seedlings averaging only about 40 cm height in two years. Balboa did not find much difference between the ability of different species to be multiplied via vegetative propagation, with the exception of *P. tamarugo*. This species could not be propagated by any of the methods tried.

In Africa, M. Beshir and O. Diagne both studied *A. seyal*, Beshir conducting provenance comparisons in the greenhouse and Diagne examining growth of one provenance in the field. In any case, this species invites study only because it's there; the spiny, spindly branches do not provide good fodder even for goats.

In the humid areas, most projects examined several exotic species and therefore had more species in common. *Leucaena leucocephala*, *A. mangium*, *A. auriculiformis*, and *Gliricidia sepium* were studied by several grantees. Overall, leucaena did well, but not spectacularly, in areas with soils that were basic to neutral. The striking successes were the dramatic growth and productivity of the two Australian acacia species, *A. mangium* and *A. auriculiformis*, in acidic soils. In the Congo, Thailand, and Kenya, *A. auriculiformis* outperformed all native and, in almost all cases, most exotic species. It demonstrated a particularly impressive growth rate not only in areas with acidic soils but also in those that were prone to drought, flooding, and other problems. A close second in the Congo and Thailand was *A. mangium*. Although not as spectacular as auriculiformis, mangium had better form for traditional forestry uses. Unfortunately, the Mexican study did not include these species, and none of the species tested in Mexico attained a height growth even close to that of *A. auriculiformis* and *A. mangium*. It would have been useful to see whether the two Australian species would do well in Mexico where the soils and climate of the study sites were very dissimilar to the conditions in either the Congo or Thailand.

Several grantees carried out provenance trials, comparing different varieties of the same species. In view of the small amount of species improvement that has been done with fast-growing, nitrogen-fixing, and other tropical trees, it is not surprising that the grantees found tremendous variation among provenances for all species examined.

Several projects examined the suitability of different species for fodder production. Results to date suggest that leucaena and gliricidia should make superior animal feeds. The fact that gliricidia is used for fodder in goat production systems throughout Indonesia, and that leucaena is used widely all over the tropics for animal food, supports these findings.

Although most proposals mentioned the need for fuelwood, few projects actually included studies to measure either the quantity or the quality of fuelwood produced by fast-growing species. The Mexican study, which did have a fuelwood component, found that under coastal lowland conditions, *Piscidia communis*, a native species, produced the highest fuelwood yield and therefore was judged the best fuelwood species. Leucaena, which did have an overall higher quality wood than *P. communis*, was not the best in the Mexican trials because a root rot problem depressed its biomass yield. The Thai project also evaluated the firewood potential of several species and, surprisingly, found that, although leucaena again had the highest spe-

cific gravity, mangium had the highest caloric content and thus was a better fuelwood species.

Three projects addressed the question of whether fast-growing species could be suitable for industrial use. Thailand, Congo, and Kenya all found that among the species examined, *A. auriculiformis* and *A. mangium* were suitable for use as pulp and in papermaking. *A. auriculiformis* was found to have the highest pulp yield followed by *A. mangium* and *L. leucocephala*. *Calliandra calothyrsus* and *Gliricidia sepium* were found to be unacceptable in Thailand and *A. autocarpa* was less desirable than the other two acacias in the Congo study.

Only R. Escalada in the Philippines conducted a systematic study of green manure yield. He found that gliricidia had the best coppicing ability and thus the best production of green manure over repeated cuttings. The coppicing results of Kovith Yantaseth (Thailand) and Enrique Pardo (Mexico), though not planned to measure green manure yield, support this conclusion. Interestingly, while Escalada and Pardo found that *Albizzia falcataria* coppices almost as well as *G. sepium*, Kovith did not find that to be the case in Thailand.

NITROGEN FIXATION

The species originally selected for study were all nitrogen fixing, and enhancement of this capability was an important goal of the early projects. However, it is very difficult to find nodules on a growing tree in most species, and few researchers were able to isolate rhizobia. Response to inoculation was studied by Torres, Balboa, Diagne, Kovith, Majid, Beshir, and Diangana. Although there were exceptions, such as Diagne's work on *Prosopis juliflora* in Senegal, most investigators reported no response to inoculation in the field. Since many of the most promising species, like auriculiformis and mangium, nodulate with rhizobial strains, which are widespread in tropical soils, it is not surprising that a more pronounced inoculation response was not seen. A notable exception was the exotic *P. juliflora* in Senegal, which, like leucaena, is nodulated by a specific type of fast-growing rhizobia not normally abundant in tropical soils. On the other hand, many of the tree species tested exhibited overall poor growth, and other environmental factors may have limited their response to inoculation. Only one of the projects attempted to measure the amount of nitrogen fixed by trees in the field; that aspect of the work is not yet complete.

Two projects examined the usefulness of nitrogen-fixing trees in agroforestry. In the Philippines, Escalada examined four species of nitrogen-fixing trees for yield, soil quality, and erosion control when intercropped with corn and cassava on steep hillsides. The corn studies show clearly that alley cropping with *Albizia falcataria*, in particular, enhances corn yield. In addition,

A. falcataria and *gliricidia* (*gliricidia sepium*) appear to be beneficial in reducing soil erosion on cropped hillsides. In a similar study in India, P. N. Unni quantified the effects of planting leucaena, gliricidia, and indigofera in rows between coconut and cocoyam plants and between rows of cassava. The preliminary results suggest that, while adding leguminous trees to a 30-year-old coconut plantation will not significantly increase coconut yields in three years, it does enhance the total system yield by increasing the yield of the cocoyam. Similarly, the presence of leguminous trees in the cassava area led to enhanced cassava yields. Quantitative data from experiments like these support the contention that agroforestry can play an important role in providing sustainable agricultural options for the wet tropics.

The multiplication of elite individual trees through tissue culture and vegetative propagation is a goal being actively sought by researchers around the world. For many species whose out-crossing nature and genetic variability make low-cost seed production unrealistic, vegetative propagation is a better way to produce superior planting materials. But tissue culture is a difficult area, part science and part art, where success occurs infrequently.

For this reason, CRG was not willing to fund a large number of tissue culture projects. In Chile, Orlando Balboa undertook studies to determine if it was possible to vegetatively propagate elite individuals of several prosopis species. Although he was able to obtain rooted cuttings and plantlets for several, their survival in the field was unacceptably low, only 7 percent. Similarly, it appears that Halos in the Philippines will be able to obtain rooted plantlets of only one of the two pine species she is studying to try to generate insect-resistant lines. Callus induction has been achieved with *Pinus caribea* but not with *Pinus keysia*.

Phenological studies are probably the least glamorous of all botanical endeavors, but without knowledge of the breeding systems of a species it is impossible to optimize its potential through genetic selection and breeding. Three BOSTID grantees conducted phenological studies on species that had received little attention heretofore. Balboa in Chile and Ulf Karlin in Argentina both gathered valuable information on the reproductive biology of different species of prosopis, while Panas Buranasilpin is documenting the phenology of *A. auriculiformis* and *A. mangium*. In the Thai study, phenological information will be critical to develop a promising hybrid of these two species, which was discovered by the grantee in one of the field sites. Since this hybrid has the desirable characteristics of both parents plus hybrid vigor, it presents an exciting opportunity to obtain a tree with good form, fast growth rates on acid soils, drought tolerance, good pulping qualities, insect resistance, and which fixes nitrogen. If this hybrid fulfills its apparent potential, it may be one of the most significant outcomes of the projects funded by the tropical trees research program.

NOTES

1. *Agroforestry in the West African Sahel*, 1984; *Firewood Crops: Shrub and Tree Species for Energy Production.* Volume 1 1980, volume 2 1983; *Sowing Forests from the Air*, 1981; *Mangium and other Fast Growing Acacias for the Humid Tropics*, 1983; *Calliandra: A Versatile Small Tree for the Humid Tropics*, 1983; *Casuarinas: Nitrogen-Fixing Trees for Adverse Sites*, 1983; *Leucaena: Promising Forage and Tree Crop for the Tropics*, 1984; *Tropical Legumes: Resources for the Future*, 1979. National Academy Press, Washington, D.C.
2. *Forestry Research Needs in Developing Countries—Time for a Reappraisal?* World Bank, Washington, D.C. 1981.
3. Members of the working group: Frederick Owino, University of Kenya; Charles Davey, North Carolina State University; Yvon Dommergues, Centre Orstom de Dakar, Senegal; Joann Roskoski, University of Hawaii; Lloyd Frederick, AID; Carl Gallegos, AID; Judith Bale and Jeffrey Gritzner, BOSTID. John Torrey, Harvard Forest, and Harold Keyser, USDA, also contributed.
4. The members of the advisory group were J. Lawrence Kulp, Weyerhaeuser Company, Chairman; James L. Brewbaker, University of Hawaii; Carl Gallegos, A.I.D.; William T. Gladstone, Weyerhaeuser Company; Joann Roskoski, University of Hawaii; Fred R. Weber, International Resource Development and Conservation Services, Boise, Idaho; Jeffrey Gritzner and Michael Greene, BOSTID.
5. Participants in the advisory group meeting were Dwight Baker, Battelle Kettering Research Laboratory, Ohio; James L. Brewbaker, University of Hawaii; Jeffrey Romm, University of California, Berkeley; Cherla Sastry, IDRC, Singapore; and V.K. Vamadevan, Center for Water Resources, Management and Development, Kerala, India; Jeffrey Gritzner, Michael Greene, and Tresa Bass, BOSTID.

Mosquito Vector Field Studies

Some of the most pernicious infectious diseases known are transmitted by mosquitoes. The most prevalent, malaria, affects between 100 million and 300 million people at any time and has a higher mortality rate than cancer—nearly all in the Third World. The data are unreliable because, in some places, malaria is so common that it is known simply as fever, and all fevers are called malaria. In many regions, the identity and/or behavior of the mosquito vectors of the disease are not well known, and attempts to control either the vector or the parasite have been futile. Some claim that the paucity of research on malaria, compared, for example, to cancer, is the best demonstration of the lack of scientific resources applied to Third World problems.

This was one of the concerns of the joint BOSTID-IOM (Institute of Medicine) Advisory Committee on Biomedical Research and Development (ACHBRD), which recommended this area to CRG. Part of the problem is that in the United States, there is little support for training malaria researchers, and worldwide the number of capable researchers is low.[1] Thus, the opportunity for BOSTID to support mosquito vector research in developing countries coincided with a concern about the shortage of U.S. researchers pursuing careers in medical entomology, and it was hoped that ways would be found to involve U.S. scientists in the projects. The U.S. capability to deal with vector-borne diseases was later the subject of a separate study carried out under ACHBRD auspices.[2]

In adopting this as one of the areas of concentration, CRG set the following as goals of the program:

- Achieve greater understanding of the biological adaptation of mosquitoes and other vectors to their environment, including new habitats, repro-

MOSQUITO VECTOR FIELD STUDIES GRANTEES

Marco Suarez	Malaria Eradication Service, Colombia. *Genetic Variation among* Anopheles albimanus *Populations and Relationships to Vector Competence, Ecology and Geographical Distribution.*
R. Valderrama	University of Antioquia, Colombia. *Dynamics of* Anopheles-*Human Interaction in Endemic Malaria Areas.*
J.S.M. Peiris	University of Peradeniya, Sri Lanka. *Vector Biology and Vector Competence of Man-Biting Mosquitoes in an Urbanized Environment and an Area Under Agricultural Development.*
Chang M.S.	Medical Department, Sarawak, Malaysia. *Bionomics of Two* Mansonia *Species and Their Response to Insecticides.*
F.P. Amerasinghe	University of Peradeniya, Sri Lanka. *Ecology of Mosquito Vectors and Vector-borne Diseases in a New Irrigation Project.*
Jeffrey Hii	Tropical Disease Research Center, Sabah, Malaysia. *Genetic Variation of the* Anopheles balabacensis *Complex and its Relationship to Malaria Transmission.*
C. Prasittisuk	Ministry of Public Health, Thailand. *Comparative Longitudinal Studies of Malaria Vector Infection Rates in Different Ecological Areas.*
Visut Baimai	Mahidol University, Thailand. *Malaria Vectorial Capacity of* Anopheles dirus *Complex.*
E. Tikasinghe	Caribbean Epidemiology Center, Trinidad and Tobago. Toxorhynchites moctezuma *as a Control Agent for* Aedes aegypti.
Louis Mukwaya	Uganda Virus Research Institute. *Complexes of* Aedes simpsoni *and* Ae. africanus *in East Africa; Vector Competence, Genetic and Ecological Differentiation.*
Yasmin Rubio	School of Malariology, Venezuela. *Biology of* Anopheles nuneztovari *and its Role in Malaria Transmission.*
S.M. Mpofu	Blair Research Laboratory, Zimbabwe. *A Study of Seasonal and Altitudinal Patterns of Malaria Transmission.*
O. Forattini	University of Sao Paulo, Brazil. *Relationships of Mosquito Feeding Patterns to Vectorial Capacity in Diverse Ecological Settings.*
Margaret Dix	Universidad del Valle, Guatemala. *Assessment of* Salvinia auriculata *as a Plant Larvacide for Malaria Control.*

Titus Mukiama	University of Nairobi, Kenya. *The Ecology and Possible Control of Malaria Vectors with Extracts of* Melia volkensis.
M. Rodriguez	Malaria Research Center, Mexico. *Isolation and Identification of Potential Pathogens for Anopheline Mosquitoes.*
Abdiel Adames	University of Panama. *Relationships of Mosquito Vectors and Waterbirds in the Potential for Transmission of Two Arboviruses.*
G. Calderon	National Institute of Health, Peru. *Dynamics of Malaria Transmission in a New Settlement Zone.*
S. Diallo	University of Dakar, Senegal. *Ecology of Malaria Vectors in a Zone Undergoing Desalinization and Agricultural Development.*
S. Upatham	Mahidol University, Thailand. *Studies on the Bionomics of* Anopheles maculatus *and its role in Malaria Transmission.*
Sakol Panyim	Mahidol University, Thailand. *Development of DNA Probes to Differentiate Sibling Species of* Anopheles dirus *and* An. Maculatus.
Louis Mukwaya	Uganda Virus Research Laboratory. *Taxonomy and Population Genetics of* Aedes simpsoni *Complex.*

ductive behavior, population density, sequence of vectors and associated organisms, and seasonal fluctuations.

- Assess the magnitude and extent of the selection of mosquito vector populations for resistance to conventional insecticides and other control methods.
- Develop and test new methods and systems of mosquito and other vector control on a regional or national basis.
- Strengthen institutional capabilities to conduct basic field studies on mosquito vectors.
- Analyze the socioeconomic factors affecting mosquito vector control.

Field research on mosquito-borne disease is notoriously difficult. It must be carried out, by definition, in infested places. It can be difficult to identify the infected and infective specimens. In the case of malaria, for example, even in the most endemic areas, a very small percentage of the female mosquitoes caught in the field are infected with *Plasmodium*. Traditionally, these are processed by manual laboratory dissection under a microscope, and detection of the parasite is difficult. In many years of field operations, the malaria service of Thailand, a country with a severe malaria problem, had detected only a handful of infected wild-caught mosquitoes.

Also elusive is the problem of control. Much of the control effort is dedicated to destroying mosquito larvae. But mosquitoes follow a life strategy that the ecologists call r-type. Each female produces up to 300 offspring each oviposition and provides no care; under normal conditions only a few survive to propagate the species. It is unclear whether under these conditions attempting to kill larvae has any effect on disease. It may be that control efforts only determine which few larvae survive, with an unintentional selection in favor of stronger individuals, so that disease may actually be increased by certain types of control programs.

Another problem relates to catching the mosquitoes. If it is not known which species is the principal vector of disease in an area, it may be necessary to target in the field those that bite humans, as opposed to species that prefer animal blood or plant juices before ovulation. According to most mosquito researchers, the most reliable method of catching man-biting species is by the so-called human bait catch. In this technique, groups of workers sit with their legs exposed and catch the mosquitoes that land on them, preferably, but not certainly, before they bite. This introduces ethical problems related to risk of disease, especially for diseases for which there are no effective prophylactic regimens. This problem was discussed in detail for the BOSTID program by the National Academy of Sciences Committee to Review Human Studies, and a policy was recommended by the grantees at their Third Coordination Meeting. This topic will be discussed below.

ORGANIZATIONAL MEETING

The organizational meeting took place in Washington, D.C., April 19-21, 1982. It followed by a few days a meeting in Gainesville, Florida, sponsored by AID, which proposed priorities for AID-supported research. Those recommendations concentrated on control strategies and interventions, but participants at the BOSTID meeting said that there was much basic research on mosquitoes remaining to be done and few sources of support. A limited amount of research funding was available from the World Health Organization (WHO), but this could be used only for malaria research, leaving important arboviruses almost without attention. The WHO representative proposed that BOSTID concentrate exclusively on vectors of diseases other than malaria, but others felt that malaria was still the most important problem and lacked adequate research support. Subsequent developments bore this out; the program received many times more proposals dealing with malaria than with all other diseases.

Areas of research recommended for study were epidemiology of mosquito-borne pathogens, population dynamics, genetic aspects and taxonomy, life table studies, surveillance, and biological control. To tie it all together,

the participants suggested a general goal: to define the natural history of mosquito vector populations, which allows development of sound control strategies leading to the reduction or prevention of disease in a defined geographical area. This would include activities such as "incrimination" of vectors; characterization of genetic variation; measurement of vector population dynamics, density, and behavior; determination of vector capacity, vector competence, and disease transmission dynamics; identification and assessment of natural predators and pathogens of vectors; understanding vector ecology in relation to human activities; evaluation of vector control methods; and development of new methods for basic vector biology field studies.

It was noted later that the projects that were funded adhered faithfully to this list. However, because of the large number of vector species and the wide geographical variations observed, it was difficult to delineate the coherent body of knowledge created by the BOSTID program. This state of affairs might have been predicted at the organizational meeting and the focus drawn a little more sharply. But the other horn of the dilemma was the small number of capable vector biologists in the Third World to do the research, and a narrower focus necessarily restricts the pool of potential applicants.

CRG accepted the recommendations of the organizational meeting, and the appropriate announcements were prepared and distributed. A broadside mailing was sent to the membership of the American Mosquito Control Association and subscribers to the *Arbovirus Exchange Newsletter*.

ADVISORY GROUP

By the time of the June 1985 meeting of CRG, fifteen grants had been awarded and the first coordination meeting had been held. But CRG was concerned that, while many of the individual projects would produce basic knowledge about the biology of, or genetic variation among, mosquito species, the information would have mainly local application and not necessarily lead to strategies for vector control beyond a limited geographical area. CRG wished, rather, to see the mosquito vector research (MVR) program develop a coherent body of knowledge and experience that would advance the field and facilitate applications of technologies for mosquito vector control. In addition, the number of proposals received was declining by 1985, and there was need for a new approach to recruiting. CRG asked that an advisory group of experts be convened to suggest possible approaches and opportunities for reorientation of the program to achieve more coherence among the projects. However, it was made clear that broadening the scope to include other vectors, in addition to mosquitoes, would not be acceptable.

The advisory group convened on October 7, 1985, in Washington, D.C.[3] The vice chairman of CRG articulated the concerns of the committee that there may be too much emphasis among the approved projects on morphology and genetic variation and insufficient comparability among projects. But the group responded that the scope and substantial focus of the MVR program were "excellent" and did not need major alteration. Qualified investigators had been identified from a very small pool in developing countries, and dissemination of program information had been thorough. They were more concerned about two peripheral aspects of the organization of the program.

This group again expressed the interest of the MVR community in the United States opportunities for collaboration among U.S. and developing country investigators in this field. In none of the other areas were objections expressed so clearly and frequently about the inability of the BOSTID Research Program to support U.S. researchers. In particular, the desirability of having U.S. postdoctoral investigators associated with BOSTID projects was mentioned by every interested group, including ACHBRD and the organizational meeting. But the advisory group went further and elaborated a detailed proposal to systematically associate U.S. postdoctoral researchers with the BOSTID MVR projects, and they even offered to help locate suitable candidates.

CRG later accepted this recommendation in principle, but wished to consider each candidate and each grant on a case-by-case basis. Staff polled the MVR principal investigators for interest in accepting a postdoctoral researcher, and the leader of the Venezuelan project responded positively. A suitable candidate (who happened to be Canadian) was located by the U.S. consultants to the project, and a two-year work plan was developed; additional funding for salary, travel, and expenses (including a laptop computer) were added to the grant. Unfortunately, the scheme ran into problems. This project was carried out by the School of Malariology in Maracay, but the host institution was legally the Pan American Health Organization (PAHO). Venezuelan law prohibited the School from accepting a foreign grant, and PAHO stepped in and agreed to accept the grant and manage the funds on behalf of the school. Therefore, the postdoctoral researcher would have to be contracted under PAHO regulations, which did not permit a guaranteed two-year contract. To protect the researcher and her career, BOSTID insisted on confirmation in writing that the contract be automatically renewed up to a two-year limit. But despite these written assurances, further problems developed. This was the only experience with placement of postdoctoral investigators within the BOSTID program because the program funds were cut soon afterwards.

The other recommendation made by the MVR advisory group had to do with evaluation of proposals. The BOSTID Research Program requires

evaluation of proposals in writing by specialists for decision by a separate, generalist panel. This is apparently unusual in the biomedical community, and on several occasions dissatisfaction with this method had been articulated. The MVR advisory group proposed that a review panel be formed for the MVR program, on a trial basis, to evaluate proposals in lieu of the independent written reviews. (The decisions would still have to be made by CRG according to the rules of the program.) This was tried for one round of proposals, but it was found unsatisfactory by the staff and abandoned. The problem lay with the pregrant visits. Staff were accustomed to visit applicants armed with four or five detailed written reviews, sometimes contradictory, which provided an adequate basis for revision of the original proposal, but left enough uncertainty so that the CRG decision remained in doubt, even were the applicant to adopt all the changes suggested by the various reviewers. In contrast, the views of the review panel were expressed briefly and definitely, leaving no options. Applicants might have been led to believe that if they took the suggestions of the review panel when they revised their proposals they would be funded, which was not necessarily the case. The study section was also more expensive and time-consuming for the staff, and the experiment was not repeated.

COORDINATION MEETINGS

The first coordination meeting of the mosquito vector researchers was a regional meeting held in Panama in August 1984. Only the grantees from Africa and Latin America were included, since they were seen to be, in general, less advanced technically than the Asian group. Much of the meeting was dedicated to workshops and reviews of techniques and procedures. It was almost a complete overview of the state of the art: field sampling and collection methods, taxonomic problems, microbial pathogens (for biological control), colonization of mosquitoes, and electrophoresis. Tutorial workshops were held on field sampling and collection, taxonomy and identification of mosquitoes, and mosquito pathogens. No attempt was made to recommend a common protocol for all researchers, but there was agreement to use more than one method of sampling and identification, wherever possible, to calibrate techniques.

The groundwork for what is perhaps the major contribution of the BOSTID mosquito vector project was laid at the second coordination meeting held in Washington, D.C., in April 1986. For two days, the grantees met at BOSTID headquarters to discuss the progress of their projects. The meeting then moved to a laboratory at the Uniformed Services University of the Health Sciences (USUHS) for a three-day, hands-on workshop offered by staff of USUHS, researchers from the Walter Reed Army Institute for Research (WRAIR), and Michael Service of the Liverpool School of Tropical Medi-

cine. The objective was to learn to apply two relatively new techniques based on the enzyme-linked immunosorbent assay (ELISA) for detection of malaria sporozoites and for identifying the source of blood meals. During the week following the coordination meeting, the grantees attended the American Mosquito Control Association annual meeting in New Orleans, where most of them presented papers at one of the regular program sessions of the meeting.

Development of the ELISA applications, principally by Robert Wirtz and his associates at WRAIR, represented an important milestone in mosquito research. Detection of *Plasmodium* infection in wild-caught mosquitoes had always been done by manual dissection of individual insects; the infection rate in the wild is very low and the rate of detection is small. Therefore, incrimination of malaria vectors was labor intensive and time consuming. Similarly, the identification of the blood meal found in the mosquito's midgut is a way of separating the man-biters from those that feed on other sources, but has required painstaking chemical analysis.

The ELISA method makes both of these measurements more rapid and possibly simple enough for field application. WRAIR was interested in assisting the BOSTID grantees, both to help them obtain reliable data and to see whether the technique could be used in the field in tropical countries. WRAIR provided each of the grantees with a partial ELISA kit and a test protocol free of charge. Those grantees who wished to incorporate the method into their projects would submit a protocol for approval by WRAIR and BOSTID, and BOSTID would purchase the necessary reagents and supplies from WRAIR for the grantees. Subsequently, WRAIR and USUHS personnel visited a number of the grantees to assist with the application of the method. The impact on the ongoing projects was dramatic; results were reported that could not have been achieved with earlier technologies. This was one of the best examples of the collaboration that BOSTID had hoped to foster among a group of developing country grantees working on a common problem and U.S. scientists. Both gained from the collaboration; the Americans' knowledge and technology were magnified by the existence of the BOSTID network of researchers.

The third coordination meeting was held in Patthaya, Thailand, in April 1987. There was a featured session on larval ecology, in which three U.S. experts led a discussion of biological control, and a special workshop was offered by grantee Sakol Panyim of Mahidol University to demonstrate the technique of DNA probes for separation of sibling species that he had developed as part of his BOSTID-supported research. The chief malaria vector in Thailand is *Anopheles dirus*, which is not a single species but is composed of at least four "sibling species," which are difficult to identify morphologically and have significantly different behavior and biting habits. Before Sakol's development, they could only be distinguished by intensive

morphological studies and using slow laboratory electrophoretic processes. Sakol's method can be applied rapidly to identify several of the species in the field. A new proposal was presented by some of his colleagues at Mahidol to validate the technique and use it to incriminate malaria vectors in endemic areas where the vectors had never been conclusively identified before.

It was also at this meeting that the policy of human bait was discussed and a workable policy was recommended to CRG, the NAS Committee to Review Human Studies (CRHS), and other mosquito researchers and donors. This policy and the arguments that led to it are discussed in the following section.

The last coordination meeting was held in December 1988 in Washington, D.C. Many of the experts from USUHS, WRAIR, the National Institutes of Health, and others who had collaborated with the grantees during the course of the program were present as the grantees presented their results. A field trip took them to the Eastern Shore of Maryland where they observed the equipment and discussed the strategy of the State of Maryland Mosquito Control Program. Mosquitoes are a major nuisance near the saline wetlands of Eastern Maryland, and may serve as carriers of disease. The heavy equipment, vehicles, and aircraft mobilized by the state agents stand in notable contrast to the meager resources available for mosquito vector control in most tropical and malarious countries. Some felt this was not a reflection of the relative wealth of the State of Maryland and of the countries involved, but rather the greater political interest in controlling a pest that annoys the affluent than in controlling the carrier of malaria, which affects mainly the poor. Some of the grantees were also critical of the quantity of chemicals applied to the wetlands in Maryland without prior testing on nontarget species; this criticism displeased the Maryland officials. However, all chemicals used by the Maryland officials have met the test criteria of the Environmental Protection Agency.

HUMAN BAIT POLICY

One of the conditions imposed on the BOSTID Research Program when it was founded was that projects using human subjects or those in which researchers were at risk of disease or injury had to be approved by CRHS. This committee was convened to satisfy guidelines of the Department of Health and Human Services, which also governed AID programs. The committee reviewed all BOSTID projects in which subjects or researchers were at risk. Although it never actually rejected a project, it sometimes added conditions to a project, usually relating to invasive procedures or consent forms. But since the first mosquito project was presented, the committee made it clear that it had been profoundly troubled by the use of human bait in catching mosquitoes.

The first MVR project presented to CHRS was from Marco Suarez in Colombia. When CHRS questioned the human bait catches, Suarez assured them that all human bait collections would be subject to WHO guidelines, and he enclosed a copy. Although this document was reviewed by BOSTID staff and by CRHS, it apparently was not carefully read by either. In any case, each time the question of human bait arose, as it did in nearly every MVR proposal, CRHS raised the same questions, and finally a policy was drafted that insisted that all projects follow WHO guidelines.

The questions raised were not trivial. Researchers argued that human bait catches (euphemistically called "landing catches" without indicating what or whom they were landing on) were essential to the research. No one argues that the paid mosquito catchers were not at risk of disease. But were they more at risk than if they remained in their villages? They were possibly at greater risk of being bitten but less at risk of disease if they took prophylactic drugs. But for some diseases there was no prophylaxis available, like resistant malaria or some arboviruses, and sometimes the catchers refused to take drugs until they had symptoms. All research groups offered chemotherapy to catchers who caught disease, and in most cases the scientists themselves took their turn at mosquito catching. Was there any significance to a consent form if the worker is being paid for catching mosquitoes, except to inform him of the risk? Finally, CRHS tired of entering the same debate and resolving it with the same formula, and asked to see the WHO guidelines once again. At this point it was noticed that the WHO guidelines were mainly concerned with scientific use of human bait collections and had nothing to say about the safety of the catcher.

With some embarrassment, BOSTID staff contacted WHO and other international organizations concerned with mosquito research. The responses were not consistent, and an official of the Tropical Disease Research Program wrote that there were no guidelines for the safety of collectors. Not all respondents even agreed that direct landing methods (the standard method of allowing the mosquito to land on the skin of the catcher) were even necessary. One expert recommended double net catches instead. In this scheme, a human sleeps inside a double net that traps the mosquito without permitting a bite. Others argued that some species will not enter a double net.

With the concurrence of CRHS, the question was put to the assembled grantees and experts at the Patthaya coordination meeting. They were asked to devise concrete guidelines or criteria for deciding when human bait direct landing catches should be used to catch mosquitoes. It was suggested that since such guidelines appeared not to exist, the recommendation might well have wider application.

Most of the grantees agreed that landing catches were indispensable for some research, and providing catchers with prophylaxis and chemotherapy

made the risk to locally recruited catchers acceptable, in the sense that it is comparable with other ordinary activities carried out in the villages. Risk can never be entirely eliminated, and is also present, for example, in a virology laboratory in the United States. The risk must therefore be weighed against the expected value of the research, and this must be decided by a review committee. Therefore, instead of devising criteria for application of landing catches, the group elaborated a series of questions designed to assist CRHS or other institutional review boards and reviewers of scientific proposals assess the necessity for human bait catches. These questions are contained in the box below.

RESEARCH RESULTS

There were twenty active grants in the MVR program. Two additional grants were made, one to Burma and one to Zimbabwe, but these were never implemented because of political violence in one case and administrative problems in the other. A third project, in Colombia, made little progress because the principal investigator was unable to make use of procedures to receive the BOSTID-procured equipment in the country and because he began to receive death threats from drug dealers, suspicious of his activities catching mosquitoes in remote areas. Consequently, activity on the project was suspended and the grant was allowed to expire.

The remaining nineteen projects were among the most productive in the BOSTID Research Program, and between them they produced more than one hundred papers. They could be grouped into four categories: malaria (eight projects), biological control (four projects), ecological changes (five projects, three of which also dealt with malaria), and other (one filariasis and three arbovirus projects).

Two grants in Colombia and one in Malaysia looked at genetic variation within a single species of malaria vector. Suarez found chromosomal differences between mosquitoes from the highland and lowland regions of Colombia, which were reflected in biting patterns and behavior. These results are somewhat discouraging for purposes of mosquito control. They imply that it is not sufficient to incriminate one particular species as the principal vector of malaria in an area; even if its biology and ecology are well known, it will be necessary to repeat the studies to be certain that there has been no major genetic shift within the population. The Colombian study dealt with *Anopheles albimanus*, the principal vector in South America. In Malaysia, Hii found similar geographic variation among *An. balabacensis*, an important vector in Indonesia, Malaysia, and the Philippines.

The other malaria projects dealt with the incrimination and bionomics of malaria vectors. In these projects, new technologies played an important role. For example, an early project in Thailand sought to incriminate *An.*

JUSTIFICATION FOR HUMAN BAIT COLLECTIONS OF MOSQUITOES

• Scientific Justification. Why are human bait collections necessary to the aims and objections of the research? What objectives will not be met without use of this method, and what is their relationship to the specific aims of the project?

• Alternative approaches. Are alternatives to the use of unprotected human bait collections feasible, including use of the double nets? Can alternatives to unprotected human bait collectors be used to satisfactorily address specific aims of the research?

• Assessment of disease risk. To what arthropod-borne pathogens will collectors be potentially exposed? Provide an assessment of disease risk (in quantitative terms, if possible). What is the potential severity and risk of fatal outcome or permanent sequelae for each pathogen?

• Susceptibility and protection of exposed personnel. Define the susceptibility of human bait collectors in terms of naturally acquired immunity (e.g., serological testing); protection afforded by chemoprophylactic agents or vaccines; and age, sex, and other risk factors.

• Informed consent. Define steps taken to assure that exposed personnel are fully informed of the risks and hazards associated with the work. Provide a copy of the voluntary consent form used to assure that this information has been provided to, and understood by, those personnel. If the project compensates personnel exposed to risk, explain how such compensation will be provided (e.g. increased pay and medical fees).

• Surveillance for infection and disease. Describe procedures for a medical surveillance program. How will workers be systematically followed for infection and disease potentially acquired during participation in the study?

• Medical care. Will workers receive medical care for diseases acquired as part of their participation in the study? How will they be compensated for losses resulting from work-related illness or injury?

maculatus, an important vector in neighboring Malaysia, which was widespread in a highly endemic area of southern Thailand. The researchers were confident that *maculatus* was the major vector and should be the target of control efforts. But during the three year project, they failed to find a single *maculatus* mosquito infected with the malaria parasite using traditional dissection methods. Two years later, a similar BOSTID project was

initiated by the Ministry of Public Health Antimalarial Program. The difference was that the ELISA technique pioneered by the Walter Reed Army Institute of Research was now available to the researchers. They found infected mosquitoes and were able to develop reliable statistics to support their conclusions. A similar study using the ELISA techniques in Venezuela by Yasmin Rubio incriminated *An. nuneztovari.*

Similarly, the DNA probe developed by Sakol Panyim to distinguish the sibling species of *An. dirus* was utilized directly in a follow-up BOSTID project led by Visut Baimai and his colleagues. They were able to determine which of the sibling species of *An. dirus* are the major vectors and begin a study of their ecology and behavior to generate information that can be useful to the antimalarial program.

Four of the grants sought biological control agents against known vector mosquitoes. Projects in Kenya and Guatemala studied botanical agents, a Mexican project looked for microbials, and a project in Trinidad and Tobago used another mosquito species as a predator. All of these were somewhat controversial.

The Mexican project was organized and promoted by a group of researchers from midwestern U.S. universities. One of the most successful larvacidal agents was a biological toxin produced by a bacterium, *Bacillus thuringensis* var *israelensis*, and commonly called B.t.i. It works effectively against bottom-feeding larvae but has to be reapplied at approximately two-week intervals. What was intriguing to the U.S. researchers was that it had been found through a search in Israel of dead or moribund larvae and then culturing the infecting pathogens. They suggested that a search in Mexico might also be fruitful. CRG funded it without enthusiasm. They regarded this kind of project as a "fishing expedition," where there were no preliminary results suggesting the existence of an agent more potent than B.t.i. Many similar proposals were received after this one, but none was funded. The Mexican group, in fact, found no agents useful for mosquito control, but they did find a pathogen that was effective against the Mexican fruit fly and a fungus that is effective against the velvet bean caterpillar, which attacks soybeans. But these were similar to other pathogens previously discovered, and no further development was carried out.

The Kenyan and Guatemalan projects sought larvacides of botanical origin. Margaret Dix's group at the Universidad del Valle had noted that larval densities were low in natural ponds covered with the aquatic weed *Salvinia auriculata*, which is common in tropical waters. Critics argued that *Salvinia* forms a dense mat, which may physically prevent larvae from reaching the surface to breathe; the same characteristic causes it to block waterways and ponds and become a nuisance in some places. Dix attempted to isolate an active chemical ingredient in *Salvinia*, but it was found to be effective against mosquito larvae only in very high doses. The

University of Nairobi project led by Titus Mukiama yielded a similar story. The plant was *Melia volkensis*, a tree that grows beside bodies of water and appears to inhibit larval growth. Again, an active agent was isolated, but it demonstrated larvacidal properties only in extremely high doses. The search for botanical pesticides is probably worthwhile, but such projects should be funded at a very low level until and unless a potent effect can be demonstrated.

Perhaps the most interesting project in this category was carried out by the Caribbean Epidemiology Center, a PAHO dependency located in Trinidad. It involved *Toxorhynchites moctezuma*, a large mosquito that neither bites man nor carries disease, but whose larvae feed on the larvae of container-inhabiting mosquitoes, including *Aedes aegypti*, the major vector of dengue fever in the Caribbean. Elijah Tikasingh proposed an ideal setting for the evaluation of "*Tox*" as a control agent: Union Island, which belongs to St. Vincent, has about 3,000 people living in two villages, which are two miles apart and separated by a hill. There was currently no dengue on Union Island, so it was judged safe to use for a trial by introducing "Tox" in one village and using the other as a control. There was a slight danger of a different kind: if after securing the informed consent of the villagers in some appropriate way, dengue should break out during the course of the trials, BOSTID, or even some other U.S. agency, might be blamed for "causing" the outbreak. Fortunately this did not occur.

Other criticisms of the experiment were more serious and the project stimulated a lot of controversy among CRG members. Questions involved the choice of Tox species, the economics of importing the larvae from Trinidad to Union Island instead of rearing the Tox on the island, and, finally, the failure of the researchers to monitor the number of adult mosquitoes in the two villages by human bait capture, which left the results inconclusive. After the project ended without definitive results, BOSTID contributed additional funds for one more trial with fresh introduction of Tox, but unfortunately the *Aedes* population was so high by the time Tox were reintroduced that control to a low level was not possible.

Perhaps the most important discovery in the area of biological control was made by the two Colombian researchers, assisted by Gerald Marten of the East-West Center, a BOSTID consultant who visited the projects. They found a strong negative correlation between the population of larvae of *An. albimanus* in ponds and lakes and the abundance of the copepods of genus *Mesocyclops*. Marten proposed that these copepods may be predators of anopheline larvae, and urged a follow-up, but the grantees declined to divert any of their resources to studying copepods.

Those projects studying the relation of human activity and ecological change to mosquito-borne disease incidence were among the most successful. The most definitive were the projects based at the University of Peradeniya

in Sri Lanka led by J.S.M. Peiris and F.P. Amerasinghe. They dealt with the Mahaweli project, a monumental effort to control the country's largest river and create new settlements and irrigated lands. Forested land is being converted to farmland and settlements, and the research question is what effect this will have on mosquito-borne disease incidence. Vectors of several viral and parasitic diseases were monitored in an uncut forested zone, a zone in transition, and a zone dedicated to settlement, and inhabitants were surveyed for serological status. The results were unequivocal. Vector species were found in the forest, awaiting the arrival of human settlers, and disease incidence rose in newly established areas. The results have now been published in the scientific literature, and the AID mission in Colombo has been advised of the significance of the findings. This situation was, in fact, widely predicted, but it had never been documented so clearly.

A similar situation existed in Senegal, where the Bignona River has been diverted for agricultural development and for the creation of a desalinated zone for irrigation. One expected result of the desalinization was replacement of the moderately ineffective malaria vector *An. melas,* which breeds in brackish water, with the highly efficient *An. gambiae*, which requires fresh water. This could result in large increases in malaria incidence if no control program is initiated. But unfortunately, although all the experts expected a definitive result, the study was inconclusive because of the investigators' failure to measure the (presumably declining) densities of *melas.* This happened despite three extended consultant visits, training of a researcher at FAO in Rome, and participation of the principal investigator in three coordination meetings.

A project in Peru set out to measure the effects of new human settlements on anopheline mosquito ecology in the Amazonian jungles of Peru. The project received a setback after one year, when a group of terrorists invaded the settlement and forced the researchers to choose another field site. Nevertheless, Guillermo Calderon and his colleagues were able to identify and incriminate the principal vectors and document some of the reasons that malaria was such a severe problem to new settlers. Many of the settlers came from other areas and did not have protective antibodies to *Plasmodium vivax* as did, for example, the local Indians. Mosquitoes bite primarily in early evening when many people are exposed. DDT spraying has been ineffective, in large part because it is usually sprayed on interior walls, and many Amazonian dwellings have no walls. The conclusion was that control of adult mosquito populations was likely to be impossible, and that attention should be shifted to control of larvae. Unfortunately, the larval ecology of these species was not studied.

In a similar vein, Oswaldo Forattini's project in the State of Sao Paulo in Brazil observed several different vectors of arbovirus and malaria to determine taxonomy, biting habits, and ecological characteristics in an area in

which settlement patterns are changing. There seems little doubt that some of these species are poised to interact with man invading their environment and cause epidemic situations among populations that have not previously been exposed to the diseases.

The importance of careful taxonomy in mosquito research was emphasized by Louis Mukwaya's project in Uganda. Mukwaya was motivated by the observation that there is no endemic Yellow Fever in the Buganda district of eastern Uganda, even though *Aedes simpsoni*, which is a demonstrated yellow fever vector in the Bwamba district of the country, is plentiful. The mystery was resolved when he discovered that *Ae. simpsoni* is really a species complex with two distinct subspecies, one of which does not bite man. The two subspecies vary in population density from locality to locality, and control efforts should be aimed at tilting the ecological balance slightly in favor of the non-anthropophilic subspecies.

One project dealt with vectors of filariasis. The Government of Malaysia had refused to mount a control campaign against the *Mansonia* vectors of filariasis distinct from the spraying done to control malaria. The object of Chang Moh Seng's project was to determine whether the anti-malarial spraying was also effective against *Mansonia*, and to test alternative strategies. *Mansonia* is difficult to control at the larval stage because they attach to the underwater roots of swamp-forest plants. The project found that anti-malarial spraying of wells was ineffective against *Mansonia*, but targeted spraying of malathion at the correct time did significantly reduce outdoor biting densities. An attempt to use B.t.i. on the swamps to attack larvae had limited success.

A project in Panama aimed to show that waterbirds act as intermediate hosts to the virus causing St. Louis and Venezuelan Equine Encephalitis by isolating the virus in the nestlings. Unfortunately this project was halted for administrative reasons, and the results were inconclusive.

NOTES

1. One member put it this way: The first consequence of the success and popularity of DDT was the eradication of the medical entomologist.
2. *Manpower Needs and Career Opportunities in the Field Aspects of Vector Biology: Report of a Workshop.* Washington, D.C., National Academy Press, 1983.
3. Participants in the advisory group meeting were George B. Craig, University of Notre Dame (NAS member); David Pimentel, Cornell University (CRG member); William Reisen, Arbovirus Field Station, Bakersfield, California; Robert Washino, University of California, Davis; Graham White, London School of Hygiene and Tropical Medicine.

Rapid Epidemological Assessment

Epidemiological data form the main core of support for public health policy in the United States, and a major governmental agency, the Centers for Disease Control (CDC), is dedicated principally to carrying out epidemiological studies. CDC has high prestige among the U.S. public, and, despite the efforts of the U.S. tobacco industry, epidemiological data are widely accepted as a picture of reality. Epidemiology is a subject of study in U.S. medical schools, and doctorates are awarded in the field by many of the nation's graduate universities.

This state of affairs, unfortunately, is not widespread in much of the world, including the developing countries. Epidemiologists are in very short supply, and reliable epidemiological data are often not available to decision makers. Apart from the lack of trained people, there are two reasons for this: one is the high cost of carrying out a major longitudinal study and following a cohort group over many years, as is often the practice in the United States; the second is the lack of supporting infrastructure and data base, such as reliable vital statistics and hospital clinical data. The science of epidemiology was developed in the industrialized countries, and in many ways it is not compatible with the needs and resources of the Third World.

The concept of rapid epidemiologic assessment (REA) was proposed by the joint BOSTID-Institute of Medicine Advisory Committee on Health and Biomedical Research and Development in 1981 to bridge that gap. It is meant to describe methods that, because of their simplicity, low cost, or rapidity, are well suited to the needs for epidemiologic information of developing countries. The goals established by CRG for this program were:

RAPID EPIDEMIOLOGIC ASSESSMENT GRANTEES

Sultana Zaman	University of Dhaka, Bangladesh. *Rapid Epidemiologic Assessment of Childhood Disability Using Community Health Workers.*
H. Flores	Universidade Federal de Pernambuco, Brazil. *Potential of Liver Retinol Reserves Measured at Autopsy as Indicator of Vitamin A Deficiency in Populations.*
F. Mardones	University of Chile. *Prediction of Malnutrition Risk in Infants.*
C. Ferreccio	Ministry of Health, Chile. *A Case-Control Study of Vaccine Efficacy in the Field: Antityphoid Oral Vaccine.*
C. Raabe	Association for Health Research, Costa Rica. *Lot Quality Assurance Sampling for Monitoring Health Care.*
Osman Galal	Nutrition Institute, Egypt. *Risk Assessment: Identification and Monitoring of Fetal Malnutrition.*
A. Augustin	Child Health Institute, Haiti. *Rapid Assessment of Health Status of Non-Users of Services in Population-Based Systems.*
Venkataswamy	Aravind Eye Hospital, India. *Assessment of Rapid Survey Techniques for Ophthalmic Health Planning and Monitoring.*
M. Thorburn	University of the West Indies, Jamaica. *Low-Cost Methods for the Rapid Assessment of Childhood Disability.*
Elsa Sarti	Directorate of Epidemiology, Mexico. *Risk Factors Associated with Rural Taeniasis and Cysticercosis.*
J. Baltazar	Nutrition Center of the Philippines. *Water, Sanitation, and Diarrhea: Comparing Case-Control and Prospective Methodologies.*
C. Ngelangel	University of the Philippines. *Case-Control Study of Late Diagnosis of Breast Cancer: Hospital Visitors as Controls.*
F Mardones	University of Chile. *A Malnutrition Risk Assessment Instrument for Infants.*
W. Freire	Center for Planning and Social Research, Ecuador. *Positive Predictive Value of Hemoglobin Measures for Program to Control Iron Deficiency Anemia.*

E. Kestler	Guatemala Social Security Institute. *Risk Assessment: Development of an Instrument to Detect Pregnant Women at High Risk of Delivery of Low Birthweight Infants.*
H. Delgado	Institute of Nutrition of Central America and Panama, Guatemala. *Determination of the Value of School Children's Height Measurements as a Tool for Nutritional Surveillance.*
C. Lanata	Nutrition Research Institute, Peru. *Development of Survey Methodology to Assess Childhood Health Status and Service Utilization.*
E. Domingo	University of the Philippines. *Standardization of Simple Method for Identifying Infants at Risk of Becoming Hepatitis-B Carriers.*
Z. Hasan	Jinnah Postgraduate Medical Center, Pakistan. *Rapid Epidemiologic Assessment of Childhood Disability Using Social Workers.*

- To develop simplified epidemiologic methods to assess a particular health problem or cluster of related health problems;
- To investigate the utility of REA survey methods for assessing the adequacy of disease surveillance systems or clinic records;
- To adapt REA methods to serve as program management or evaluation tools; and
- To develop REA methods to provide population-based information on births and infant mortality.

But REA, as was pointed out, is a new concept. It is not a standard discipline and very few references in the literature exist. AID also had difficulty with it; although it was approved by CRG in December 1981, and a small discussion meeting was held with AID in early 1982, AID concurrence for the research area was not received until September 1982.

ORGANIZATIONAL MEETING

The organizational meeting was held January 3-5, 1983. The participants recognized that the REA program would be dealing with a novel approach in a field whose fundamentals are not well known in the developing countries. They cited examples of innovative approaches to epidemiology that have been carried out in the developing countries, but that had not been thought of previously as belonging to a subfield of their own. The participants anticipated that it might be difficult to convey to potential applicants the objectives of the program, and suggested that the announce-

ments be designed with great care. They proposed that all projects considered for review and funding should meet all the following criteria:

- The method in question should be closely related to a health planning or management decision at a local, regional, or national level.
- The objective should not be to carry out a health survey per se; the primary aim should be methodological.
- The method being tested should be applicable to a variety of similar settings.
- The methodology under development should be simple and inexpensive.
- The data collection and analysis techniques could be taught or reproduced, and could be carried out in a timely fashion.
- The health problem or program being addressed should be justified by its importance to national health goals, size of program budget, or high prevalence, incidence or number of disability days.
- The health problem selected can be prevented or treated by currently available technologies.

They also developed a similar list of criteria for projects that should not be funded, including, in particular, studies of tools for clinical screening and diagnosis or for decision making at the individual level, and they suggested a set of examples of research studies that could be included in the program.

As matters developed, the apprehensions of the organizational meeting were fully justified. To identify potential grantees, CRG staff consulted with national and international organizations in the health and epidemiologic areas. Questionnaires were mailed worldwide to seek names of additional persons likely to be interested in the program. The program announcement was circulated widely, and CRG staff spent extra effort commenting on ideas presented in letters of inquiry. But during the first year, only thirty-four proposals were received, of which seven were approved. Most of the proposals involved only descriptive studies, and CRG asked for a revision of the announcement to reflect the emphasis on development of epidemiologic methods. But concerns remained within CRG and AID about appropriate focus in this research area.

ADVISORY GROUP ON REA METHODS

Following the January 1984 CRG meeting, two consultants[1] were engaged to examine the proposals that had been received in this area, conduct literature searches and interviews, and prepare papers to assist CRG to change the focus of the program and identify the constraints to obtaining viable proposals from developing country investigators. These papers were presented to an advisory group for comment on May 11, 1984. The group was asked to consider four options:

- Alter the process of soliciting proposals and providing proposal preparation assistance in this one area by emphasizing or requiring linkages with U.S. institutions.
- Alter the announcement to express the program goals more clearly without modifying them.
- Change the major goal of the program area, removing the emphasis on methods, and fund epidemiologic surveys in one or two health areas.
- Phase out the REA area if other donors are covering it sufficiently or if there is no investigator interest or capability.

The consultants found few references to REA in the scientific literature. One of them went to a meeting of the International Clinical Epidemiology Network meeting in Thailand and met many potential grantees. In a manner reminiscent of the BNF organizational meeting, she was exposed to the argument that every country had its own health survey priorities that were not being met, and that BOSTID should simply fund those, instead of seeking to divert researchers to develop innovative methodologies. Both consultants recommended abandoning the original REA objectives to some degree.

But the advisory group of experts did not agree. They felt that, basically, the goal of the REA project was valid and should remain unchanged. They indicated that the projects funded to date were consistent with project guidelines, and the others were rejected for appropriate reasons. They asked that the announcement be rewritten to provide better guidance to developing country researchers about the types of proposals sought, with more examples given. They suggested three themes for illustration:

- Develop better means of identifying high risk individuals for program interventions.
- Determine the relative contribution of selected important diseases to the burden of illness of a given population.
- Assess the effectiveness of a health program.

Techniques should be faster, simpler, or cheaper than those currently in use, and be reasonably accurate. The proposal should demonstrate how decision making and resource allocation will be influenced, and should justify the selected subject as an important health problem.

Curiously, the pattern that later evolved and brought concrete meaning to the REA program was not suggested by the advisory group but was developed in practice by CRG. This was the validation of a rapid or simpler methodology against a "gold standard" in the form of a survey carried out by traditional, accepted methods. In this way, several REA projects were linked to other larger, ongoing, or recently completed studies funded by other agencies. Had this suggestion been included in the early announcements it might have generated additional proposals of this type, and it would

also have clarified in concept that what was desired was the validation of REA techniques as applied to a given problem. The phrase "development" of REA techniques did not seem to convey the same meaning. As it was, REA had the highest proposal rejection rate of all the project areas. In an attempt to provide continuing theoretical guidance to the area, BOSTID contracted with Johns Hopkins University for the part-time services of Gordon Smith, an assistant professor of epidemiology with special interest in REA, to work with grantees and new applicants and to write articles promoting the idea of REA.

COORDINATION MEETINGS

The first coordination meeting was held in Washington, D.C., September 23-27, 1985. By then there were ten grantees. Their projects could be divided into two groups: 1) identification of individuals and groups at high risk, and 2) evaluation of program performance and impact on morbidity, mortality, and nutrition. Experts were invited to describe the state of the field and their own work as it related to the two topics. Sandra Huffman of Johns Hopkins University and Alfred Zerfas of the University of California, Los Angeles, spoke on risk factors, and Richard Cash of Harvard, John Briscoe of the World Bank, Max Woodbury of Duke University, and William Taylor of CDC spoke on program evaluation. On the second day, Harris Pastides of the University of Massachusetts led a workshop and demonstration on the use of microcomputers for epidemiologic investigations. He distributed copies of public domain software and advised grantees on purchase of microcomputers and software for their own projects. The grantees asked that a special workshop on microcomputer applications be offered to the data processing personnel of each project. In fact, similar workshops were held for the ARI grantees, but such an activity was never included in the REA program.

By the second coordination meeting, held in Lima, Peru, March 30-April 3, 1987, there were seventeen grantees, and the focus of the program was a bit more clear. This was demonstrated by the new subtopics into which the project reports were organized: sampling methods, screening for risk factors, surrogate measures of health status, and design of case-control studies. Case-control studies proved to be an important tool in REA and, although the concept was not new, they were being used and validated in novel applications in the developing countries. Two grants were dedicated to lot quality assurance sampling (LQAS) and BOSTID had commissioned a monograph on the subject; this proved to be one of the most exciting developments in the REA program. LQAS will be discussed in more detail below.

A highlight of the meeting was a workshop on data entry and editing, linkage of files, and data analysis, led by Beatrice Selwyn of the University

of Texas. A laptop computer, new on the market at the time, was demonstrated, and several were ordered by grantees for their projects. Grantees agreed that computers are very useful in the field for verification and preliminary analysis of data; direct entry of data into the computer should be avoided, however, unless a hard copy could immediately be generated for backup.

At this meeting the grantees decided to submit papers as a group to form a special issue of an international journal, and selected the *International Journal of Epidemiology* as an appropriate choice. Gordon Smith agreed to write an introductory article describing REA and the BOSTID program, and all grantees decided to submit papers first to BOSTID for peer review before submitting them to the journal, to maximize the number of articles the journal would accept.

The grantees devoted a half-day session to the problem of how to influence health ministries and policymakers. They found a commonality of problems, from Brazil and Haiti to Bangladesh and the Philippines, with politics playing as important a role as science on the impact and visibility of their work.

The central event of the week was the visit to the field sites and the computing center of the Institute of Nutritional Research, hosted by Claudio Lanata. The field station at Campo Grande is located in a squatter settlement on the outskirts of Lima. All homes in the community were constructed illegally, but the government provides electricity and health service, while water and bus service are provided by other "illegal" enterprises. The institute has carried out a cluster survey on the causes of chronic diarrhea and used the results to validate in this community the new LQAS method. Other participants were as interested in seeing the structure of the community and the health service as in the results of the project. The institute also set up a computer center to serve the project in another part of Lima. For the other grantees, it was instructive to see the highly imaginative and innovative use of linked microcomputers in the center and in the field. Computers are installed in the vans used by field-workers in remote areas, powered by the vehicle battery; data are entered by the drivers. In addition to allowing efficient recording and processing of data, it allows the field teams to make preliminary analyses to check the validity of the data. Early results thus obtained are shared with the villagers and strengthens cooperation between the communities and the research team.

The third meeting was held in July 1988 in Kingston, Jamaica, after it was already clear that the BOSTID Research Program would no longer award grants. This was of particular concern to the REA researchers because there was no other obvious source of support for this new area, and AID had shown little interest in this BOSTID program. It had taken nine months to secure AID concurrence to begin the REA program, and AID

staff frequently spoke against REA proposals at CRG meetings, arguing that the proposals were not "innovative." In any case, the meeting produced lively discussion because many grantees had finished their projects and were eager to present their results. Much of the meeting was devoted to discussion of the papers for the special edition of the *International Journal of Epidemiology* dedicated to REA and the papers of the BOSTID grantees.

RESEARCH RESULTS

Significant progress was made by the grantees in two main areas. One was the development of survey methods using low sample sizes, principally the case-control study method and the LQAS method. Low sample size, if sufficient accuracy is maintained, means reductions in cost, in size of survey staff, and, perhaps most important, in the time required before survey results can be announced. The second area was to determine risk factors or surrogate indexes for a given condition or disease, which enables agencies to identify those most likely to be sufferers and to monitor effectively the health status of a community.

The search for mathematical techniques that enable sample sizes to be reduced without significant loss of accuracy is not a new idea, of course, and many innovative techniques were developed during the smallpox eradication campaign and the World Health Organization Expanded Program on Immunization (EPI). Yet these techniques are not valid for all situations, and even the EPI cluster-sampling method can be difficult to apply accurately in some situations. One newer technique is the case-control method, which was developed for study of chronic diseases, but which may have advantages for other conditions as well. In this method, patients are found who display the condition under study. Then, for each case, a number of controls is selected, generally from the same population as the case, and matched for whichever variables are to be controlled. The method of selecting the controls is crucial, and the projects that sought to validate the case-control method under given circumstances were, in effect, testing the system for selection of controls and analysis of data, since the mathematics underlying the method are universally accepted. The question of whether the BOSTID REA projects were studying the practical application of an established technique in a developing country context or redundantly verifying the mathematical formalism underlying the technique confused reviewers and CRG members on more than one occasion.

Four projects applied the case-control methodology to new situations. In Haiti, Antoine Augustin of the Child Health Institute wanted to determine why some families did not use the free, government-supported health services. If the nonusers turned out to be from the low-income, poor-health segment of the population spectrum, it would pay for the government to

make an effort to recruit them. On the other hand, if these were the wealthier people who probably patronize private physicians, nothing should be done. As in most of the REA studies, it was the result of the study that was of greatest interest to the investigator; validation of the new methodologies was carried out principally because BOSTID required it, and it served to confirm the survey conclusion. In fact, this survey did provide a new perspective on the nonusers of the health services and their attitudes toward disease and treatment, while demonstrating the validity of the case-control method using vaccination record as an objective parameter of health-service use.

Two case-control studies in the Philippines approached the problem of validating the methodology directly. Jane Baltazar of the College of Public Health, University of the Philippines, took advantage of an ongoing prospective study by a group from the University of North Carolina. It concerned the effects of improved environmental sanitation on diarrheal disease incidence in the city of Cebu. Using this long-term traditional study as the "gold standard," she repeated the surveys using case-control methodology. Unfortunately, the advantage of the case-control method was illustrated in the fate of the project: the case-control study was completed in a matter of months during 1985; the results of the prospective study were not available until late 1989. Corazon Apolinar-Ngelangel of the University of the Philippines College of Medicine approached the validation problem in a different way. Her study sought to determine why so many Philippine women seek medical help for cases of breast cancer very late compared with other countries, and the methodological objective was to evaluate different ways of selecting the controls. The conventional way is to seek out neighbors and friends of the case as controls; the innovation proposed, which would save considerable time and expense and avoid some other technical problems if shown to be valid, is to use hospital visitors of other patients in the ward. Ngelangel aimed to show that the case-control methodology yielded the same results for two different ways of selecting controls.

The fourth case-control study, which is somewhat controversial, explores other technical problems with the methodology. Catterine Ferreccio of the Ministry of Health in Chile is evaluating the efficiency of an anti-typhoid oral vaccine that was distributed in 1984. But the vaccination campaign was universal, and for each case of typhoid, where the patient may or may not have received the full dose of vaccine, it is impossible to find a matched control with the same vaccination history. This project reexamines the mathematical basis for case-control studies to find the correct application for vaccine efficacy studies.

Arguably, the most important contribution of the BOSTID REA program was the set of LQAS studies. This is a small-sample-size technique bor-

rowed from industrial quality control. The problem is to design a quality-control sampling system that can "pass" or "reject" a "lot" without testing a large number of items in the lot. The LQAS solution requires very small samples, of order 12-25, independent of lot size, but requires the sample and the pass-reject criteria to be selected in a careful way that is highly sensitive to the desired level of reliability (that is, tolerable probabilities of rejecting a "good" lot or passing a "defective" one). Change "lot" to "health region" and "good/defective" to "vaccinated/unvaccinated," and the LQAS method can be applied to the evaluation of vaccination coverage by a health service, for example.

Two projects applied LQAS to epidemiologic questions. The project of Claudio Lanata of the Institute of Nutritional Research in Peru was the first application of the technique in a developing country setting, and he worked closely with the developers of the methodology, George Stroh of the Centers for Disease Control and Stanley Lemashow of the University of Massachusetts. The LQAS method was applied to estimate the health status and health service utilization in a peri-urban region of Lima, where it was compared for accuracy and cost-effectiveness to a cluster survey already completed. It was then used to evaluate a massive immunization campaign of the Ministry of Health near Lima and also in a remote mountain area. The conclusions were surprising and appeared to call into question the validity of the method: the vaccination campaign resulted in no significant increase in immunization coverage! However, a check with the health services revealed that in fact there had been severe shortages of vaccine combined with overvaccination of older children. The Ministry of Health was informed and became interested in applying the technique on a routine basis. CRG gave unusual support to this project by commissioning a handbook on use of LQAS by Stroh and Lemashow,[2] and by granting a follow-up award to Lanata to prepare a manual and training program for use by the Peruvian Ministry of Health. The handbook was widely distributed by BOSTID, but the additional effort to assist the health ministry was of little avail when the Institute for Nutritional Research ran into administrative and economic difficulties, in common with the rest of the country.

The other LQAS project was undertaken by Luis Rosero of the Institute for Health Studies in Costa Rica. This project was born under an institutional cloud, and it never emerged completely. The proposal was originally submitted to BOSTID by a research fellow at a U. S. institution who sought to incorporate a BOSTID-funded LQAS study in a larger project supported by PAHO. During the site visit, staff discovered that Rosero had signed on with PAHO because he was under the misapprehension that only Americans could apply for BOSTID funds. However, staff were able to help him reformulate his proposal, so it was supported as a separate project, with the American as an unpaid consultant. Rosero's idea was imaginative: to

apply LQAS as a sampling scheme within the files of the health units to identify those whose service or coverage is defective. Finally, however, Rosero left the country with the project uncompleted, and the U. S. researcher published some of the data under his own name, thanking BOSTID for support while failing to mention either Rosero or his colleagues.

The other research direction, in addition to low-sample-size surveys, was the identification and validation of risk factors for illness and of surrogate indexes to measure the state of health of a given population. Twelve grantees were involved in this effort. Three of them collaborated directly in the same protocol, coordinated with a group from Columbia University. The aim was to validate a simple questionnaire (Ten Questions, or TQ) to assess the prevalence of childhood disability disorders in three countries: Bangladesh, Jamaica, and Pakistan. The questionnaires were administered in rural communities by local health workers, and the instrument was validated by follow-up examinations by physicians. The Bangladesh project later was extended so the instrument could be applied in the wake of the serious flooding of early 1989 to determine the fate of disabled children relative to normal children. Only the Jamaican project is complete, and it is characterized by unexpectedly low specificity (many false positives). Final conclusions await the reports of the other two centers and the analysis by the Columbia researchers.

The use of local health workers is the subject of a project of the Aravind Eye Institute in India, headed by V. K. Venkataswami. There, local, nonprofessional health workers are trained to screen for cataracts, and their accuracy is confirmed independently by ophthalmologists. This system can be used both for epidemiologic surveys and referral of patients for surgery.

In Guatemala, schoolteachers were trained to carry out a different survey. Hernan Delgado and his colleagues at INCAP developed, and validated through the use of community surveys, a system for evaluating the nutritional status of a community, from infants to the elderly, using the height distribution of schoolchildren in a single grade as indicator. This survey has now been carried out on a national level and will soon be adopted on a regional basis. The survey, carried out in 1986, revealed that malnutrition was a serious problem in five departments and 100 municipalities in the country, and priority action was called for.

The height of schoolchildren in the Guatemalan project is used as a surrogate index for community malnutrition (not necessarily indicating malnutrition in the individual schoolchild). Another surrogate index was identified in a project at the Federal University of Pernambuco in Brazil, led by Hernando Flores. He looked at the level of retinol in the livers of children who died of various causes and concluded that the state of vitamin A deficiency in the population as a whole could be monitored. The validation was done through a survey of the live population. He was also able to demon-

strate the value of a massive dose of vitamin A supplement to deficient cases. A vitamin A program based on this study was implemented in a neighboring city with government support.

One project was funded principally because the epidemiology of the disease under observation had not been studied, and it presented some unusual difficulties peculiar to the developing country context. Porcine cysticercosis is caused by direct consumption of food contaminated with pig feces containing the larvae of the tapeworm, *Taenia solium*. It is difficult to secure the cooperation of those at risk in the community, in part because of the presumption of unhygienic conditions implied by contracting the disease,[3] and in part because raising pigs domestically and marketing infected animals is illegal in the communities studied by Elsa Sarti and her associates. The problems are compounded by the difficulty of diagnosing the infection both in man and animal; cysticercosis in man is often mistaken for epilepsy. Assistance on diagnosis was provided by a group at CDC in Atlanta, who had developed an ELISA-based test for the encysted larvae, and the completed project will create a national surveillance and control system that would be applicable to other developing countries with endemic cysticercosis.

Two projects explored the use of specific, low-cost clinical tests for screening purposes and prevalence estimates. Wilma Freire looked at the use of hemoglobin as a predictor of response to iron therapy among anemic pregnant women in the highlands of Ecuador, and found it a useful measure. It was proposed that the method be applied in a nationwide survey to see whether an intervention program was necessary. To our knowledge this has not happened; Freire, on the other hand, was given an important promotion following her capable performance on the BOSTID project.

The other project dealing with a clinical test explored the use of capillary blood surface antigen of hepatitis B virus (HBaAg) as a surrogate marker for the "e" antigen (HBeAg) for detection of HB infection among pregnant women in the Philippines. The importance of this study by Ernesto Domingo and his associates is that "positive" pregnant women are at risk of passing the hepatitis B infection to their newborn babies, who could be vaccinated promptly; further, the standard for detection, the "e" antigen, is more costly to detect. This successful project demonstrated that the HBsAg was a highly sensitive and specific, as well as cost-effective, indicator of infection of pregnant women. Moreover, the test on capillary blood dried on filter paper could be performed by trained village health workers at an accuracy comparable with that of medical technicians.

Finally, three grantees in Chile, Egypt, and Guatemala were concerned with identifying risk factors for low birthweight and infant malnutrition. In the Egyptian project, Osman Galal used village midwives, or dayas, to make the anthropometric measurements. There were two obstacles to overcome: first, the dayas were illiterate and could neither read nor record instrument

readings, and second, parents are traditionally afraid of the "evil eye" and are loath to let strangers handle the newborn. Both were overcome by use of religious symbols and special color-coded instruments developed by the Program for Appropriate Technology in Health (PATH), and incidence of low birthweight in Egypt was measured in a cost-effective way.

Identification of reliable risk factors is of considerable importance in developing countries that have limited resources for interventions and therefore must choose the target populations carefully. Francisco Mardones of Chile reduced a large number of candidate variables to a few using multivariate analysis. He found that the best indicators of infant malnutrition and failure to grow were the quality and type of floor in the home, as a socioeconomic measure, and a new quality they named "maternal competence," which was scored from observation of the behavior of the mother in the clinic. Edgar Kestler in Guatemala developed a detailed data collection and computerized analysis package that could be applied at the local level to anticipate women at risk of having low birthweight infants. Since the study was cosponsored by the Guatemala Social Security Institute, there was good reason to hope that the system would be put into practice directly.

NOTES

1. Lynne Galler, Harvard University, and Virginia Hight Laukaran, the Population Council, New York.
2. Lemashow, Stanley, and George Stroh, Jr. *Sampling Techniques for Evaluating Health Parameters in Developing Countries.* Board on Science and Technology for International Development. Washington, D.C.: National Academy Press. 1988.
3. However, Gilbert Otto, retired professor of parasitology who served with BOSTID as a consultant on mosquito vector research, recalled that in a long career he had seen only two cases of porcine cysticercosis—both Johns Hopkins University professors!

Diagnosis and Epidemiology of Acute Respiratory Infection in Children

Acute Respiratory Infection (ARI) is one of the two leading causes of child mortality in the world. The other is diarrheal disease, for which there is a treatment that is effective in many cases—oral rehydration therapy. There is no similar "magic bullet" for ARI, and it has been somewhat more difficult to develop effective treatments because of the difficulty of establishing the causal agent or agents for specific cases. In fact, the incidence in developing countries is about the same as in advanced countries, but the mortality rate is twenty times higher. (The rate corresponds to the death rate from ARI in the United States about eighty years ago.) The number of deaths is significant: five million a year, which is equivalent to a Boeing 747 full of children crashing with no survivors every half hour, every day, all year. Why do the developing country children die when U.S. children don't? It was not known whether different pathogens were involved (ARI in the United States is generally caused by viruses), whether malnutrition plays a major role, or even what is the specific cause of death. The difficulty of the problem is compounded by the fact that developing country children have other infectious diseases, may be malnourished, and may not be brought to the clinic until it is too late.

Few epidemiologic and etiologic studies had been carried out in developing countries, and the findings were often inconsistent. CRG was further influenced by the argument that on the basis of studies in Papua New Guinea and the Philippines, the World Health Organization was considering recommending antibiotic treatment for all children with ARI. Many felt that this recommendation was unjustified and likely to exacerbate the overuse of antibiotics, which leads to evolution of resistant strains of bacteria; however, once a standard treatment is prescribed by WHO, an etiologic study like the one BOSTID contemplated might be considered unethical. (Ulti-

mately, antibiotics were provided in BOSTID studies after specimens were taken, so this was never an issue.) CRG was moved to proceed promptly and include researchers in Papua New Guinea and the Philippines among the BOSTID grantees.

CRG set the following goals for the area:

- Adapt and develop rapid diagnostic methods appropriate for clinical surveillance in developing country settings.
- Identify the viral and bacterial pathogens most frequently responsible for severe cases of ARI.
- Identify the clinical syndromes associated with particular respiratory infections and establish their incidence and severity in different socioeconomic and geographic populations.
- Assess the effectiveness of treatment for ARI among different clinic populations.

ORGANIZATIONAL MEETING

The organizational meeting for this program area was held at the University of North Carolina in connection with a workshop held during May 18-20, 1983, and cosponsored by the Edna McConnell Clark Foundation and the Pan American Health Organization. In a sense, this meeting most closely approximated the ideal organizational meeting in that seven of the twelve institutions that ultimately would receive grants were represented and participated in the design of the program. The proceedings of the workshop were published in *Pediatric Research.*[1]

The organization of the BOSTID program fell on the third day of the symposium, after extensive review of the work that had been undertaken in developing countries and discussion of the most critical problems not yet resolved. It was recognized that clinical studies in developing countries to correlate causative pathogens with syndromes had rarely been undertaken, and that very little funding had been available for etiologic studies of ARI. The participants thought the most important task for BOSTID was to elucidate the etiology and epidemiology of ARI in children in both hospital- and community-based studies. They felt that the studies should be strongly coordinated to ensure compatibility and comparability of results obtained from different populations. They classified the following issues as most important:

- Assessment of the incidence, severity, and fatality rates of infections caused by specific pathogens in different populations;
- Description of the clinical and radiological features of ARI that are associated with specific pathogens; and
- Identification of important risk factors for infection by specific pathogens.

It was also strongly suggested that to qualify for funding, the proposed research must include identification of bacteria and viruses, and must not simply examine risk factors for undiagnosed acute respiratory disease. This was an important recommendation because it requires a minimum level of laboratory capability to make those diagnoses. When the proposal was adopted by CRG, this meant that many research teams were not eligible because they could not meet that criterion. It would be a challenge to reach the poorest populations in settings that lack the minimal virological and bacteriological capability.

The issue came to a head at a meeting of the CRG Executive Committee in February 1984, which rejected several proposals to study high-mortality populations. Moreover, AID representatives were concerned about a possible inconsistency between requiring coordinated studies following a common protocol and Congress's dedication of the research funds to "innovative" research. The committee asked staff to convene a meeting of experts to advise on these issues and on the overall question of whether these studies would finally be able to establish whether bacteria or viruses are more important for ARI in developing countries.

The advisory group meeting took place on May 4, 1984.[2] The group noted that the organizational meeting had emphasized the importance of collecting a comparable body of data on ARI in different populations, and the announcement was almost prescriptive in describing the data to be taken according to a certain methodology. Most applicants who had the capability were complying with that guideline. The group agreed that, while these individual grants may not be characterized by U.S. scientists as "innovative," the studies are technically challenging and may be considered innovative in the context of developing countries. Most of the participants did not consider the announcement unduly restrictive, considering the goals of the program to generate a coordinated group of studies whose results might be combined to provide important information for designing intervention and prevention programs. They went further and recommended that grantees adopt a common record of clinical symptoms, a common classification of clinical syndromes, and a common record of treatment and outcome, and urged that this recommendation be brought before the grantees at the forthcoming coordination meeting.

The question of carrying out research in high-mortality countries was set aside when the staff reported that negotiations were under way with institutions in Thailand, Bangladesh, Pakistan, Egypt, Peru, and Colombia. Ultimately, grants were awarded to four of these six, as well as Nigeria, Kenya, and Papua New Guinea, where high-mortality populations were studied.[3]

Whether these studies would be sufficient to determine the pathogens responsible for severe ARI was a more difficult question. The sample sizes were too small for statistical certainty, but identification of trends and ma-

ACUTE RESPIRATORY INFECTIONS IN CHILDREN GRANTEES

M. Weissenbacher	University of Buenos Aires, Argentina. *Etiology of Lower ARI: Relation to Clinical Features and Environmental Variables.*
M. Rahman	International Center for Diarrhoeal Disease Research, Bangladesh. *Causes of Acute Lower Respiratory Tract Infections in Hospitalized Children.*
F. Sutmoller	Oswaldo Cruz Foundation, Brazil. *The Etiology and Risk Factors of ARI in a Favela Population.*
I. Borrero	Universidad del Valle, Colombia. *An Etiologic, Epidemiologic, and Clinical Study of ARI.*
Jose Cruz	Institute of Nutrition of Central America and Panama. *Epidemiology and Etiology of ARI in a Low-Income Urban Population: Identification of Nutritional and Other Risk Factors.*
T. Tupasi	Tropical Disease Research Foundation, Philippines. *Etiology of Childhood ARI.*
A. Ghafoor	National Institute of Health, Pakistan. *Determination of the Etiology of ARI in Children Attending Outpatient Clinics.*
M. Grandien	National Bacteriology Laboratory, Sweden. *Quality Control of Diagnostic Reagents and Reference Laboratory Services for BOSTID Grantees.*
S. Suwanjutha	Mahidol University, Thailand. *Etiology and Development of ARI in an Urban Community and Hospital.*
M. Peluffo	Ministry of Public Health, Uruguay. *Identification of Etiology and Risk Factors of Childhood ARI in the Community.*
M. Alpers	Institute of Medical Research, Papua New Guinea. *Viral and Bacterial Pathogens Responsible for ARI in Young Children.*
C. Oyejide *W. Aderele*	University of Ibadan, Nigeria. *Etiology of ARI in Low Income Urban Children: Hospital and Community Studies.*
E. Wafula	University of Nairobi, Kenya. *Clinical and Familial Study of ARI in a Rural Area.*

jor differences among populations was possible. A few members of the group, including Nobelist Frederick Robbins, felt that the number of studies already approved at that time (eight) could generate enough data to establish the major pathogens, and no further grants need be awarded, unless they addressed areas specifically not covered.

FIRST COORDINATION MEETING

The first coordination meeting of grantees and U.S. advisors took place June 26-29, 1984. Each grantee outlined the objectives for the project and plan of work, and visitors from other agencies described their ongoing work on ARI. The meeting then turned to the problem of compatibility of data from different research teams. Participants broke into three working groups to address problems associated with 1) hospital-based studies, 2) community-based studies, and 3) sampling and laboratory techniques for all studies. Each group prepared recommendations for all grantees to adopt, and reported back to the plenary for agreement.

The first two working groups prepared questionnaires for hospital and community studies, with core and optional questions to be asked of patients and controls in all studies. Grantees would be free to add questions but not to omit or change the core questions. To ensure compatibility of data, the participants discussed selection of children, design of studies, and use of standard forms for recording data—one for hospital-based studies and another for community-based studies. Participants agreed on the importance of deciding early in the program how the analysis will be done so data will be collected and coded correctly. They requested advice from BOSTID for all grantees in the selection of computers and software packages for these studies.

The third group reached agreement on the best specimens for detecting different pathogens, when to take blood cultures, how to do viral cell cultures and rapid viral diagnoses by immunofluorescence, and how to do bacterial culture and antigen detection. This group identified the pathogens to be sought in all projects:

- Viruses
  - respiratory syncytial
  - influenza A and B
  - parainfluenza 1, 2, and 3
  - adenovirus
- Bacteria
  - *Streptococcus pneumonia*
  - *Haemophilus influenzae*
  - Group A *Streptococcus*

They also recommended the types of specimen required for the diagnoses and the specific cell lines and media to be used for isolation of these agents. They agreed on the need for a systematic and central source of high quality reagents and cell lines. And finally they requested that a laboratory manual containing all pertinent technical details be prepared. The group also suggested that once the laboratory manual was ready, the laboratory personnel from each project should meet together for training in the techniques.

There was also a discussion of the requirements of the National Academy of Sciences Committee to Review Human Studies for compliance with NAS guidelines, especially regarding the documentation of informed consent. The meeting ended with a trip to Children's Hospital in Washington, D.C., to observe the facilities for diagnosis of respiratory pathogens. In retrospect, the recommendations made by this meeting formed the core of the BOSTID ARI program and set up the regime for the disciplined adherence to agreed protocols that characterized the program.

LABORATORY MANUALS AND PROCEDURES

Two laboratory manuals were prepared by the BOSTID ARI program. A first draft of *Laboratory Procedures for Diagnosis of Viral Respiratory Tract Infections* was prepared by Lou Potash of Flow Laboratories in Virginia. It was reviewed by an advisory panel on diagnosis of respiratory viruses,[4] which met on December 17, 1984. Members of this panel revised and expanded all sections, and John Maassab and Mark Steinhoff at the University of Michigan coordinated the final draft. It was designed for use by virologists and technicians who have training and experience in virology but not necessarily with the respiratory viruses. The other manual, *Procedures for Diagnosis of Respiratory Bacterial Pathogens*, was begun with a staff review of the *World Health Organization Manual on Bacteriology of Respiratory Pathogens*, 1984. Sections from this manual were adapted for use by the BOSTID grantees by a working group that met December 18, 1984,[5] with further contributions by Dan Granoff and Patricia Charache. Each manual contains a complete set of laboratory procedures suitable for adoption by the grantees. Additional laboratory procedures and problems were added as needed. They also provided for verification of the laboratory data by reference laboratories. Laboratories at the Washington University in St. Louis, the Johns Hopkins University, the Boston Children's Hospital, and the Centers for Disease Control agreed to verify and type various pathogens, and this was a key part of the procedure.

The manuals were prepared in draft to serve as the basis for training workshops in viral and bacterial diagnoses and to permit the laboratory workers from the projects to revise and agree to the protocols as they worked through them together. The workshop on viral diagnoses was led by John

Maassab in Ann Arbor, Michigan, for two weeks in May 1985, and the one on bacterial diagnoses was directed by Patricia Charache at Johns Hopkins University a month later. For the laboratory participants, it was a valuable experience to meet their counterparts in the other projects and to share some of the benefits of international cooperation that the principal investigators enjoyed. From the recommendations of the workshops and final review of the panel members came the completed manuals, which were distributed to all grantees and, on request, to applicants for ARI grants.

DATA MANAGEMENT

An advisory meeting on epidemiological design and selection of microcomputers and software was held January 7-8, 1985.[6] The participants offered suggestions on study design, interviewing, data coding, entry, monitoring, and analysis. They then turned to the question of specific recommendations of hardware configurations and software packages, emphasizing use of microcomputers, with manufacturers selected mainly for availability of local service. They recommended that a manual be prepared on the design of community- and hospital-based studies and data collection and management, and that this be followed up with a workshop. C. Oyejide agreed to prepare a draft manual in time for the next coordination meeting.

The second coordination meeting was held July 22-26, 1985, and it was dedicated mainly to challenges in epidemiology and data management of the ARI projects. Following the discussion of research status, successes, and problems, Oyejide presented her manual as an example for each group, which should adapt it to suit its own studies, staff, and facilities. The meeting subsequently divided into discussion groups, with one group working on study design, population sampling, community organizing, and planning. The other group addressed questionnaire design, recruitment and training of field staff, and meetings with community leaders.

Data management was also treated by two distinct groups, one for hospital-based and one for community-based studies. "Dummy tables" were prepared for data presentation, both for scientific papers and presentations and also for presentations at future coordination meetings, to standardize definitions and facilitate comparisons. The meeting ended with a visit to the Microbiology Laboratories of the Johns Hopkins University in Baltimore.

In January 1986, a data management workshop was held at the Asian Institute of Technology in Bangkok, Thailand. It was led by Harris Pastides of the University of Massachusetts and Beatrice Selwyn of the University of Texas; Pastides prepared a manual for use at the workshop, and BOSTID purchased and distributed the recommended software packages for use by all groups.

A follow-up workshop was held for the same group at the fourth coordi-

nation meeting in June 1987 at the University of Maryland in College Park. This time the emphasis was on data analysis and how to use the computer to test hypotheses. Grantees brought examples of their own data on diskettes, and worked together with the help of Selwyn and Pastides to begin the analysis of the large and complex data sets.

PATHOGENESIS OF ARI

The U.S. community of researchers with interests in ARI had taken an active and participatory interest in the ARI program, beginning with the organizational meeting in North Carolina and including a large volume of proposal reviews, advisory meetings, and visits to grantees. In late 1986, Floyd Denny of the University of North Carolina, Stephen Berman of the University of Colorado, and Judith Bale of BOSTID convened a meeting to look at whether the BOSTID projects would adequately answer the basic question relating to pathogenesis: why do the children die? A date was chosen so that the pathogenesis meeting would immediately precede a coordination meeting of principal investigators, so that grantees might be represented at the pathogenesis meeting and the conclusions of the meeting could be shared with them. The group met December 4-5, 1986.[7]

The most probable scenario affecting children with ARI in developing countries is initial infection by one of the common respiratory viruses followed by secondary bacterial infection. Children in developing countries seem to be more susceptible than Western children to bacterial infection, which can cause severe disease and death. Contributing factors are likely to be compromised immune systems, malnutrition, and other infections. The exact causes of death are also in question, although both respiratory failure and shock due to septicemia are common. Unfortunately, the research on this topic is frequently hampered by the difficulty in most countries of obtaining permission for autopsies.

LATER COORDINATION MEETINGS

The Third Coordination Meeting in December 1986 began with reports from the projects and a report of the pathogenesis meeting, but most of the time was spent with small groups holding discussions on topics such as diagnosis of viral and bacterial pathogens, data management and analysis, clinical aspects, and coordination and management of ARI teams. The decisions were summarized in a ten-page circular for distribution and discussion with the key researchers in each project. For example, where the principal investigator was a virologist, the information concerning bacteriology, epidemiology, data analysis, and clinical aspects had to be transmitted to the appropriate researcher for each group.

The Fourth Coordination Meeting in June 1987 began with a data analy-

sis workshop. The main topic on the agenda was the organization of data and planning for publication of research results. An international symposium was planned for announcement of the results a year later, and the grantees began the preparation of their papers. They also decided to publish papers from all research groups in one place, aiming for a special edition of an international journal. (The papers were later published by *Reviews of Infectious Diseases*.)

SITE VISITS AND TRAINING

It was clear from the outset that most grantees would require a good deal of assistance from international collaborators. All the projects were highly multidisciplinary; some elements were weaker and others stronger in each center. Consultants would be required for laboratory procedures, epidemiology, and data management and analysis, and reference laboratory services would be necessary to confirm rapid diagnoses and type certain pathogens. Since collaboration and conformity to agreed protocols were required, it was decided that links would be established based on the discipline. For example, instead of having one collaborating researcher or institution in the United States work with each of the grantees, advisors in each field—such as virology, bacteriology, data management—would visit a number of the grantees, repeatedly where possible. Thus, epidemiologists Pastides and Selwyn together worked with principal investigators and analysts at the data management and analysis workshops, and followed up with site visits to projects in all regions. Charache participated in both the virology and bacteriology workshops and followed up with researchers in Latin America, Asia, and Africa. Arnold Monto visited Floyd Denny and Alan Kendal who also assisted in Africa. Kenneth McIntosh, Dan Granoff, and Mark Steinhoff assisted researchers in Asia. Monto assisted researchers in all regions. When extended visits were required to solve major laboratory problems, technical staff from Boston Children's Hospital, Johns Hopkins, and Washington University spent one to three weeks in the grantees' laboratories. Assistance with clinical protocols was provided by Berman in Asia and Latin America. The ARI program was particularly demanding of expert assistance to grantees, and the success of the ARI program owes much to the dedication and voluntary efforts of the advisors.

SYMPOSIUM ON ETIOLOGY AND EPIDEMIOLOGY OF ACUTE RESPIRATORY INFECTIONS IN YOUNG CHILDREN

The symposium was held at the National Research Council's Beckman Center in Irvine, California, October 20-22, 1988. More than thirty papers were presented by the several members of each research team who were present. Advisors and representatives of AID and WHO also participated.

Apart from the grantees' papers, there were overview presentations from the advisors, papers from other developing country and ARI researchers, and reports from three discussion groups with recommendations for future action. The papers and summaries of the discussion were published in the November/December supplement of the *Reviews of Infectious Diseases.*[8]

RESEARCH RESULTS

The primary motivation for the ARI program was to determine the causative agents in developing countries, and ascertain why the outcomes appeared to be so different from those in the industrialized countries. In fact, the studies show the etiology of ARI in young children to be remarkably similar in different areas of the developing world and in industrialized populations. A respiratory pathogen was identified in about half the cases observed in the BOSTID studies, which is roughly the same rate of identification in studies conducted in industrialized countries. The failure to diagnose half the cases may be attributed to lack of sensitivity of diagnostic methods, difficulties in diagnosis caused by previous antibiotic treatment, admission to the hospital late in the course of the disease, or other agents that were not specifically sought.

Bacterial isolations were made from blood culture in 20-30 percent of the specimens examined. This rate is also similar to that observed in Western studies. Isolation rates would have been higher from pleural fluid but these specimens were frequently unavailable. Lung aspirates, which are the standard for bacterial diagnoses, were not taken in the BOSTID studies because investigators considered the procedure to place the child at an unjustified risk.

Streptococcus pneumoniae is the major cause of severe ARI in developing countries. This was established in previous diagnoses of lung aspirates from severely ill children and was observed again in these BOSTID studies. *Haemophilus influenzae* was found to be the second major bacterial cause of ARI and *H. influenzae* type b is the strain responsible for most of these. While studies in industrialized countries report that non-encapsulated *H. influenzae* rarely causes invasive disease in healthy children, in developing countries such as Pakistan and Papua New Guinea, these pathogens were found responsible for epidemics of bacteremic pneumonia. That this organism is invasive in this setting has not been established.

Bacterial diagnosis is made more difficult in many Third World countries because of the unlimited availability of antibiotics. Antibiotics are obtainable without prescription from entrepreneurs who have no medical or pharmaceutical training and who sell any antibiotics they happen to have. As a result, most of the children admitted to hospital studies have received at least one and sometimes several antibiotics.

RSV was consistently the most significant viral pathogen causing ARI in the populations investigated. While not generally life threatening in industrialized populations, this virus is associated with serious and life-threatening ARI in developing country children. The order of importance of other viruses varied with study sites, but parainfluenza 1, 2, and 3, influenza A and B, and adenovirus were all responsible for serious illnesses, although not as consistently nor frequently observed as RSV.

One persistent problem was the difficulty of diagnosing severe ARI. There is no commonly accepted definition of clinical syndromes, no clinical or microbiological means of routinely distinguishing between bacterial and viral pneumonia for a timely intervention, and no simple, effective therapy that can be prescribed and carried out by mothers and health workers. Since definitions for clinical syndromes of ARI vary significantly in different hospitals, BOSTID studies focused on signs and symptoms as well as radiology for each case. Management of ARI cases was generally based on the recommendations of WHO, although pediatricians varied as to details. BOSTID requirements were limited to recording the treatment and outcome of each case.

In these studies, health workers observed children once or twice weekly. To be classified as having an acute respiratory infection, the child must have rales, stridor, wheeze, respiration rate >50, cyanosis, or retractions. To document an illness as a new episode, the child must have been free of ARI symptoms for at least one week. The incidence of ARI was observed to be four to ten episodes per year, with most projects having six to eight episodes per year.

In previous comparisons of ARI incidence in several populations around the world, it was concluded that the incidence of ARI is similar in Third World and industrialized populations. However, such comparisons have been complicated by variations in case definitions and by the longer duration of ARI in developing countries. Third World children spend a much greater part of their childhood ill with an ARI than do their Western counterparts.

Measurements taken over the last several decades in Third World and Western populations have shown that mortality rates due to ARI decrease over time in parallel with improvements in socioeconomic status. For many populations, however, improvements in socioeconomic status are coming about too slowly. ARI mortality may be decreased more effectively by identifying specific risk factors and trying to change them. The BOSTID studies identified risk factors that distinguished the severely ill children from their healthy cohorts. Those factors that are noted in most studies were crowding, large family size, hygiene and sanitation (all related to transmission), and age, nutritional status, immunization status, mother's education, and smoke pollution (all related to the susceptibility of the host).

Measures that can be recommended to lower ARI mortality amount to improvements in primary health care in general. They include promotion of immunization against childhood infections, improved access to health care, training for mothers on recognition and treatment of ARI, promotion of birth spacing and maternal health care to reduce the number of low birth weight infants, and assistance with good nutrition and breastfeeding.

FUTURE OF THE ARI PROGRAM

Participants at the symposium noted that enormous data bases had been established, but not yet completely analyzed. The first priority was to "mine" the data. Yet the grants were all coming to an end, and the BOSTID program had been curtailed because of budget cuts.

Negotiations were begun in early 1988 with the AID Office of Health for new funding, apart from the BOSTID Research Program, to continue the ARI program and address some of the research priorities to be identified by the symposium participants. The AID staff pointed out that a program that had been in existence for more than five years would need a formal evaluation before AID could consider funding it. A small panel was formed, and with unusual energy and hard work, it produced an evaluation in three months.[9] The evaluation recommended continuation of the program, but efforts to secure funding from AID were unsuccessful.

Following the symposium, BOSTID reallocated some of the savings from the research program, mostly from three large grants that were never initiated because of violence and political problems in the host countries, and, with AID encouragement, dedicated these resources to continuing the data analysis and publishing the ARI results. A new committee, the Committee on Acute Respiratory Infections in Third World Children, chaired by Denny,[10] was formed to approve proposals for additional funds for data analysis from the grantees and assist with the preparation of publications. This committee has itself identified areas for further research, and is preparing a proposal to funding agencies to carry on the work. It intends to prepare a National Research Council publication on the status of ARI research and the implications for public health policy.

NOTES

1. Pediatric Research *17*: 1023-1076 (1983).
2. Participants at the advisory group meeting were Samuel Asper, Educational Commission for Foreign Medical Graduates, CRG member and chair; Stephen Berman, University of Colorado, Boulder; Joseph Cook, Edna McConnell Clark Foundation; Roger Glass, National Institutes of Health; John La Montagne, National Institutes of Health; Adel Mahmoud, Case Western Reserve University, Cleveland, Ohio, CRG member; Robert Parrott, Washington Children's

Hospital; Frederick Robbins, Institute of Medicine; Arnold Monto, University of Michigan, Ann Arbor, visiting scholar at BOSTID; Judith Bale, Tresa Bass, Michael Greene, BOSTID.

3. BOSTID staff also made a considerable effort to develop projects in India, Burma, and Nepal. The project in India was approved on two occasions. In the first instance, there was a long delay for Indian Government approval of the project, and the investigators accepted funds from the Canadian Government instead. After the Canadian-supported project ended, the Indian researchers applied again and were approved for funding by CRG, only to have the entire program suspended because of budget cuts. A promising project was being developed in Burma when the program was suspended. In contrast, BOSTID staff and advisors visited Nepal on several occasions to assist promising research groups to develop viable proposals, but without success.

4. Members of the advisory panel on viral diagnoses were Patricia Charache, Johns Hopkins University, Baltimore, Maryland; Jose Cruz, Institute of Nutrition of Central America and Panama, Guatemala (grantee); Frederick Hayden, University of Virginia, Charlottesville; Fabio Luelmo, PAHO; H. Maassab, University of Michigan, Ann Arbor; Kenneth McIntosh, Boston Children's Hospital; Arnold Monto, University of Michigan, Ann Arbor; Judith Bale, BOSTID. Thomas Elliott was staff consultant.

5. Participants in the advisory panel on bacterial diagnoses were: Claire Broome, Centers for Disease Control; Patricia Charache, Johns Hopkins University, Baltimore, Maryland; Jose Cruz, Institute for Nutrition of Central America and Panama, Guatemala; Mary Jane Ferraro, Harvard University, Cambridge, Massachusetts; Dan Granoff, Washington University, St. Louis, Missouri; Fabio Luelmo, PAHO; Judith Bale, BOSTID. Thomas Elliott was staff consultant.

6. Participants at the advisory meeting on data management were Patricia Charache, Johns Hopkins University, Baltimore, Maryland; Jeanne Cushing, Public Applied Systems, Columbia, Maryland; Harry Foxwell, American Chemical Society, Washington, D.C.; Peter Lachenbruch, University of Iowa, Iowa City; Arnold Monto, University of Michigan, Ann Arbor; C. Oyejide, University of Ibadan, Nigeria (grantee); Beatrice Selwyn, University of Texas, Houston; Mark Wolff, Johns Hopkins University, Baltimore, Maryland; Judith Bale, Tresa Bass, Michael Greene, BOSTID.

7. Participants were Floyd Denny, University of North Carolina, Chapel Hill; Stephen Berman, University of Colorado, Boulder; John Brooks, University of Rochester, Rochester, New York; Richard Johnston, Children's Hospital, Philadelphia, Pennsylvania; Michael Katz, Columbia University, New York, New York; Gerald Keusch, Tufts University, Medford, Massachusetts; Kenneth McIntosh, Boston Children's Hospital, Massachusetts;

Catherine O. Oyejide, University of Ibadan, Nigeria (grantee); Richard Stiehm, University of California, Los Angeles; Judith Bale, Michael Greene, BOSTID.
8. Reviews of Infectious Diseases. 1990. Vol. 12, Suppl. 8.
9. An Interim Evaluation of the BOSTID Research Program on Acute Respiratory Infections in Children, Board on Science and Technology for International Development, May, 1988. Members of the panel were William Jordan, National Institutes of Health, Chairman; Larry Anderson, Centers for Disease Control; Pamela Johnson, AID; Calvin Kunin, Ohio State University, Columbus; Kenneth McIntosh, Boston Children's Hospital. Consultant to the panel was Peggy Sullivan, University of Texas, Houston.
10. Membership of the Committee: Floyd Denny, University of North Carolina Medical School, Chapel Hill; Stephen Berman, University of Colorado, Boulder; Patricia Charache, Johns Hopkins University, Baltimore, Maryland; W. Paul Glezen, Baylor College of Medicine, Houston, Texas; Kenneth McIntosh, Boston Children's Hospital, Massachusetts; Harris Pastides, University of Massachusetts, Amherst; Beatrice Selwyn, University of Texas, Houston. Staff director: Judith Bale.

Conclusions

The BOSTID Research Program was primarily aimed at generating scientific knowledge in six research areas, and any evaluation of its success or failure must begin with the achievements made in each of the program areas. These have been discussed in the previous chapters. Beyond those, one must examine the performance of the individual projects, and how BOSTID acted to maximize the successes and minimize the failures. One may ask how the countries and the institutions have benefited for the long term, and how the capability to do high-quality research has been increased. Finally, what were the major lessons learned for international cooperation in science development?

CRG indicated at an early stage that the primary purpose of the program was to perform reliable, publishable research on specific scientific problems, and most of the decisions made by CRG were consistent with that policy. The selection of problem areas and projects was based on the gaps in knowledge that could be filled by field work in the developing countries rather than on short-term gains to participating institutions. For example, CRG made clear that it would not support site-specific screening of cultivars or microsymbionts, even where this was a national priority or the assigned mandate of an institution, but would only fund projects that contributed to the larger picture. One must look at the individual projects to assess the overall impact. Why did certain investigators not perform well and certain projects fail? How did the grantee institutions benefit and improve their capability to carry out research and address the critical problems of their countries? In other words, did this program whose primary goal was to generate good research on certain problems in developing countries also succeed in building capability to carry out national goals?

RESEARCH CAPABILITY

There are serious obstacles to doing good research in developing countries. With some notable exceptions, investigators do not, in general, publish as much, nor are their papers cited as often (the two traditional measures of scientific performance), as scientists of the same age and training working in the advanced countries, including their former classmates at U.S. graduate schools. (One scientist who trained a grantee in a U.S. laboratory said of him that he could probably do great things if he worked in the United States. The implication was that great things were not expected of him in his own country.) There are a number of reasons for this—constraints peculiar to, or more acute in, developing countries. Among the constraints identified by the BOSTID Research Program, three stand out.

1. Operational difficulties and lack of resources. It is difficult and often more expensive to do anything that involves capital or institutional resources in a developing country, and research is not an exception. For a scientist this may mean that supplies and materials are difficult to obtain and of uncertain quality, basic equipment is lacking, institutional regulations are cumbersome, government bureaucracy is intractable or corrupt, and laboratory conditions are crowded or uncontrolled. Library resources are a special problem; where they are inadequate it is very difficult for researchers to remain current with the latest knowledge and techniques, and they are more likely to have scientific proposals and papers rejected by donors or publishers for lack of adequate references. The problem can vary from the situation of some researchers in Mexico, whose laboratories and libraries are relatively well supplied, but who have to contend with frequent political strikes and changes of policy and direction with every new government, to cases in some African and Latin American countries where researchers must supplement the project with their own personal resources and some may even work without pay because inflation has consumed that part of the grant money earmarked for salaries. Greater dedication and effort is generally necessary to complete a good research project in developing countries than in the United States.

It is difficult to know how to cure these problems, because they are often representative of every sector and every aspect of society. As was suggested by a member of the National Academy of Sciences Committee to Review Human Studies, speaking of the ethics of a program that treated malnourished children and then returned them to the home situation where they had originally become malnourished because there were no resources to do otherwise, "underdevelopment itself is unethical." No exception can be expected for scientific research. The ingenuity of scientists has overcome many problems (like impenetrable customs services), and some anec-

dotes about creative schemes to import research equipment have reached the proportion of legend. Other conditions, like runaway inflation, make any economic activity in society problematical, and research, too, suffers. No formulas are available, except economic development, to overcome operational difficulties in developing countries.

2. Lack of career recognition. In countries without a long scientific tradition, research may not be considered a legitimate activity, even for a "scientist." In such places, no allowance is made for research when assigning teaching loads, and research productivity may not count toward promotion or salary increases. Or it may be counted in ways which show no appreciation for the nature of science, as in one Middle Eastern university, which requires a certain number of papers before a professor can be promoted (although no work time is allocated to actually doing the research), but, in order to "encourage collaboration," only multi-authored papers count! One can imagine the kind of collaboration that this encourages. More commonly, in an antithesis of this policy, no credit at all is given for publication of research papers, so that even scientists who have the interest and drive to do research have no motivation to write up the results and publish them.

The destructive result of all these variations on a theme is that in too many places the distinction between doing good, publishable work and just "doing research" is blurred. There is no more reward or recognition for excellence than for passing the time with work that is never published. This is almost an environmental disease, which corrupts the workplace and destroys young researchers. It is a large part of the difficulty that many otherwise capable developing country researchers have with writing persuasive proposals that are designed to solve a real problem. It is, in a way, the most serious problem of science in developing countries.

Culprits here include local-language, unrefereed, journals that publish articles without regard for international standards of quality. Recent efforts to include more of such journals in the international citation services does no credit to international science. Science prizes for excellent research and salary differentials to those who bring in international grants and publish papers in international journals are among the acknowledgments that would help to strengthen the career of a scientist.

3. Lack of a scientific community. A scientific community is more than a group of scientists working in the same country. A true community of scientists read and discuss each other's work, meet for seminars and exchange of ideas, and review each other's papers and proposals. The community provides stimulation and information on new results, and acts as a sounding board for ideas and proposals. The intellectual nourishment pro-

vided by other scientists is so essential that it generally goes without comment in the United States, and rarely since Einstein worked alone in the patent office has anyone accomplished anything important in total isolation (even Einstein in his first relativity paper thanks a friend for helpful discussions). Yet isolation is what many scientists must contend with in some developing countries, where scientific discussions among colleagues are a rarity.

For BOSTID grantees, the coordination meetings provided intellectual nourishment, and their great popularity with the researchers and the intensity of discussion demonstrated how intensely the need was felt. Grantees were also occasionally asked to review new proposals received from other countries, which they did conscientiously, though some had never reviewed a proposal before. These experiences should be duplicated at the national level. Governments should support national scientific meetings and offer small research grants on a peer-reviewed, competitive basis.

A direct result of this minefield of obstacles for the researcher is that the single best indicator for success of a research project is the character of the principal investigator. Character, distinct from scientific competence, includes entrepreneurial ability to seek solutions to operational problems, force of personality to gain the cooperation of others, energy and persistence to overcome bureaucratic obstacles, and desire to accomplish high quality work. For BOSTID staff, this kind of grantee was frequently the most demanding, calling often to request services, trying to extend the budget or time period, applying for other grants from BOSTID or other agencies, and generally making himself or herself visible and demanding. But the same successful personality traits often made the individual particularly ingratiating to the staff. One example was the situation at one African university where BOSTID had made five grants. Four of the five investigators complained that they were unable to obtain use of vehicles promised by the university. The fifth never mentioned it. He just requested the vehicle "early and often," and remembered the dispatcher with some produce at harvest time; he always had the vehicles he needed. His project was one of the most successful.

In many cases, the assistance and collaboration of U.S. scientists was effective in filling the gaps. Critics, and even some friends, of the BOSTID program argued that the collaboration would have been more effective and the projects stronger if money had been available to support the research of the U.S. collaborators. But the administration of the program would have been much more complex if U.S. proposals were joined with the developing country proposals, and the amount of money available for researchers in the developing countries would have been less. Even so, U.S. collaborators and advisors played an important part in the success of most of the better projects.

Another method to improve the quality of projects was to improve the

quality of proposals through research planning and proposal-writing workshops. These were led by BOSTID staff, and usually hosted by "neutral" or national institutions in the countries, like USAID, the International Rice Research Institute, or the Andean Pact. They lasted two days. The first day was dedicated to a review of the "principles" of problem definition, proposal preparation, and budget estimation. On the second day, participants analyzed four real examples of proposals submitted to BOSTID, together with the peer review comments. Finally, each participant was invited to present his or her research idea orally in the form of a proposal: problem definition, objectives, scientific background, etc.

The success of the workshops was mixed. In some countries, an increase in the number of acceptable proposals and grants awarded by BOSTID was noted; in the Philippines particularly, it was dramatic. In other countries, the workshops appeared to have no impact whatever. In future workshops, where time permits, there should be an interval for participants to work on their proposals, and for individual consultations during a final day.

Scientists in Africa face some especially daunting problems even though sub-Saharan Africa is a high priority for development agencies. High population growth rates, decreasing national incomes, and poor working conditions and facilities for trained people make it a difficult place for them to do research. BOSTID awarded fifteen grants to sub-Saharan African institutions: six in Kenya, three in Senegal, two each in Nigeria and Uganda, and one each in Congo and Zimbabwe. This is fewer than in the other developing regions, and probably reflects the smaller number of scientists working in Africa. One of the Kenyan grants was to the International Council for Research in Agroforestry and will not be included in the generalizations that follow. Of the fourteen remaining grants, five resulted in publications in refereed journals (one of BOSTID's criteria for success), three others are considered by staff to have produced some unpublished results of value, and five were not considered successful. In dollar terms, about $1.5 million was awarded (about ten percent of the program in dollars and thirteen percent in number of grants). Those that resulted in publications spent about $450,000 of the total. For the BOSTID Research Program as a whole, the fraction of the grantees who publish is about sixty percent; for Africa the figure quoted above is thirty-five percent, but is based on only fourteen cases.

One of the successful African grantees is an expatriate from India. The other successful projects were characterized by strong interaction with foreign scientists—U.S., French, and German. Only two of the remaining nine projects had as much assistance. This would suggest that until the fundamental working environment is improved, the African projects particularly will profit from frequent visits of advisors and short-term investigators training abroad.

Unfortunately several kinds of problems worked to perhaps the unique disadvantage of African projects in the BOSTID experience. They included:

- Personal problems in working relations of investigators that made it difficult to get the resources needed.
- Difficulties of having to do "inappropriate" tasks, like spending inordinate time collecting equipment from airport customs because the institution would not provide the service.
- Overburdening of well-known investigators with paid and volunteer assignments by international agencies to the extent that they could not carry out their own research. This is a natural consequence of the small number of senior researchers and the large number of active development agencies in Africa.
- Inefficient management of funds by grantee institutions, to the disadvantage of the investigators, because of fierce turf battles among underfunded academic departments that were supposed to be collaborating.

On the other hand, BOSTID saw in Africa examples of the most sincere dedication to the project, at personal cost and even personal risk. Visiting advisors commented on investigators' persistence and energy in the face of some nearly insurmountable obstacles. This experience suggests that investigator-instigated research programs with technical support for researchers like the one under discussion could be effective in assisting the active scientists. In the long term, programs to train additional scientific manpower are needed.

India also presented a unique problem. It was the only country that specifically required government approval before BOSTID could award a grant. Other countries required approval before a proposal could be sent to an international donor, but the approval was usually pro forma, and BOSTID was often unaware of the requirement. In India, proposals were received, albeit unofficially, the pregrant visits were made, and proposals were approved by CRG before the difficult process of seeking government approval was even initiated. The process of seeking government approval was so time consuming and frustrating that few researchers cared to undertake it before they were assured of approval in advance.

In 1983, three proposals from India were approved by CRG. For nearly two years, the principal investigators attempted to secure government approval, with the assistance of the USAID mission and several visits by BOSTID staff. Meanwhile, they participated in all coordination meetings and workshops. One investigator, Jacob John of the Christian Medical College in Vellore, was fortunate to receive an offer of support for his project from the Canadian International Development Research Center (IDRC), and after a visit to India by the prime minister of Canada, the IDRC project was suddenly approved and he withdrew his proposal from BOSTID. The

other two were approved about six months later, in late 1985. In 1986, two new Indian proposals were approved, and in 1987, Dr. John finished his Canadian-supported project and proposed a follow-on to BOSTID. None of these latter three received Indian government approval before BOSTID grants were discontinued in late 1987.

No reason was ever given for the failure to approve the funded projects. No official ever admitted his opposition, and all asserted that the problem was in some other office or bureau. On the other hand, the two grants that were approved and the research carried out encountered no interference by the government, neither in receiving and exchanging foreign currency, importing equipment, international travel, nor reporting to BOSTID. One of them did encounter a problem with his dean, who insisted that all correspondence from BOSTID be addressed to him (the dean); BOSTID reluctantly complied, at the request of the researcher, and there was no further difficulty.

CAPACITY BUILDING

CRG emphasized scientific merit and value of research results in the selection of grantees, since they believed that this was the most effective strategy for building research capability. A few alternative (and more expensive) approaches that have been tried elsewhere are institution building (equipment procurement and long-term training at selected institutions), twinning of university departments with U.S. universities, and use of resident expatriate experts.

There are three measures of the capability of a research group: its human and material resources, productive output, and its reputation or national and international recognition. The recognition factor is an area where BOSTID was unusually effective. International recognition, scientific reputation, and prestige are the intangible assets of a scientist that are both measured by, and determine whether, he or she is awarded grants, is invited to scientific meetings, commands resources within the institution, and participates in international scientific correspondence.

There was no long term degree training in the BOSTID Research Program. The emphasis was on one-week to two-month visits to U.S. or other international laboratories for specific training and on one-day to two-week workshops on specialized techniques, which were often held during coordination meetings. Examples of the shorter workshops were the training on ELISA and DNA probes for MVR grantees, the workshop on clinical diagnoses in ARIs, the sessions on ^{15}N and serological methods for BNF grantees, the workshop on soil analysis for FGT grantees, and the sessions on statistical applications for computers given to REA grantees. The longer workshops included laboratory courses on diagnosis of respiratory viruses

and bacteria, data management and analysis given to ARI grantees, and the application of molecular genetic techniques to field experiments offered for BNF grantees. The effectiveness of these workshops was measured by the extent to which these techniques were correctly incorporated into the projects. ARI grantees adopted the diagnostic and data analysis methods, most with substantial improvement in their capability. Some of the MVR grantees redesigned their projects to take advantage of the ELISA methods. Nearly all BNF grantees incorporated ^{15}N measurements into their projects and obtained quantitative results, and all participants in the Mexico course introduced molecular genetics experiments into their projects. These workshops were focused and immediately applicable for the studies at home and did not have the drawback of long term or general training that frequently woos young scientists away from the problems in their own countries.

Purchase of equipment was an important part of every project. BOSTID only purchased equipment that was directly applicable to the project, and checked during project visits that the equipment was in working order. Whenever possible, equipment came with a maintenance contract and/or with a supply of spare parts. Often, its arrival was timed to coincide with the visit of an advisor who would help to install or test the equipment. Supplies and reagents were also provided by BOSTID; while these were consumed during the course of the project, the identification of sources of supply and quality control methods should be helpful for future research. Finally, reference laboratory services were provided to the grantees in the BNF and ARI programs, which enabled grantees to calibrate the precision of their laboratory techniques for future work.

The recognition received by grantees for their participation in the BOSTID Research Program can be seen in several ways. A few grantees were awarded high national prizes and medals for their research: two were awarded the equivalent of "Scientist of the Year," and one received a medal that had never been awarded to a civilian before. Three became heads of their institutions. On the other hand, three others lost their positions. More significantly, with assistance from BOSTID, many more grantees published papers in refereed journals. Nearly all have made international contacts and participated in international meetings, which were inaccessible previously. And some have already seized other opportunities: some of the viral laboratories assisted by BOSTID for the ARI project have become the central laboratories in their countries for AIDS monitoring. Many have received research grants from other donors, but since they were all skillful enough to have received a grant from BOSTID in the first place, one can only speculate as to what part their enhanced experience, publication list, laboratory facilities, and name recognition may have played.

COMMENTS FROM GRANTEES

In September 1986, as the planned eight-year term of the BOSTID Research Program was approaching its end, BOSTID surveyed some of the grantees for ideas that might help plan the hoped-for renewal of the program. Although they were asked only which features of the program they would retain and which they would change, their comments throw some light on their view of the BOSTID program and improvements that could be made.[1] Some of these are repeated below:

> "The present format of the coordination meetings for grantees is an excellent one and should as a whole remain unaltered. . . . The idea of a workshop on some kind of subject following the coordination meetings is a nice one. This can be on a technique such as ELISA or immunofluorescence, DNA probes, electrophoresis, or computer usage and software.
>
> "BOSTID research grants should have a training element to give a chance for continuity. American graduate students should be supported to spend a limited time to work on the projects supported by BOSTID. . . . Post-doctoral fellows should spend about a year either working on the BOSTID supported project or on any other project agreed upon.
>
> "Principal investigators . . . should be supported at the end to spend some kind of sabbatical leave of about six months in a laboratory in the United States to write up their work and carry out investigations . . . this would rejuvenate them and enable them to keep abreast of the advances in science in the developed world." [Louis Mukwaya, Uganda]

> "We have been involved in three projects which received funds from the same agency (AID) and administered by three different groups. One is the CRSP Title XII on beans, the second is the amaranth grant [BOSTID], and the third is a project on coffee pulp, supported by the Science Advisor. I believe we have contributed with knowledge and practical applications in the three projects. However, the two which have been more attractive are the first two. The basic reason has been the interaction with the other scientists working on the same project from different angles. . . . Something which is also of value is that there is prestige when a grant comes from NAS or universities. This has to be recognized.
>
> "The grantees' meetings have been useful, but they could be more useful if an outside technical committee would review the results and discuss them with the researchers. Given the reduced availability of funds, it seems the number of areas should be reduced to enhance those which show a greater promise, and to reinforce the evaluation of research results. The funds should be concentrated in areas which will pay off, not in supporting activities which rather than help may interfere with development." [Ricardo Bressani, Guatemala]

> "The BOSTID project and grant has been an immense help to our entomology group and the SEM by enabling us to carry out a well organized and sustained research program. In the past the SEM has been involved in various

research projects . . . , but these projects were either on an 'ad hoc' and/or collaborative basis, which resulted in very few long term benefits to our human or physical infrastructure and were often not entirely relevant to our problems. In addition to the scientific results of our projects, the BOSTID grant has also provided other benefits, such as:

a. physical infrastructure (laboratory, insectary, equipment)

b. human infrastructure (training in and out of country)

c. sensitizing higher officials to the importance and results of good research.

Therefore, in any evaluation of the BOSTID program . . . we would hope that benefits other than purely scientific results also be considered. We would also strongly recommend that BOSTID or other funding involving a minimum of bureaucracy as is now the case continue to be available because . . . by the end of this grant to study *An. albimanus* we will have the complete infrastructure in place (really the most difficult part) and be able to immediately attack other problems." [Marco Suarez, Colombia]

"Let me make some comments on the REA component. First, this is practically the only program that could identify, test, and disseminate new methodologies. I agree that the grantees' meetings are helpful, but what is lacking is action to ensure that a new technique, once discovered, could be fully developed and applied. By just funding new basic research that will end in publications, the chance that those innovative techniques will be implemented is not great. What should be done next are active promotion and operational studies to implement the methods developed. That will reduce the gap between researchers and health planners, so BOSTID could see at the end the benefits of its research results. BOSTID should review all results from their studies and decide which interventions or methods are important to be promoted and then see ways to implement them. . . .

"I also hope the BOSTID program will continue, because it has demonstrated to be a unique, effective, and very useful way to stimulate and channel research activities." [Claudio Lanata, Peru]

"I am in favor of BOSTID bringing together the grantee researchers at a national or subregional level with appropriate experts and AID to discuss more general scientific problems. . . .

"I think that the national science and technology councils of a particular country could be informed of the research program by BOSTID but the granting of funds should not be channeled through the national agencies but coursed through the institution of the researcher. I believe the present setup that we are following is much better and more flexible." [Rudolfo Escalada, Philippines]

"In trying to comment on the BOSTID Research Program, I would like to focus at three different levels: my research grant, the nitrogen fixation program, and the whole BOSTID program.

"My research grant: Our institution . . . has twenty researchers, twenty technicians, and about twenty-five students; it is well equipped and we have a

sophisticated methodology and ambitious goals. We have internal support from the university and [the government]. Under these conditions, what is the actual influence of a grant from the National Academy of Sciences?

"In the last years, Mexico has gone through a very difficult economic situation, and funding from the university and CONACYT has decreased to very low levels, in particular for equipment, travel, and operation. I could say my grant from NAS has been essential to maintain our level of productivity. Most important has been the fact that the grant is operated directly from NAS and the grantee without going through a national council.

"I have found particularly encouraging the meetings with experts and with other grantees, and this has stimulated us to get into some collaborative projects. . . . It has been of great benefit to appreciate and understand research at the field level and we are sure that our basic research will be connected to field problems in the future.

"The Nitrogen Fixation Program: At this level I have the impression that although these are some excellent projects, several of the projects are not really scientific research but just screening of different types. Most of the projects are oriented to a short term application and few have really ambitious goals that include fundamental research. In this regard, the BNF program should be considered as a whole and we should ask if it is a comprehensive program that covers from fundamental to applied research; if it includes the best groups in the area working in developing countries as well as the best experts; and if there is a good flow of information among them. It is my view that although the program is good, it could be better if we pay attention to some facts:

- More attention should be given to fundamental research in the areas of molecular biology, biochemistry and physiology. We should recognize the best groups working in BNF in developing countries and suggest them to be incorporated.
- We should stimulate the exchange of information at the level of the whole program: grantees, experts, and National Academy of Sciences staff. This could be done by: 1) continuing the annual meetings; 2) developing computer networks for communications to enhance the collaboration between grantees; 3) organization of experimental workshops with the participation of grantees and experts that could lead to the advancement of the program, and 4) promoting academic exchange between grantees in such a way that some of them could serve as co-advisors of other projects.

"[As for] the whole BOSTID program: I would suggest the introduction into the program of new research areas that are of due scientific impact in Third World countries. One of preeminent importance would be the study of the biology of infections and parasitic diseases.

"As a last comment, I would like to stress that much of the success of the BOSTID program has been due to some features of the present organization. One of them refers to the fact that everything has been done working directly with the grantees, and not by dealing with national science and technology councils that could interfere with the accomplishment of some of our goals." [Rafael Palacios, Mexico]

TERMINATION OF THE PROGRAM

In November 1987, CRG met and approved fourteen grants. Scarcely one month later, the Congress cut $2 million from the budget of the Office of the Science Advisor of AID for 1988. The report of the Senate Appropriations Committee's Subcommittee on Foreign Operations, which handles the AID Budget, made clear that this sum was to be taken from the BOSTID Research Program; more precisely, the amount granted to BOSTID could not exceed $2 million, although the amount expected by BOSTID for 1988 was $4.5 million. The reason given was "the failure of the NAS to provide its own resources in support of the collaborative research program funded by AID."

While the cut itself was neither altogether unexpected nor fatal, the reaction to it was. There was known to be unhappiness in the Senate Subcommittee on Foreign Operations because, as told to BOSTID by an Appropriations Committee staffer, there was a feeling by key Subcommittee staff that the Institute for Scientific and Technical Cooperation (ISTC), which had been killed by the Senate Appropriations Committee in 1979, had been revived "contrary to the will of Congress" and brought to the NAS by its current president, Frank Press (who had promoted ISTC from his position as Science Advisor to President Carter before he became president of the NAS). In fact, the AID grant for the research program required no approval from Press, and he was elected president of the NAS well after the grant had been made. Nevertheless, it was expected that some difficult discussions were in store before the program could be continued beyond the eight-year expiration date.

What was a surprise was the application of the budget limitation to FY1988, the current year. This had two immediate effects. The grants that had been awarded (with the successful applicants already notified) in November 1987 could not be funded and had to be retracted. Moreover, in light of the likelihood that the funding cap would not be lifted in the foreseeable future, a decision was made at the highest levels of the National Research Council and AID to bring the BOSTID Research Program to an end.

The November 1987 meeting turned out to be the last meeting of CRG. Although no new grants could be awarded, the program continued to support the existing projects, coordination meetings were held, and effort was concentrated on producing publications. Completed grants were combed for unspent funds, and these were reprogrammed, mostly to continue the data analysis for the ARI program, which had run severely short of both time and money to carry out the recommendations of the October 1988 ARI Symposium in California. AID granted a no-cost extension of the research program grant until January 1992, when all projects will be over.

The experience gained in the program has continued to find other applications. In August 1988, AID and BOSTID entered into a $10 million five-

year cooperative agreement through which BOSTID provides scientific support and technical assistance to grantees of the PSTC research grants program operated by the Office of the Science Advisor.

Meanwhile, BOSTID is attempting to apply the experience to other programs. A five-year grant was awarded by USAID/Islamabad to operate a BOSTID-type research program in Pakistan. All grants would be awarded to Pakistani researchers on one area: increasing agricultural productivity of stressed lands in Pakistan. BOSTID will have a cooperator, the Pakistan Agricultural Research Council, which will work side-by-side with BOSTID to administer the program and thus learn the methodology and philosophy. Grantees will be selected by a binational CRG, but awarded by BOSTID. The impact of this program on a national level will be of great interest in the future.

LESSONS LEARNED

The primary realization brought to BOSTID by the Research Program was that research in developing countries cannot be supported in the same way that it is in the United States; i.e., proposal evaluation on the basis of written submissions only and transfers of funds without attendant technical assistance. Written proposals in English often are poor indicators of the capability or intentions of developing country researchers, and inadequate library facilities and international contacts often means that an extended period of discussions and revisions are required before research protocols are ready for funding. For the same reasons, contacts and exchanges with researchers in other countries must be integral elements of research projects if worthwhile and publishable research results are desired. Management of the program is labor-intensive and more expensive than for research programs in the United States, but failure to make the effort and investment will cause many of the projects to be unproductive, with a greater waste of resources.

Another important observation was the role that BOSTID, as a U.S. funder of developing country scientists, was expected to play beyond grant-giving. Of course, many scientists wrote to BOSTID seeking funds, even where their interests were outside of the six areas. But others also wrote for scientific advice, for technical assistance unrelated to research grants (university curriculum, for example), for names of U.S. contacts, for news of meetings and study opportunities in the United States, and to vet research ideas without asking for money. Some scientific organizations wanted to establish formal relations and sponsor joint activities. For many, BOSTID was considered to be a channel to the U.S. scientific community. This experience may be relevant in case the call for an ISTC is ever renewed, because some of these functions were contemplated for the ISTC. The fact

is that there really is no U.S. institutional counterpart to the science and technology research councils found in many developing countries, and a central focus for foreign researchers seeking U.S. contacts, or vice versa, is missing. The largest U.S. research funders, like NSF and NIH, have small or narrowly focussed international programs and limited resources for participating in international cooperative activities. The BOSTID experience contains many clues of what an ISTC, dedicated to international scientific and technological cooperation, ought to be.

NOTE

1. The request letter made the suggestion that, in the future, BOSTID might work more closely with national science and technology councils or other governmental institutions, and the grantees' comments were invited. This is the provocation for the criticism of these national institutions in the grantees' remarks.

Appendix A
Committee on Research Grants

Frederick Seitz (Chairman), President Emeritus, Rockefeller University, New York, New York*

Francisco Aguirre B., Director, Instituto Centroamericano de Investigacion y Tecnologia Industrial (ICAITI), Guatemala City, Guatemala

George A.O. Alleyne, Director, Area of Health Programs Development, Pan American Health Organization, Washington, D.C.

M. Anandakrishnan, Policy, Analysis, and Research Division, UNCSTD, United Nations, New York, New York

Samuel P. Asper, President, Educational Commission for Foreign Medical Graduates, Washington, D.C.

Adnan M. Badran, President, Yarmouk University, Irbid, Jordan*

A. Richard Baldwin, Vice President, Cargill, Inc., Minneapolis, Minnesota*

Teresa Salazar de Buckle, UN Industrial Development Organization, Vienna International Centre, Vienna, Austria

Louis Berlinguet, Science Attache, Canadian Embassy, Paris, France

Robert H. Burris, Department of Biochemistry, University of Wisconsin, Madison, Wisconsin

Charles C. Carpenter, Chairman, Department of Medicine, Case Western Reserve University, Cleveland, Ohio*

James Chin, Chief, Infectious Diseases Section, State Department of Health Services, Berkeley, California

W. Ronnie Coffman, Department of Plant Breeding and Biometry, International Agriculture Program, Cornell University, Ithaca, New York

---

* Indicates an original committee member.

Joseph A. Cook, The Edna McConnell Clark Foundation, New York, New York

Carl Djerassi, Department of Chemistry, Stanford University, Stanford, California

Joy C. Dunkerley, Senior Fellow, Resources for the Future, Washington, D.C.*

Arturo Gomez-Pompa, Director of U.C. Mexus, University of California, Riverside, California

Carl W. Hall, Dean, College of Engineering, Washington State University, Pullman, Washington*

Jake Halliday, Battelle Kettering Laboratories, Yellow Springs, Ohio

Dale D. Harpstead, Chairman, Department of Crop and Soil Sciences, Michigan State University, East Lansing, Michigan

Nicolai Herlofson, Secretary-General, International Foundation for Science, Stockholm, Sweden*

Ann M. Hirsch, Department of Biology, University of California, Los Angeles, California

Norman E. Johnson, Vice-President, Weyerhaeuser Company, Tacoma, Washington

John A. Katili, Director-General, Ministry of Mining, Jakarta, Indonesia*

J. Laurence Kulp, Vice-President, Research and Development, Weyerhaeuser Company, Tacoma, Washington

Aklilu Lemma, Senior Advisor, Technology for Health and Development, UNICEF, United Nations, New York, New York

Adel A. Mahmoud, Department of Medicine, Case Western Reserve University, Cleveland, Ohio

Leonardo Mata, Professor and Director, Instituto de Investigaciones en Salud, Ciudad Universitaria "Rodrigo Facio," San Jose, Costa Rica

Alejandro Melchor, Director, Asian Development Bank, Manila, Philippines*

Thomas P.C. Monath, Director, Division of Vector-Borne Viral Disease, Centers for Disease Control, Fort Collins, Colorado

Robert P. Morgan, Department of Technology and Human Affairs, Washington University, St. Louis, Missouri

Walter B. Mors, Professor of Phyto Chemistry, Instituto de Ciencias Biomedias, Federal University of Rio de Janeiro, Brazil*

David R. Nalin, Director of Clinical Research, Merck, Sharp and Dohme Research Laboratory, West Point, Pennsylvania

Thomas R. Odhiambo, Director, International Centre of Insect Physiology and Ecology, Nairobi, Kenya*

Daniel Okun, Kenan Professor Emeritus, Environmental Sciences and Engineering, University of North Carolina, Chapel Hill, North Carolina

Efraim Otero, Fundacion Santa Fe de Bogota, Asociacion Medica de Los Andes, Bogota, Colombia

David Pimentel (Vice Chairman), Professor of Insect Ecology, Department of Etomology, Cornell University, Ithaca, New York*

Hugh Popenoe, Director, International Programs in Agriculture, University of Florida, Gainesville, Florida

Vulimiri Ramalingaswami, Director, All-India Institute of Medical Sciences, New Delhi, India*

Roger R. D. Revelle, Science, Technology and Public Affairs, University of California, San Diego, California*

Robert E. Shope, Arbovirus Research Unit, Yale University School of Medicine, New Haven, Connecticut

H. Guyford Stever, Chairman, Commission on Engineering and Technical Systems, National Research Council, Washington, D.C.*

John G. Torrey, Harvard Forest, Harvard University, Petersham, Massachusetts

Clifton R. Wharton, Jr., Chancellor, State University of New York, Albany, New York*

Appendix B
The CRG Program
A Member's Perspective
John G. Torrey

I joined the CRG program in the summer of 1984—after it was well under way. I attended the first CRG meeting in Washington in June 1984, then participated in the coordination meeting on fast-growing trees in Jalapa, Mexico, in October 1984, and hosted the coordination meeting of November 1986 at the Harvard Forest. I remained with the program until its termination, attending committee meetings three times each year in Washington, D.C. During that period the program I was most directly involved with—fast-growing nitrogen-fixing trees—was broadened and its title changed to the Tropical Trees Program. I had previously been deeply involved in a meeting on Casuarinas held in Canberra, Australia, in August 1981, which had direct BOSTID participation. From that meeting came a substantial volume on Casuarinas, entitled *Casuarina Ecology and Management and Utilization*, published by the CSIRO, Melbourne, Australia, and a more popular BOSTID study by Noel Vietmeyer entitled *Casuarinas: Nitrogen-Fixing Trees for Adverse Sites* published in 1983 by the National Academy Press.

Although my expertise was in nitrogen-fixing trees, especially actinorhizal plants, I brought to the program a knowledge of *Rhizobium*-legume symbioses and a background in laboratory-based plant physiology. I was conversant with the material we read on fast-growing nitrogen-fixing trees and the content of the program on biological nitrogen fixation as well. These were the two programs of the six that I knew best. I was also familiar with the grain amaranth studies and followed that program closely.

Even so, all CRG members were expected to read and understand the proposals and projects in all six programs. This expectation was met by the committee members to a remarkable degree. During the course of our meetings, I learned a great deal about mosquito vectors, acute respiratory

infections in children, and rapid epidemiological assessment. Our homework was extensive, but our understanding was facilitated by the presence at each of our CRG meetings of committee members who were expert in each of the subject areas. There was a lot of give-and-take on all progress reports and decisions. The discussions and decisionmaking were given direction and impetus by the staff member in charge of each program who had intimate knowledge of each project and knew the project leader and the detailed logistics involved.

One of the most difficult tasks in the BOSTID program was the identification and recruitment of suitable, talented, and even slightly experienced grantees in each subject area who could be expected to outline and submit an appropriate research project proposal that qualified for CRG approval and BOSTID support. In my judgment, of all the programs the one on tropical trees suffered most from this problem. Even though BOSTID had been involved earlier in publication of a number of volumes on agroforestry and tropical trees for developing countries, little of this experience was reflected in the successful recruitment of project leaders in this subject area. Even so, during the course of the program, some first-rate investigators were funded and their programs substantially facilitated.

The staff of the CRG worked hard and in diverse ways in the recruitment process. Although the entire search process was never fully clear to me, I felt this step was the weakest link in the program on fast-growing trees. The program in biological nitrogen fixation had a more clearly defined constituency at the outset and was successful in recruiting from a broad group of already identified scientists and institutions.

Once approved for funding, a grantee was given all the support possible for achieving success—in a way unique to the BOSTID program, so far as I know. The CRG staff was involved directly and in detail in advising on experimental design, arranging for expert consultants from around the world to assure the best scientific plan, facilitating the availability of materials and equipment, and providing ongoing advice. Regular site visits by the CRG staff were made to smooth institutional budget matters and to check on progress and problems as well as competency. At regular intervals the grantees all assembled for exchange of information, for mutual confidence building, and for cooperative activities directed toward collaboration and accomplishment. The CRG staff person in charge of each subject area became well acquainted with each grantee as well as some of the other participants in the project and the institutional setting within which the grantee operated. This intimate knowledge of the grantee made possible the most useful logistical support. The executive director of the CRG also knew all of the grantees personally and the circumstances of their research programs. This hands-on approach to each project by the CRG staff provided the strongest possible form of support for each grantee at all stages.

CRG committee members were also involved in this support process, attending coordination meetings of the grantees on occasion, providing direct advice on research methods, assisting in the choice of experimental materials, editing written reports, and facilitating the organization of reports for publication. In all cases, the responsibility for the scientific work was left in the hands of the grantee, but support and encouragement came consistently and reliably from CRG and BOSTID personnel. Leadership from among the grantees themselves developed spontaneously and became an integral part of the support structure of the program.

The success of the BOSTID program in all areas rested heavily on the CRG staff. A remarkably dedicated group of staff members was assembled during the relatively short life of the BOSTID program and an extended network was created in each of the subject areas.

The sudden termination of funding and the rapid demise of the program was a great disappointment to all concerned.

Appendix C
BOSTID Project on BNF in Gramineae in Brazil

Johanna Dobereiner

The establishment of the BOSTID Research Program in 1981 seemed at last to fill a gap between the highly advanced science in the north and the extremely simple and conventional AID, FAO, or UNESCO programs designed for countries where scientific projects were nonexistent. Such programs attempted to transfer research results from temperate, highly advanced countries to the less developed tropical countries in the southern hemisphere, and to adapt them to the local conditions. They usually lacked originality and often failed to achieve the expected results, but they did train people and put them in contact with colleagues from advanced scientific centers. In many poor countries this was the best that could be hoped for.

There are, however, a number of developing countries, also in the tropical belt, designated by AID as advanced developing countries, where effective, reliable scientific activities are already under way in several fields and where support, cooperation from advanced countries, and, perhaps most important, cooperation among themselves, could help advance scientific projects that would have enormous impact on the development of these countries. This was exactly what the BOSTID program proposed, and that, with time, has progressed to make the BOSTID projects so special and so successful.

The BNF program was perhaps one of the best examples. The grant evaluations initially made in meetings with the grantees individually were frightening to many of them. They were therefore changed to group discussions where the grantees presented their results and accepted constructive criticism from fellow grantees in a more relaxed setting. These annual coordination meetings, held each time on the site of a fellow grantee, not only permitted all of us to observe other laboratories and their problems and solutions (usually typical for developing countries and very different from

those of U.S. laboratories), but also permitted an active exchange of ideas, fueled by the expert participants. Deep friendships all over the world united the BNF grantee group, which, it is hoped, will permit continuing trust and cooperation.

The requirements for financial reporting were simple and non-bureaucratic and the auditors rarely had cause for complaint. Some unavoidable problems arose from currency conversion in countries like Brazil, where inflation (and hence currency devaluation) is very high. Equipment purchases by BOSTID staff were always efficient, and delays in arrival were due principally to local problems with customs.

We were fortunate to obtain two successive grants, and the BNF program of EMBRAPA, in Brazil, certainly was strengthened substantially by them. The first grant, "BNF by plant bacteria associations in tropical grasses and cereals," enabled us to deepen the understanding of the associations of wheat and sorghum with azospirilla. It became clear that certain strains could be established under field conditions within roots, while others established preferentially on the root surface. In both cereals, the strains that established within roots proportioned most reproducible effects on N incorporation and grain. Using N^{15} labeled soil, however, we showed that the increases in N incorporation in wheat caused by inoculation with two such strains were due to a more efficient assimilation of soil N and not to BNF. By using nitrate reductase negative mutants we were then able to confirm that it is the bacterial nitrate reductase that enhances nitrate uptake through its reduction in the roots, which then is transported to the tops as amino acids.

Attempts to quantify BNF in association with several forage grasses (two *Bracchiaria* spp and *Paspalum notatum*) by the N^{15} isotope dilution method became very successful after some necessary adjustments of the methodology. These experiments, for the first time, showed substantial denitrogen fixation in association with grasses in the field. There were significant differences between plant species, and the nitrogen derived from the atmosphere was between 20 and 40 percent of the total N incorporation (10-40 kg per hectare per year).

Still more impressive results were obtained with sugarcane. An initial experiment in 50-liter pots, also by the N^{15} isotope dilution method, demonstrated that in one cultivar more than 50 percent of the plant nitrogen was coming from the atmosphere. Total N balances confirmed the data, which, extrapolated to one hectare, would total more than 100 kg N per year. Three other varieties were less effective in stimulating BNF.

With this promising data, the controversy about the potential of BNF in Gramineae associations appeared to be solved, and it seemed logical to continue this research in a second project, slated to start in 1985. The BOSTID staff suggested that since we had so much effective legume BNF

research going on in our laboratory, an approval would be considerably easier. However, we decided to accept the challenge and stay with the grasses; the second BOSTID project then proved that sugarcane can obtain all the nitrogen it needs for high yields (up to 200 tons of fresh canes per hectare) from BNF. In a concrete-bottomed tank filled with 80 tons of nitrogen deficient N^{15} labeled soil, 3 out of 10 sugarcane cultivars, fertilized with PK and minor elements and regularly irrigated, produced 3 consecutive cuts without any decline, extracting the equivalent of more than 200 kg N per hectare every year. One of the cultivars is a primitive type of *Saccarum spontaneum,* which is used for breeding; the second is the cultivar most commonly planted in the poor sugarcane-growing area in the northeast of Brazil where farmers can barely afford fertilizer. The third cultivar has been bred for poor soils in the Sao Paulo area and, because of its vigorous growth, has recently replaced other cultivars.

The data could not be explained by associations with low numbers of the known diazotrophs on or in roots, and, therefore, attempts to find new nitrogen-fixing bacteria led to the discovery of *Acetobacter diazotrophicus,* an entirely different diazotroph, which grows best with 10 percent sugar, fixes N^{15} in the presence of high nitrate levels, and occurs in roots, stems, and leaves of sugarcane but not in soil or in other plants, except, so far, for sweet potatoes and cameroon grass, both of which contain much sugar and are propagated vegetatively. This led to the conclusion that we found an endophyte that is propagated vegetatively by cuttings, and is therefore restricted to sugarcane and similarly propagated plants.

These recent experiments explain the lack of response of sugarcane to N fertilizers in Brazil, observed for many years, and are creating enthusiastic responses from sugar growers and alcohol distillers all over the country. These results made headlines in the Brazilian press because they may help to save the highly visible Brazilian fuel alcohol program, which today produces 13 billion liters of alcohol a year for more than 4 million cars running on 95 percent ethanol.

Appendix D
Proposal Evaluation Criteria

After a proposal has been received by the BOSTID Committee on Research Grants, it is sent on to a reviewer for expert evaluation. When evaluating the proposal, the reviewer is asked to consider the guidelines listed below. (However, if the proposal does not conform to the guidelines, it should be judged carefully for: relevance to the research area, scientific importance of the proposed research, and application to developmental goals. We do not wish to overlook the inspired researcher who follows a novel path.)

1. Problem Definition

   Is the problem to be solved clearly stated? Is it a problem of general importance for international development rather than one of only local interest?

2. Research Objectives

   Are the objectives clearly stated? Do they conform with the research planned? Are they reasonable in relation to the present state of our knowledge and the time frame of the project? Will the objectives, if accomplished, be a valuable contribution to the particular field?

3. Research Plan

   Is it based on sound principles? Is the overall research plan optimal to accomplish the objectives? Should it be broadened to include other populations, environments, studies, experiments, etc., or should it be narrowed in

focus? Are the major assumptions clearly stated? Is the budget and staffing reasonable? What changes would you recommend?

4. Research Methodology

Is there enough information to judge the adequacy of the methodology? Is the methodology adequate to accomplish the stated objectives? Are there alternate methods you would propose that are more suitable? Are there additional measurements, methods, or analyses that should be added or used? Will the data permit reasonable conclusions to be drawn? Is the choice of equipment appropriate? Has other published work been taken into account? Are there other changes you would recommend? (Specific comments on the detailed methodology would be welcomed.)

5. Institutional Capability

Does the institution posses the necessary resources to complete the project? Is the research team (including short term assistance of international experts) of sufficiently high caliber? Would you recommend any special training, including visits to other institutions, in initial phases of the project?

The following form is attached to the proposal to assist the reviewer in the evaluation.

PROPOSAL #
TITLE:
PRINCIPAL INVESTIGATOR:
INSTITUTION:
COUNTRY:
REVIEWER:

Problem Definition. Clarity. Consonance with BOSTID program announcement. Relation to other published work. Long term benefits. General Interest. Recommended changes.

Institutional Capability. Qualifications of the research team. Institutional support. Choice of consultants. Training required.

Research Objectives. Clarity, reasonableness, time frame, contribution. Recommended changes.

Research Plan. Optimum, soundness, broadness, budget, staffing. Recommended changes.

Research Methodology. Adequacy, up to date, alternate method, additional measurements. Recommended changes.

Summary. Recommendation for modification and/or funding.

Appendix E
Research Grants Program Publications List

GRAIN AMARANTH

Alfaro, M. A., A. Martinez, R. Ramírez and R. Bressani. 1987. Rendimiento y composición química de las partes vegetativas del amaranto (*Amaranthus hypochondriacus*, L.) en diferentes etapas fisiológicas. Arch. Latinoam. Nutr. 37(1): 108-121.

Alfaro, M. A., R. Ramírez, A. Martinez and R. Bressani. 1987. Evaluación de diferentes niveles de harina de amaranto (partes vegetativas) en sustitución de alfalfa para conejos en crecimiento. Arch. Latinoam. Nutr. 37(1): 174-185.

Bressani, R. 1983. The protein quality of raw and processed grain amaranth. Amaranth Newsletter 3: 1-3.

Bressani, R. 1983. The protein quality of raw and processed grain amaranth. Amaranth Newsletter 3.

Bressani, R. and J. M. Gonzalez. 1984. Potential use of the amaranth vegetative matter residue in ruminant feeding. Preliminary study. Amaranth Newsletter 4: 4-5.

Bressani, R. 1985. Some comments on amaranth grain research needs. Amaranth Newsletter 4.

Bressani, R. and J. M. Gonzalez. 1986. The nutritive value of the amaranth seed calyx as tested in growing chickens. Amaranth Newsletter 1.

Bressani, R. and C. Mendoza M. 1987. Nutritional and functional characteristics of extrusion-cooked amaranth flour. Cereal Chem. 64(4): 218-222.

Bressani, R., J. M. Gonzalez, L. G. Elias and M. Melgar. 1987. Effect of fertilizer application on the yield, protein and fat content, and protein quality of raw and cooked grain of three amaranth species. Plant Foods Hum. Nutr. 37(1): 59-67.

Bressani, R., L. G. Elías, J. M. González and R. Gómez-Brenes. 1987. The chemical composition and protein quality of amaranth grain germ plasm in Guatemala. Arch. Latinoam. Nutr. 37(2): 364-377.

Bressani, R. L. S. Kalinowski, M. A. Ortiz and L. G. Elias. 1987. Nutritional evaluation of roasted, flaked and popped *A. caudatus*. Arch. Latinoam. Nutr. 37(3): 525-531.

Bressani, R., J. M. Gonzales, J. Zuniga, M. Breuner and L. G. Elias. 1987. Yield, selected chemical composition and nutritive value of 14 selections of amaranth grain representing four species. J. Sci. Food Agric. 38(4): 347-356.

Bressani, R., L. G. Elias and C. De Bosque. 1988. The supplementary value of amaranth leaves to cereal grain-based diets. Amaranth Newsletter 1.

Bressani, R. 1988. Amaranth: the nutritive value and potential uses of the grain and by-products. Food Nutr. Bull. 10(2): 49-59.

Bressani, R. and L. G. Elías. 1989. The proteins of grain amaranth. Food Rev. Int. 5(1): 13-38.

Bressani, R., L. G. Elias and A. Garcia-Soto. 1989. Limiting amino acids in raw and processed amaranth grain protein from biological tests. Plant Foods Hum. Nutr. 39(3): 223-234.

Del Valle, R., A. Sanchez-Marroquín, M. Escobedo, R. Avitia, H. Bourges, S. Maya and M. Vega. 1987. Development and evaluation of a low-cost infant formula containing amaranth (*Amaranthus cruentus*). Arch. Latinoam. Nutr. 36: 480-493.

Duriyaprapan, S., P. Buranasilpin, J. Watanakul, S. Chitnawasarn and S. Tanpanich. 1987. Amaranth: Future Plant Protein. 38 pp. Bangkok: Thailand Institute of Scientific and Technological Research. (In Thai)

Garcia, L. A., M. A. Alfaro and R. Bressani. 1987. Digestibility and nutritional value of crude oil from three amaranth species. J. Am. Oil Chem. Soc. 64(3): 371-375.

Garcia, L. A., M. A. Alfaro and R. Bressani. 1987. Digestibility and protein quality of raw and heat-processed defatted and nondefatted flours prepared with three amaranth species. J. Agric. Food Chem. 35(4): 604-607.

Gonzalez, L. G. and R. Bressani. 1987. A guide to amaranth grain cultivation summary of experiences at the INCAP experimental farm. Amaranth Newsletter 2.

Graham, G. G., J. Lembcke and E. Morales. 1989. Protein value for children of soft-endosperm maize, alone and with toasted Amaranth flour. Nutr. Res. 9(8): 859-866.

Graham, G. G., J. Lembcke and E. Morales. 1990. Post-prandial plasma aminograms in the assessment of protein quality for young children: maize and grain amaranth alone and combined. Eur. J. Clin. Nutr. 44: 35-43.

Gudu, S. and V. K. Gupta. 1987. Male sterility in grain amaranth (*Amaranthus hypochondriacus* ex-Nepal) variety Jumla. Euphytica 37: 323-326.

Gudu, S. and V. K. Gupta. 1988. Electrophoresis as an aid for identification of various species and cultivars of grain amaranth. East Afr. Agric. For. J. 52(4): 244-250.

Gupta, V. K. 1984. Grain amaranth: a new crop for Kenya. Amaranth Newsletter 2: 3-5.

Gupta, V. K. and M. Pal. 1987. Grain amaranth germplasm collection in Kumaon-Garhwal Himalayas, India. Amaranth Newsletter 4: 1-6.

Gupta, V. K. and S. Gudu. 1990. Inheritance of some morphological traits in grain amaranthus. Euphytica 46: 79-84.

Imeri, A. G., L. G. Elías and R. Bressani. 1987. Amaranto: una alternativa tecnológica para la alimentación infantil. Arch. Latinoam. Nutr. 37(1): 147-159.

Imeri, A., R. Flores, L. G. Elías and R. Bressani. 1987. Efecto del procesamiento y de la suplementación con aminoácidos sobre la calidad proteínica del amaranto (*Amaranthus caudatus*). Arch. Latinoam. Nutr. 37(1): 160-173.

Imeri, A., J. M. Gonzalez, R. Flores, L. G. Elías and R. Bressani. 1987. Variabilidad genética, y correlaciones entre rendimiento, tamaño del grano, composición química y calidad de la proteína de 25 variedades de amaranto (*Amaranthus caudatus*). Arch. Latinoam. Nutr. 37(1): 132-146.

Julsrigival, S., C. Senthong, P. Wivutvonvana, V. Pataro and D. Tiyawalee. 1985. Varietal yield trials in grain amaranth. J. Agric. 1(1): 42-49.

Kalinowski, L. Sumar, O. B. Galdos and J. P. Navarro. 1986. Descriptores Para Amaranthus. 3d Edition. Programa Nacional de la Kiwicha Universidad Nacional del Cusco.

Kalinowski, L. Sumar, B. Pedersen and B. O. Eggum. 1987. The nutritive value of amaranth grain (*Amaranthus caudatus*). Plant Foods Hum. Nutr. 36: 309-324.

Lopez, M. and R. Bressani. 1987. The true metabolizable energy of amaranth (*Amaranthus* sp.) seed in poultry. Amaranth Newsletter 3.

Mendoza-Montano, C. and R. Bressani. 1987. Nutritional and functional characteristics of extrusion-cooked amaranth flour. Cereal Chem. 64(4): 218-222.

Morales, E., J. Lembcke and G. G. Graham. 1988. Nutritional value for young children of grain amaranth and maize-amaranth mixtures: effect of processing. J. Nutr. 118(1): 78-85.

Sanchez-Marroquín, A. 1983. Dos cultivos olvidados: el amaranto y la quinua. Arch. Latinoam. Nutr. 33: 11.

Sanchez-Marroquín, A. 1983. Procesamiento del amaranto en Mexico. Comparación nutricional del amaranto y la quinua. In Memoria Mesa Internacional sobre Cultivos Andinos. La Paz: FAO-IBTA 143-150.

Sanchez-Marroquín, A. and S. Maya. 1984. Effect of heat-treatment on amaranth seed quality. Arch. Latinoam. Nutr. 34.

Sanchez-Marroquín, A. and S. Maya. 1985. Industrial corn flour enrichment

with whole amaranth flour and milling fraction in corn based products. Arch. Latinoam. Nutr. 35(3): 518-535.Sanchez-Marroquín, A., S. Maya and M. V. Domingo. 1985. Milling procedures and air classification of amaranth flours. Arch. Latinoam. Nutr. 35(4): 620-630.

Sanchez-Marroquín, A., S. Maya and M. V. Domingo. 1985. Effect of heat treatment and milling on the seed, flour, rheology and baking quality of some amaranth ecotypes. Arch. Latinoam. Nutr. 35(4): 603-619.

Sanchez-Marroquín, A., M. V. Domingo, S. Maya and C. Saldaña. 1985. Amaranth flour blends and fractions for baking applications. J. Food Sci. 50(3): 789-794.

Sanchez-Marroquín, A., F. R. Del-Valle, M. Escobedo, R. Avitia, S. Maya and M. Vega. 1986. Evaluation of whole amaranth (*Amaranthus cruentus*) flour, its air-classified fractions, and blends of these with wheat and oats as possible components for infant formulas. J. Food Sci. 51(5): 1231-1234, 1238.

Sanchez-Marroquín, A., A. Feria-Morales, S. Maya and V. Ramos-Moreno. 1987. Processing, nutritional quality and sensory evaluation of amaranth enriched corn tortilla. J. Food Sci. 52(6): 1611-1614.

Soonthorn, D. 1987. Amaranth. Bangkok: Thailand Institute of Scientific and Technological Research. (In Thai)

BIOLOGICAL NITROGEN FIXATION

Badr El-Din, S. M. S. and H. Moawad. 1988. Enhancement of nitrogen fixation in lentil, faba bean and soybean by dual inoculation with rhizobia and mycorrhyzae. Plant Soil 108: 117-134.

Baldani, J. I., V. L. D. Baldani, M. J. A. M. Sampaio and J. Dobereiner. 1984. A fourth *Azospirillum* species from cereal roots. An. Acad. Bras. Cienc. 56(3): 365.

Baldani, V. L. D., M. A. de Alvarez B., J. I. Baldani and J. Dobereiner. 1986. Establishment of inoculated *Azospirillum* spp. in the rhizosphere and in roots of field grown wheat and sorghum. Plant Soil 90: 35-46.

Baldani, V. L. D., M. A. de Alvarez B., J. I. Baldani and J. Dobereiner. 1986. Characterization of *Herbaspirillum seropedicae* gen. nov., sp. nov., a root-associated nitrogen fixing bacterium. Int. J. Syst. Bacteriol. 90: 35-46.

Baldani, V. L. D., J. I. Baldani and J. Dobereiner. 1987. Inoculation of field-grown wheat with *Azospirillum* spp. in Brazil. Biol. Fertil. Soils 4: 37-40.

Bilal, R. and K. A. Malik. 1987. Isolation and identification of N2-fixing zoogloea-forming bacterium from Kallar grass histoplance. J. Appl. Bacteriol. 62(4): 289-294.

Bilal R. and K.A. Malik. 1987. Seasonal variation in rhizospheric popula-

tion of diazotrophs and root associated nitrogenase activity of some wheat mutants. Pak. J. Bot. 19(1): 29-41.

Bilal R., G. Rasul, K. Mahmood and K. A. Malik. 1990. Nitrogenase activity and nitrogen fixing bacteria associated with the roots of *Atriplex* spp. growing in saline sodic soils of Pakistan. Biol. Fertil. Soils. In press.

Bilal R., G. Rasul, J. A. Qureshi and K. A. Malik. 1990. Characterization of *Azospirillum* and related diazotrophs associated with roots of plants growing in saline soils. Mircen J. Appl. Microbiol. Biotech. In press.

Bilal R., G. Rasul, M. Arshad and K. A. Malik. 1991. Associative nitrogen fixation in plants: Attachment, colonization and proliferation of diazotrophs on the root surface. Soil Biol. Biochem. (Submitted).

Boddey, R. M. (1987). Methods for quantification of nitrogen fixation associated with Gramineae. Crit. Rev. Plant Sci. 6(3): 209-266.

Boddey, R. M. and J. Dobereiner. 1988. Nitrogen fixation associated with grasses and cereals: Recent results and perspectives for future research. Plant Soil 108: 53-65.

Boddey, R. M., V. L. D. Baldani, J. I. Baldani and J. Dobereiner. 1986. Effect of inoculation of *Azospirillum* spp. on the nitrogen assimilation of field grown wheat. Plant Soil 95: 109-121.

Boddey, R. M. and R. L. Victoria. 1986. Estimation of biological nitrogen fixation associated with *Brachiaria* and *Paspalum* grasses using 15-N labelled organic matter and fertilizer. Plant Soil 90: 265-292.

Bohlool, B. B., D. F. Bezdicek, P. Somasegaran and H. Moawad. 1988. Interstrain competition for rhizosphere colonization and nodule occupancy in the pea, lentil and chickpea/*Rhizobium* symbiosis, *in* "World Crops: Cool Season Food Legumes", R. J. Summerfield, (ed.), Kluwer Academic Publ. 675-691.

Brom, S., E. Martinez, G. Davila and R. Palacios. 1988. Narrow and broad host-range symbiotic plasmids of *Rhizobium* spp. strains that nodulate *Phaseolus vulgaris*. Appl. Environ. Microbiol. 54(5): 1280-1283.

Campos, F., J. Padilla, M. Vazquez, J. L. Ortega, C. Enriquez and F. Sanchez. 1987. Expression of nodule-specific genes in *Phaseolus vulgaris* L. Plant Mol. Biol. 9: 521-532.

Cavalcante, V. A. and J. Dobereiner. 1988. A new acid-tolerant nitrogen-fixing bacterium associated with sugarcane. Plant Soil 108: 23-31.

Cevallos, J. A., M. Vazquez, A. Davalos, G. Espin, J. Sepulveda and C. Quinto. 1989. Characterization of *Rhizobium phaseoli* Sym plasmid regions involved in nodule morphogenesis and host-range specificity. Mol. Microbiol. 3(7): 879-889.

Choonluchanon, S., N. Boonkerd and P. Swatdee. 1988. Adaptation of exotic *Azolla* to tropical environment of Thailand. Plant Soil 108: 67-70.

Christiansen-Weniger, C., R. M. Boddey and J. Dobereiner. 1985. Evaluation of nitrogen fixation in sorghum cultivars inoculated with different

strains of *Azospirillum* spp. pp. 180-188, *in* Klingmuller, W. (ed.) *Azospirillum* III: genetics, physiology, ecology: proceedings of the 3rd Bayreuth azospirillum workshop. Berlin: Springer-Verlag.

Davila, G., S. Brom, M. Florcs, M. L. Girard, V. Gonzalez, M. Louzada, J. Martinez, E. Martinez, R. Placious, D. Pinero, D. Romero and A. M. Vladez. 1988. The Symbiotic Genome of *Rhizobium phaseoli*. pp. 187-191, *in* Molecular Genetics of Plant-Microbe Interactions.

De Leon, R., M. Castellanos, M. C. de Arriola and C. Rolz. 1987. Effect of dilution rate on the biological nitrogen fixation in the *Phaseolus vulgaris-Rhizobium phaseoli* symbiosis. Biotech. Letters 9(9): 665-670.

Dianese, J. C., J. Dobereiner and L. Santos. 1989. Membrane protein patterns of three *Azospirillum* species and *Herbaspirillum seropedicae*. An. Acad. Brasil Cienc. 61: 223-230.

Dobereiner, J. and F. Pedrosa. 1987. Nitrogen-fixing Bacteria in Nonleguminous Crop Plants. Science Tech Publishers, Madison, Wisconsin. p. 155.

Dobereiner, J. 1988. Isolation and identification of root associated diazotrophs. Plant Soil 110: 207-212.

Dobereiner J., V. Reis and A. C. Lazarini. 1988. New N2-fixing bacteria in association with cereals and sugar cane. pp. 717-722, *in* Bothe, H., F. J. De Brujin and W. E. Newton (eds.). Nitrogen Fixation: Hundred Years After. Proc. 7th Int. Congr. Nitrogen Fixation. Gustav Fischer, Stuttgart, Germany.

Dobereiner, J. 1990. *Azospirillum* and *Herbaspirillum*, *in* The Procaryonts. Springer-Verlak, Berlin. In press.

Falk, E. C., J. Dobereiner, J. L. Johnson and N. R. Krieg. 1985. Deoxyribonucleic acid homology of *Azospirillum amazonense* Magalhaes et al. 1984 and emendation of the description of the genus *Azospirillum*. Int. J. System. Bacteriol. 35: 117-118.

Ferreira, M. C. B., M. S. Fernandes and J. Dobereiner. 1987. Role of *Azospirillum brasilense* nitrate reductase in nitrate assimilation by wheat plants. Biol. Fertil. Soils 4: 47-53.

Flores, M., V. Gonzalez, S. Brom, E. Martinez, D. Pinero, D. Romero, G. Davila and R. Palacios. 1987. Reiterated DNA sequences in *Rhizobium* and *Agrobacterium* spp. J. Bacteriol. 169(12): 5782-5788.

Flores, M., V. Gonzalez, M. A. Pardo, A. Leija, E. Martinez, D. Romero, D. Pinero, G. Davila and R. Palacios. 1988. Genomic instability in *Rhizobium phaseoli*. J. Bacteriol. 170(3).

Folch, J. L., A. Antaramian, L. Rodriguez, A. Bravo, A. Brunner and A. Gonzalez. 1989. Isolation and characteristization of a *Saccharomyces cerevisiae* mutant with impaired glutamate synthase activity. J. Bacteriol. 171(12): 6776-6781.

Gillis, M., K. Kersters, B. Hoste, D. Janssens, R. M. Kroppenstedt, M. P. Stephan, K. R. S. Teixeira, J. Dobereiner and J. De Ley. 1989. *Acetobacter*

diazotrophicus sp. nov., a nitrogen-fixing acetic acid bacterium associated with sugarcane. Int. J. Syst. Bacteriol. 39(3): 361-364.

Gueye, M. and Bordeleau, L. M. 1988. Nitrogen fixation in bambara groundnut, *Voandzeia subterranea* (L.) Thourars. Mircen J. 4: 365-375.

Gueye, M. 1989. Amelioration de la production du voandzou au Senegal par la fixation biologique de l'azote. *Cashiers d'Information* ISRA. 2(6): 6.

Lara, M., J. L. Ortega. B. E. Olguin and F. Sanchez. 1988. Nodulin expression and nitrogen metabolism in *Phaseolus vulgaris* root nodules. pp. 617-622, *in* Bothe, H., F. J. de Bruijn and W. E. Newton. (ed.). Nitrogen Fixation: Hundred Years After. Proc. 7th Int. Cong. on N[Triple-bond] Nitrogen Fixation. Koln, Germany.

Lima, E., R. M. Boddey and J. Dobereiner. 1987. Quantification of biological nitrogen fixation associated with sugar cane using a ^{15}N aided nitrogen balance. Soil Biol. Biochem. 19(2): 165-170.

Loureiro, M. de F. and R. M. Boddey. 1988. Balanco de nitrogenio em quatro gramineas do genero *Brachiaria*. Pesq. Agropec. Bras. 23: 1343-1353.

Magalhaes, F. M. M. and J. Dobereiner. 1984. Ocorrencia de *Azospirillum amazonense* em alguns ecosistemas da amazonia. Rev. Microbiol. 15(4): 246-252.

Malik, K. A. and Y. Zafar. 1985. Quantification of root associated N2 fixation in Kallar grass as estimated by 15N isotope dilution. *in* Nitrogen and the Environment.

Malik, K. A., Y. Zafar, R. Bilal and F. Azam. 1987. Use of ^{15}N isotope dilution for quantification of N_2-fixation associated with roots of kallar grass (*Leptochloa fusca* (L)). Biol. Fertil. Soils. 4(1/2): 103-108.

Malik, K. A. and R. Bilal. 1988. Survival and colonization of inoculated bacteria in kallar grass rhizosphere and quantification of N_2-fixation. Plant Soil 110(2): 329-338.

Malik, K. A., R. Bilal, F. Azam and M. I. Sajjad. 1988. Quantification of N2 fixation and survival of inoculated diazotrophs associated with roots of Kallar grass. Plant Soil 108: 43-51.

Malik, K. A.and R. Bilal. 1989. Survival and colonization of inoculated bacteria in kallar grass rhizosphere and quantification of N_2-fixation. Nitrogen fixation with non-legumes. Kluwer Academic Publishers. pp. 301-310.

Malik, K. A., R. Bilal, G. Rasul, K. Mahmood and M. I. Sajjad. 1990. Associative N_2-fixation in plants growing in saline sodic soils and its relative quantification based on ^{15}N natural abundance. Proc. 5th Int. Symp. Nitrogen Fixation with Non-legumes, Sept. 10-14, 1990, Florence, Italy.

Martinez, E., M. A. Pardo, R. Palacios and M. A. Cevallos. 1985. Reiteration of nitrogen fixation gene sequences and specificity of *Rhizobium* in

nodulation and nitrogen fixation in *Phaseolus vulgaris*. J. Gen. Microbiol. 131: 1779-1786.

Martinez, E., R. Palacios and F. Sanchez. 1987. Nitrogen fixing nodules induced by *Agrobacterium* harboring *Rhizobium phaseoli* plasmids. J. Bacteriol. 169(6): 2828-2834.

Martinez, E., D. Romero and R. Palacios. 1990. The *Rhizobium* genome. CRC Crit. Rev. *in* Plant Sci. 9(1): 59-93.

Miranda, C. H. B. and R. M. Boddey. 1987. Estimation of biological nitrogen fixation associated with 11 ecotypes of *Panicum maximum* grown in ^{15}N labelled soil. Agron. J. 79: 558-563.

Miranda, C. H. B., Uraiaga S. and R. M. Boddey. 1990. Selection of ecotypes of *Panicum maximum* for assisted biological nitrogen fixation using the 15m isotope dilution technique. Soil Biol. Biochem. 22(5): 657-663.

Moawad, H., S. M. S. Badr El-Din, and M. A. Khalafallah. 1987. Symbiotic nitrogen fixation by two lentil cultivars in relation to *Rhizobium* strains, competition and irrigation rates. Egypt. J. Microbiol. 22: 203-212.

Moawad, H., S. M. S. Badr El-Din, and M. A. Khalfallah. 1988. Field performance of three *Bradyrhizobium japonicum* strains with two soybean (Glycine max. L.) cultivars. Biol. Fertil. Soils. 6(2): 174-177.

Moawad, H., S. M. S. Badr El-Din, and M. A. Khalfallah. 1988. Field performance of rhizobial inoculants for some important legumes in Egypt. pp. 235-244. *in* Beck, D. P., and L. A. Materon (ed.). Nitrogen Fixation by Legumes in Mediterranean Agriculture. Dordrecht:Martinus Nijhoff 32: 235-244.

Moawad, H., M. A. Khalfallah, and S. M. S. Badr El-Din. 1988. Field Assessment of the interaction between seven soybean cultivars and three *Rhizobium japonicum* strains. Egypt. J. Microbiol. 23: 2.

Moawad, H., S. N. S. Badr El-Din and M. A. Khalfallah. 1988. Persistence and competitiveness of three *Bradyrhizobium japonicum* inoculant strains in clay loam Nile Valley soil. Plant Soil 108: 137-141.

Morett, E. S. Moreno and G. Espin. 1988. Transcription analysis of the three nifH genes of *Rhizobium phaseoli* with gene fusions. Mol. Gen. Genet. 213: 499-504.

Palacios, R., M. Flores, E. Martinez and C. Quinto. 1987. *Rhizobium phaseoli*: Nitrogen fixation genes and DNA reiteration. pp. 173-179, *in* Evans, H. J., P. J. Bottomley and W. E. Newton, (eds.). Nitrogen Fixation Research Progress. Dordrecht: Martinus Nijhoff.

Pereira, J. A. R., V. A. Cavalcante, J. I. Baldani and J. Dobereiner. 1988. Field inoculation of sorghum and rice with *Azospirillum* spp. and *Herbaspirillum seropedicae*. Plant Soil 110: 269-274.

Qureshi, J. A., Y. Zafar and K. A. Malik. 1989. *Klebsiella* sp. NIAB-I: A new diazotroph, associated with roots of kallar grass from saline sodic

soils. Nitrogen fixation with non-legumes. Kluwer Academic Publishers. pp. 115-120.

Qureshi, J. A., Y. Zafar and K. A. Malik. 1988. *Klebsiella* sp. NIAB-I A new diazotroph, associated with roots of kallar grass from saline sodic soils. Plant Soil 110: 219-224.

Reinhold, B., T. Hurek, J. I. Baldani and J. Dobereiner. 1988. Temperature and salt tolerance of *Azospirillum* spp. from salt-affected soils in Brazil. pp. 234-241. *in* Klingmuller, W., (ed.) *Azospirillum IV*: Genetics, physiology, ecology: Proceedings of the fourth Bayreuth azospirillum workshop. Berlin: Springer Verlag.

Romero, D., P. W. Singleton, L. Segovia, E. Morett, B. B. Bohlool, R. Palacios and G. Davila. 1988. Effect of naturally-occurring *nif* reiterations on symbiotic effectiveness in *Rhizobium phaseoli*. Appl. Environ. Micro. 54: 848-850.

Romero, D. and R. Palacios. 1986. Molecular genetics and BNF. Bio. Nit. Fix. Bull. 7(2): 1.

Sanchez, F., C. Quinto, M. Vazquez, H. Spaink, C. Wijffelman, M. Cevallos, A. de las Penas, F. Campos, J. Padilla and M. Lara. 1989. The Symbiotic Association of *Phaseolus vulgaris* and *Rhizobium leguminosarum* bv. *phaseoli*. from "Molecular genetics of plant-microbe interactions," eds. R. Palacios and D.P.S. Verma. pp. 370-375.

Soberon-Chavez, G., R. Najera, H. Olivera and L. Segovia. 1986. Genetic rearrangements of a *Rhizobium phaseoli* symbiotic plasmid. J. Bacteriol. 167(2): 487-491.

Soberon, M., J. Membrillo-Hernandez, G. R. Aguilar and F. Sanchez. 1990. Isolation of *Rhizobium phaseoli* Tn5-induced mutants with altered expression of cytochrome terminal oxidases o and aa3. Bacteriology 172(3): 1676-1680.

Souto, S. M. and J. Dobereiner. 1984. Metodologia para medicao da fixacao de N2 em raizes de gramineas forrageiras tropicais. Pesq. Agropec. Bras. 19(5): 553-565.

Teixeira, K. R. S., M. P. Stephan, J. Dobereiner. 1985. Variacao estacional da fixacae de N2 e assimilacao de nitrato em gramineas forrageiras tropicais. Pesq. Agropec. Bras. 20(3): 319-334.

Urquiaga, S. S. and R. M. Boddey. 1987. Theoretical considerations in the comparison of total nitrogen difference and ^{15}N isotope dilution estimates of the contribution of nitrogen fixation to plant nutrition. Plant Soil 102: 291-294.

Urquiaga, S. S., P. B. L. Botteon and R. M. Boddey. 1989. Selection of sugar cane cultivars for associated biological nitrogen fixation using ^{15}N-labelled soil. pp. 311-310, *in* Nitrogen Fixation with Non-Legumes. Kluver Acad. Publ., Dordrecht, Netherlands.

Wahid, A., E. Rasul, L. Ali, Y. Zafar and K. A. Malik. 1985. Associative

nitrogen fixation in some grasses and cereals growing around Faisalabad area. Pak. J. Agri. Sci. 22(3).

Zafar Y., M. Ashraf and K. A. Malik. 1986. Nitrogen fixation associated with roots of Kallar grass (*Leptochloa fusca* L. Kunth) Plant Soil 90: 93-105.

Zafar Y., K. A. Malik and E. G. Niemann. 1987. Studies on N2 fixing bacteria associated with salt tolerant grass *Leptochloa fusca* (L.) Kunth. Mircen J. Appl. Microbol. Biotechnol. 3(1) 45-56.

TROPICAL TREES

Arce, P. and O. Balboa. 1987. Factors que inciden en la propagacion de *Prosopis chilensis*. Cien. Inv. Agr. 4: 431.

Balboa, O. and J. M. Martinez. 1985. Actividad reductora estacional de los nodulos en algunas especies de Rhamnaceae. Medio Ambiente 7: 63-72.

Balboa, O., I. Cortes and J. P. Arce. 1987. Propagacion vegetativa de *Prosopis*: Investigaciones, problemas y perspectivas. Interciencia 12: 27-31.

Chantrasiri, S. and K. Yantasath. 1988. Krathin Thepa (*Acacia mangium*), an Interesting Fast-Growing Tree. Thai Fishmeal Producers Association Journal 8: 16-22. (in Thai)

Chantrasiri, S., K. Yantasath and P. Boonklinkajorn. 1988. Fast Growing Trees for Fuelwood. Thai Fishmeal Producers Association Journal 10: 36-43. (in Thai)

Huxley, P. A. and P. J. Wood. 1984. Technology and research considerations in ICRAF's diagnosis and design procedures. Working paper No. 26 ICRAF, Nairobi. p. 49.

Huxley, P., (ed.). 1985. Methodology for the Exploration and Assessment of Multipurpose Trees (MPT's). ICRAF, Nairobi.

Huxley, P. A. 1985. Experimental agroforestry—progress through perception and collaboration? Agroforestry Syst. 3: 129-138.

Huxley, P. 1986. Rationalizing research on hedgerow intercropping—an overview. ICRAF Working Paper No. 40, ICRAF, Nairobi, Kenya. p. 140.

Huxley, P. 1987. Agroforestry experimentation: Separating the wood from the trees. Agroforestry Syst. 5: 251-275.

Huxley, P. A., R. Mead and D. Ngugi. 1987. National Agroforestry Research Proposals for Southern African AFRENA. ICRAF. Nairobi. p. 90.

Huxley, P. 1988. An ecological approach to on-farm experimentation. (with Mead, R.). ICRAF Working Paper No. 52. ICRAF, Nairobi. p. 39.

Huxley, P. 1989. Experimental Agroforestry. pp. 332-353. *in* MacKicken, K. G. (ed.). Agroforestry, classification and management. Wiley.

Huxley, P. A. 1989. The Tree/crop interface: A Project Designed to Generate Experimental Methodology. Agroforestry Abstracts. 2.

Huxley, P. A., T. Darnhofer, D. Gatama and E. Akunda. 1989. The rainfall distribution at a tree crop interface. pp. 371-382. *in* Reifsnyder, W. E. and T. Darnhofer, (ed.). Proc. of the ICRAF/WMO/UNEP Workshop on Application of Meteorology to Agroforestry systems Planning and Management. ICRAF, Nairobi, Kenya.

Huxley, P. A., E. Akunda, T. Darnhofer, D. Gatama and A. Pinney. 1989. Tree/crop interface investigations. Preliminary results with *Cassia siamea* and maize. pp. 361-370. *in* Reifsnyder, W. E. and T. Darnhofer (ed.). Proc. of the ICRAF/WMO/UNEP Workshop on Application of Meteorology to Agroforestry systems Planning and Management. ICRAF, Nairobi, Kenya.

Jordan, M. and O. Balboa. 1985. *In vitro* regeneration of *Prosopis tamarugo* Phil. and *P. chilensis* (mol.) Stuntz from nodal sections. Gartenbauwissenschaft 50: 138-142.

Jordan, M., G. Montenegro, O. Balboa and I. Cortez. 1985. Propagacion de plantas economicamente importantes en zonas aridas de Chile. Medio Ambiente 7: 53-62.

Jordan, M., J. Pedraza and A. Goreux. 1985. *In vitro* propagation of three *Prosopis* species (*P. alba*, *P. chilensis* and *P. tamarugo*) through shoot-tip culture. Gartenbauwissenschaft 50(6): 265-267.

Jordan, M. 1987. *In vitro* culture of *Prosopis* species. 3: pp. unknown. *in* Bonga, J.M., D. J. Durzan (ed.). Cell and Tissue Culture in Forestry. Dordrecht, Netherlands: Martinus Nijhoff.

Ramires, S. H. and M. Valdes. 1989. Sewage watering at the nursery improves growth and nodulation of cascarinas. Nitrogen Fixing Tree Res. Rep. 7: 87-88.

Silvester, W. B., O. Balboa and J. A. Martinez. 1985. Nodulation and nitrogen fixation in members of the Rhamnaceae (*Colletia*, *Talguenea*, *Retanilla*, y *Trevoa*) growing in the Chilean matorral. Symbiosis 1: 29-38.

Kovitvadhi, K. and K. Yantasath. 1982. Research on *Leucaena* and Other Nitrogen-Fixing Trees at the Thailand Institute of Scientific and Technological Research (TISTR). Proceedings of a Workshop "Leucaena Research in the Asian-Pacific Region" held in Singapore, 23-26 November 1982. IDRC-211 : 133-136.

Yantasath, K. 1983. Fast growing Trees for Agricultural and Industrial Purposes. Thailand Institute of Scientific and Technological Research TISTR Research News. February 1983: 2 p. (in Thai)

Yantasath, K., et al. (1985) I. Species trials of nitrogen-fixing trees. II. Spacing trials of nitrogen-fixing trees. III. Determination of biomass production of NFT using allometric regression equation. IV. Tissue analysis and heating parameters of NFT. V. Pulping and papermaking characteristics of fast growing trees. Nitrogen Fixing Tree Research Reports 3: 48-56 1985. NFTA Waimanalo, Hawaii/U.S.A.

Yantasath, K. 1985. Krathin Thepa (*Acacia mangium*), an interesting fast-growing tree. Thailand Institute of Scientific and Technological Research TISTR Special Report. 22 p. (in Thai)

Yantasath, K. 1985. A Manual for Cultivation of *Acacia mangium*. Thailand Institute of Scientific and Technological Research TISTR Special Report. 15 p. (in Thai)

Yantasath, K., et al. 1986. Research on fast growing nitrogen-fixing trees at Thailand Institute of Scientific and Technological Research. Proc. of the Symposium on Forest Regeneration in Southeast Asia. Bio-trop. Spec. Publ. No. 25: 110-120, Bogor, Indonesia.

Yantasath, K., et al. 1987. Management of Production of selected Nitrogen Fixing Trees. Proc. of His Majesty's Fifth Cycle Commemorative Conference of USAID Science Research Award Grantees. Nakhonpathom. Thailand. 24-26 July 1987. pp. 361-366. The Ministry of Science Technology and Energy/U.S. Agency for International Development/Silpakorn University.

Yantasath, K. 1987. Field Trials and Testing of Selected Species of Fast-Growing Nitrogen-Fixing Trees. Proc. of an International Workshop, Australia, August 1986 ACIAR Proc. No. 16: 176-179.

Yantasath, K., et al. 1987. Field Trials and Multipurpose Testings of Selected Fast-Growing, Nitrogen-Fixing Trees in Thailand. TISTR Special Report. 46 pp.

Yantasath, K. and J. Watanakul. 1987. New Psyllid Pest on *Leucaena* in Thailand. Leucaena Research Report 7(2): 83 NFTA, Weimanalo, Hawaii, U.S.A.

Yantasath, K. 1989. Fast-Growing Trees for Fuelwood Energy. Science and Technology Journal 3: 16-19. Thailand Institute of Scientific and Technological Research. (in Thai)

Yantasath, K. 1990. Case Study in Multipurpose Tree Species. Proc. Thai-Nordic Forest Tree Improvement Training Course in Thailand. 23 May-15 June 1990. Chiang Mai. DTEC/RFD/DANIDA/SIDA. In press.

MOSQUITO VECTOR RESEARCH

Adames, A., B. Dutary, P. Galindo, V. M. Tejeira, L. De Leon and E. Adames. 1990. Relacion entre Mosquito Vectores y Aves Acuaticas en la transmission potencial de dos arboviruses. Scientia, In press.

Amerasinghe, F. P. and N. B. Munasingha. 1985. A survey of medically important mosquitoes in Kandy. Proc. Kandy Soc. Med. 8: 30-31.

Amerasinghe, F. P. and N. B. Munasingha. 1985. Anopheline breeding in a dry zone forest in Mahaweli System-C. Proc. Sri Lanka Assoc. Advancement Sci. 41(1): 70.

Amerasinghe, F. P. and N. B. Munasingha. 1985. Further observations on

the mosquito fauna of Udawattakell Forest, Sri Lanka. Ceylon J. Sci. (Bio. Sci.) 17-18: 1-21.

Amerasinghe, F. P. 1986. Current studies on vector populations in areas under development in Mahaweli System C. pp. 14-21, *in* Colwell, R. (ed.). Proceedings of the workshop on irrigation and vector borne disease transmission. Published by the International Irrigation Management Institute.

Amerasinghe, F. P. and N. B. Munasingha. 1986. Ecology of the Japanese encephalitis vector *Culex tritaeniorhynchus*. Proc. Sri Lanka Assoc. Advancement Sci. 42(1): 1.

Amerasinghe, F. P., N. B. Munasingha and V. L. Kulasekera. 1987. Some new records of mosquitoes occurring in Sri Lanka. Mosq. Syst. 19(2): 162-166.

Amerasinghe, F. P. and N. B. Munasingha. 1988. A predevelopment mosquito survey in the Mahaweli development project area, Sri Lanka: Adults. J. Med. Entomol. 25(2): 276-285.

Amerasinghe, F. P. and N. B. Munasingha. 1988. A predevelopment mosquito survey in the Mahaweli development project area, Sri Lanka: Immatures. J. Med. Entomol. 25(2): 286-294.

Amerasinghe, F. P., J. S. M. Peiris, S. H. P. P. Karunaratne and P. H. Amerasinghe. 1988. Epidemiology of the 1987 Japanese encephalitis outbreak in the Anuradhapura area. II. Entomological aspects. Proc. Sri Lanka Med. Assoc. 101: 22-23.

Amerasinghe, F.P. 1989. Redescription of *Heizmannia (Heizmannia) greenii* (Theobald) from Sri Lanka (Diptera: Culicidae). Mosq. Syst. 21(2): 83-99.

Amerasinghe, F. P. and N. B. Munasingha. 1989. The seasonality of some abundant mosquito species in Kandy, Sri Lanka. Proc. Intern. Conf. Biol. Contr. Pests Med. Agric. Import., Madurai, India. p. 116.

Amerasinghe, F. P., P. H. Amerasinghe, N. G. Indrajith, A. M. S. Rathnayake, Y. G. Ariyarathne, W. Somapala, J. S. M. Peiris, C. Ratnayake and S. Wickremaratne. 1989. Japanese encephalitis activity in Anuradhapura during the 1988-89 northeast monsoonal period. Proc. Sri Lanka Assoc. Advancement Sci. 45: 19-20.

Amerasinghe, F. P., P. H. Amerasinghe, M. de S. Wijesundera and J. S. M. Peiris. 1989. A study of malaria in Mahaweli System-C. II. Vector aspects. Proc. Sri Lanka Med. Assoc. 102: 47.

Amerasinghe, F. P. and T. G. Ariyasena. 1990. Larval survey of surface water-breeding mosquitoes during irrigation development in the Mahaweli Project, Sri Lanka. J. Med. Entomol. 27(5): 789-802.

Amerasinghe, F. P. and T. G. Ariyasena. 1991. A survey of adult mosquitoes (Diptera: Culicidae) during irrigation development in the Mahaweli Project, Sri Lanka. J. Med. Entomol. 28(3): 387-393.

Arunagiri, C. K., S. B. Abeykoon, F. P. Amerasinghe and J. S. M. Peiris.

1987. Comparison of methods for the isolation of arboviruses from mosquitoes. Proc. Sri Lanka Assoc. Advancement Sci. 43(1): Suppl. p. 1.

Arunagiri, C. K., J. S. M. Peiris and L. P. Perera. 1986. Japanese encephalitis virus activity in the Central Province of Sri Lanka. Proc. Kandy Soc. Med. 9: 20-21.

Chang, M. S., N. Jute and J. Lah. 1988. Breeding-site productivity of the swamp forest mosquitoes *Mansonia bonneae* and *Ma. dives* in Sarawak, East Malaysia. Med. Vet. Entomol. 2: 19-28.

Conn, J. 1990. A genetic study of the malaria vector *Anopheles nuneztovari* from Western Venezuela. J. Am. Mosq. Control Assoc. 6(3): 400-405.

Conn, J. 1991. A cytogenetic analysis of the polytene chromosomes of *Anopheles triannulatus* (Diptera: Culicidae) from Western Venezuela. Genome, In press.

Faye, O. 1987. Contribution to the study of *Anophelinae* (Diptera, Culicidae) and malaria transmission in the zone of the Bignona anti-salt dam (Ziguinchor, Senegal). Ph.D. Thesis, University of Dakar, Senegal.

Faye, O., S. Diallo, O. Gaye, O. Ndir, I. B. Bah, I. Gueye, A. Victorius and O. Faye. 1990. Contribution to the study of the Anophelinae (Diptera, Culicidae) in the Bignona River basin (Senegal). I. Adult anopheline fauna. Bull. Inst. Fr. Afr. Noire Ser. A. 48(1): 90-105.

Faye, O., S. Diallo, O. Gaye, O. Ndir, I. B. Bah, I. Gueye, A. Victorius and O. Faye. 1990. Contribution to the study of the Anophelinae (Diptera, Culicidae) in the Bignona River basin (Senegal). II. Bioecology of the larvae of *Anopheles gambiae* s.l. Giles. Bull. Inst. Fr. Afr. Noire Ser. A. 48(1): 106-121.

Faye, O., S. Diallo, O. Gaye, O. Ndir, I. B. Bah, I. Gueye, A. Victorius and O. Faye. 1990. Contribution to the study of the Anophelinae (Diptera, Culicidae) in the Bignona River basin (Senegal). III. Bioecology of the females of *Anopheles gambiae* s.l. Giles. Bull. Inst. Fr. Afr. Noire Ser. A. 48(1): 122-140.

Faye, O., S. Diallo, O. Gaye, O. Ndir, I. B. Bah, I. Gueye, A. Victorius and O. Faye. 1990. Contribution to the study of the Anophelinae (Diptera, Culicidae) in the Bignona River basin (Senegal). IV. Quantitative study of malaria transmission. Bull. Inst. Fr. Afr. Noire Ser. A. 48(1): 141-152.

Forattini, O. P. and M. A. M. Sallum. 1985. A new species of *Culex* (*Melanoconion*) from Southern Brazil (Diptera: Culicidae). Rev. Saude Publica 19: 171-182.

Forattini, O. P. and M. A. M. Sallum. 1987. Studies on some species of *Culex* (*Melanoconion*), with the description of a new one from Southern Brazil (Diptera: Culicidae). Rev. Saude Publica 21(2): 123-156.

Forattini, O. P., A. de C. Gomes, D. Natal, I. Kakitani and D. Marucci. 1987. Feeding preferences of Culicidae mosquitoes in the Ribeira Valley, S. Paulo State, Brazil. Rev. Saude Publica 21: 171-187.

Forattini, O. P., A. de C. Gomes, D. Natal, I. Kakitani and D. Marucci.

1987. Developing domiciliarity of Ribeira Valley mosquitoes, S. Paulo, Brazil. Rev. Saude Publica 21(3): 188-92.

Forattini, O. P. and M. A. M. Sallum. 1989. Redescription of *Culex* (*Melanoconion*) *sacchettae* Sirivanakarn and Jakob, 1981 with the description of immature stages (Diptera: Culicidae). Mosq. Syst. (21): 117-132.

Forattini, O. P. and M. A. M. Sallum. 1989. A new species of *Culex (Melanoconion)* from the Atlantic tropical system of southern Brazil (Diptera: Culicidae). Mem. Inst. Oswaldo Cruz 84: 1-4.

Forattini, O. P. and M. A. M. Sallum. 1989. Redescription of *Culex (Melanoconion) delpontei* Duret, 1968 and *Cx. (Mel.) pereyrai* Duret, 1967, from southern Brazil. Proc. Entomol. Soc. Wash. 91: 473-485.

Forattini, O. P., A. de C. Gomes, D. Natal, I. Kakitani and D. Marucci. 1989. Feeding preferences and domiciliation of Culicidae mosquitoes in the Ribeira Valley, S. Paulo State, Brazil, with particular reference to *Aedes scapularis* and *Culex (Melanoconion)*. Rev. Saude Publica 23: 9-19.

Forattini, O. P., A. de C. Gomes and I. Kakitani. 1989. Observations on adult Culicidae in a rice field of the Ribeira Valley, S. Paulo State, Brazil. Rev. Saude Publica 23: 307-312.

Hayes, J., G. Calderon, R. Falcon and V. Zambrano. 1987. Newly incriminated anopheline vectors of human malaria parasites in Junin Department, Peru (Diptera: Culicidae). J. Am. Mosq. Control. Assoc. 3: 418-422.

Hii, J. L. K. 1985. Genetic investigations of laboratory stock of the complex of *Anopheles balabacensis* Baisas (Diptera: Culicidae). Bull. Entomol. Res. 75: 185-197.

Hii, J. L. K. and Y. S. Vun. 1985. A study of dispersal, survival and adult population estimates of the malaria vector, *Anopheles balabacensis* Baisas (Diptera: Culicidae) in Sabah, Malaysia. Trop. Biomed. 2: 121-131.

Hii, J. L. K., S. Kan, Y. S. Vun, K. F. Chin, M. S. Lye, J. W. Mak and W.H. Cheong. 1985. *Anopheles flavirostris* incriminated as a vector of malaria and Bancroftion filariasis in Banggi Island, Sabah, Malaysia. Trans. R. Soc. Trop. Med. Hyg. 79: 677-680.

Hii, J. L. K. and Y. S. Vun. 1987. The influence of a heterogeneous environment on host feeding behaviour by *Anopheles balabacensis* (Diptera: Culicidae). Trop. Biomed. 4: 67-70.

Hii, J. L. K., M. Chew, Y. S. Vun, M. Nasir and M. S. Chang. 1988. Enzyme Polymorphism of the Malaria Vector, *An. Balabacensis* (Diptera: Culicidae) Revisited - Why Sample Natural Populations? Southeast Asian J. Trop. Med. Public Health. 19(4): 689-701.

Hii, J. L. K., E. L. Peyton and V. Y. Shang. 1988. Redescription of the adult and first descriptions of the larva and pupa of *Anopheles (Cellia) sulawesi* Waktoedi, a species of the Leucosphyrus Group from Sulawesi, Indonesia (Diptera: Culicidae). Mosq. Syst. 20(1): 41-54.

Hii, J. L. K., M. H. Birley and V. Y. Sang. 1990. Estimation of survival rate

and oviposition interval of *Anopheles balabacensis* mosquitoes from mark-recapture experiments in Sabah, Malaysia. Med. Vet. Entomol. 4: 135-140.

Hii, J. L. K., M. Chew, Y. S. Vun, L. E. Munstermann, S. Panyim and Y. Yasothornsrikul. 1991. Population genetic analysis of host seeking and resting behavior in the malaria vector, *Anopheles balabacensis* (Diptera: Culicidae). J. Med. Entomol. 28: In press.

Jayanetti, S. R., H. A. S. Perera, S. S. Ariyaratne and M. de S. Wijesundera. 1987. Population dynamics and the medical significance of peridomestic mosquitoes in residential areas in Kandy. Proc. Kandy Soc. Med. 10: 2.

Jayanetti, S. R., H. A. S. Perera, S. S. Ariyaratne and M. de S. Wijesundera. 1987. Filarial carriage by peridomestic mosquitoes in residential areas in Kandy. Abst. 47th Ann. Sess. Galle Clinical Soc. p. 26.

Jayanetti, S. R., H. A. S. Perera and M. de S. Wijesundera. 1987. Observations on indoor resting mosquitoes in settlement areas in Mahaweli System C. Proc. Kandy Soc. Med. 10: 1.

Jayanetti, S. R., M. de S. Wijesundera and F. P. Amerasinghe. 1987. A study of the bionomics of indoor resting mosquitoes in Kandy. Ceylon J. Med. Sci. 30: 47-62.

Jayanetti, S. R., H. A. S. Perera and M. de S. Wijesundera. 1988. Evaluation of the CDC gravid mosquito trap for sampling peridomestic mosquitoes in the incrimination of filarial vectors. Mosq. Borne Dis. Bull. 5: 18-21.

Jayanetti, S. R., M. de S. Wijesundera and F. P. Amerasinghe. 1988. Temporal variations in relative densities of indoor resting mosquitoes in Kandy. Proc. Sri Lanka Assoc. Advancement Sci. 44: 8.

Jayanetti, S. R., M. de S. Wijesundera and F. P. Amerasinghe. 1988. Temporal variations in relative densities of indoor resting mosquitoes in Mahaweli System C. Proc. Sri Lanka Assoc. Advancement Sci. 44: 9.

Kertbundit, S., P. Rajkulchai, A. Kashemsanta and S. Panyim. 1986. Molecular cloning in *E. coli* of the DNA fragments specific for *Anopheles dirus* B. ICSU Short Rep. 6: 144-145.

Lounibos, L. P. and J. Conn. 1991. Fecundity, parity, and adult feeding relationships among *Nyssorhynchus* malaria vectors from Venezuela. Mem. Inst. Oswaldo Cruz, In press.

Lutwama, J. J. 1990. Morphological and ecological differentation in *Aedes simpsoni* complex in East Africa. Ph.D. Thesis, University of Makerere, Uganda.

Lutwama, J. J. and L. G. Mukwaya. 1988. Behavioural and ecological diversity of *Aedes simpsoni* complex (Diptera: Culicidae) in Africa. XII Int. Congr. Trop. Med. and Mal., Amsterdam.

Marten, G. G., R. Astaiza, M. F. Suarez, C. Monje and J. W. Reid. 1989. Natural control of larval *Anopheles albimanus* (Diptera: Culicidae) by the predator *Mesocyclops* (Copepoda: Cyclopoida). J. Med. Entomol. 26(6): 624-627.

Monje, C., M. F. Suarez, M. L. Quinones, M. Ramirez and C. Velez. 1987. Variacion genetica detectada electroforeticamente en poblaciones naturales del mosquito *Anopheles albimanus* en Colombia. Biomedica 6(1): 17.

Mpofu, S. M. and H. T. Masendu. 1986. Description of a baited trap for sampling mosquitoes. J. Am. Mosq. Control Assoc. 2(3): 363-365.

Mukiama, T. K. 1987. Genetic variation in wild *Anopheles arabiensis* Patton of Mwea Irrigation Scheme, Kenya. Insect Sci. Appl. 8(2): 245-249.

Mukiama, T. K. 1988. Genetics as a component of vector mosquito control in East Africa. Modern Insect Control: Nuclear Techniques and Biotechnology. IAEA-SM-301/34, pp. 163-177.

Mukiama, T. K. and R. W. Mwangi. 1989. Field studies of larval *Anopheles arabiensis* Patton of Mwea Irrigation Scheme, Kenya. Insect Sci. Appl. 10(1): 55-62.

Mukiama, T. K. and R. W. Mwangi. 1989. Seasonal population changes and malaria transmission potential of *Anopheles pharoensis* and the minor anophelines in Mwea Irrigation Scheme, Kenya. Acta Trop. 46: 181-189.

Mukiama, T. K. and R. W. Mwangi. 1990. Population and cytogenetic observations on *Anopheles arabiensis* Patton of Mwea Irrigation Scheme, Kenya. Insect Sci. Appl. 11(2): 119-131.

Mukwaya, L. G. 1986. Feeding preference by the male blowfly *Phormia regina* for some natural foods and its relation to carbohydrate, amino acid and alcohol content. Entomol. Exp. Appl. 41: 203-212.

Mukwaya, L. G., L. E. Munstermann, J. J. Lutwama and J. P. Mutebi. 1988. Preliminary studies on variations in morphology and isozymes of *Aedes simpsoni* complex and *Aedes africanus* (Diptera: Culicidae). XII Int. Congr. Trop. Med. and Mal., Amsterdam.

Munasingha, N. B. and F. P. Amerasinghe. 1986. Bionomics of *Anopheles* (*Cellia*) *vagus* in Kandy. Proc. Sri Lanka Assoc. Advancement Sci. 42(1): 129.

Mwangi, R. W. and T. K. Mukiama. 1988. Evaluation of *Melia volkensii* extract fractions as mosquito larvacides. J. Am. Mosq. Control Assoc. 4(4): 442-447.

Narang, S. K., J. A. Seawright and M. F. Suarez. 1991. Genetic structure of natural populations of *Anopheles albimanus* in Colombia. J. Am. Mosq. Control Assoc. 7: In press.

Narang, S. K., J. A. Seawright, N. L. Willis and M. F. Suarez. 1987. Genetic variability and mapping of peptidase-4 in *Anopheles albimanus*. J. Hered. 78: 278-279.

Natal, D. and D. Marucci. 1984. Aparelho de succao tipo aspirador para captura de mosquitos. Rev. Saude Publica. 18: 418-421.

Panyim, S., S. Yasothornsrikul and V. Baimai. 1988. Species-specific DNA sequence from the *Anopheles dirus* complex: a potential for efficient identification of isomorphic species. pp. 193-202, *in* Service, M. W. (ed.). Biosystematics of Haematophagous Insects. Oxford Univ. Press.

Panyim, S., S. Yasothornsrikul, S. Tungpradabkul, V. Baimai, R. Rosenberg, R. G. Andre and C. A. Green. 1988. Identification of isomorphic malaria vectors using a DNA probe. Am. J. Trop. Med. Hyg. 38(1): 47-49.

Peiris, J. S. M., C. K. Arunagiri, L. P. Perera, F. P. Amerasinghe and S. H. P. P. Karunaratne. 1987. Studies on the epidemiology of Japanese encephalitis in Sri Lanka. Proc. Sri Lanka Med. Associ. 100: 48-49.

Peiris, J. S. M., N. Jayatilleke and L. P. Perera. 1987. Viral prozone in the macrophage cell line P388D1 as mediated by interferon. Proc. VIIth Int. Congr. Virol., Edmonton, Canada. p. 200.

Peiris, J. S. M., L. P. Perera, F. P. Amerasinghe and N. B. Munasingha. 1986. Studies on arbovirus infection in the Kandy and Mahaweli System C. Proc. Sri Lanka Med. Assoc. 99: 61.

Peiris, J. S. M., L. P. Perera, C. K. Arunagiri and F. P. Amerasinghe. 1986. Arboviruses in Sri Lanka. Proc. First Intern. Conf. Impact Viral Dis. Develop. Asian Countries, Bangkok, Thailand. p. 177.

Peiris, J. S. M., L. P. Perera, F. P. Amerasinghe and N. B. Munasingha. 1987. A study of arboviruses and vectors in an area undergoing human settlement in an urban area in Sri Lanka. pp. 176-179, *in* George, T. D. St., B. H. Kay and J. Blok. (eds.). Arbovirus research in Australia. Proc. Fourth Arbovirus Symp. CSIRO-QIMR, Queensland, Australia.

Peiris, J. S. M., L. P. Perera and C. K. Arunagiri. 1987. The application of the antibody dependent plaque enhancement test in seroepidemiological surveys. Proc. VII Intern. Cong. Virol., Edmonton, Canada. p. 322.

Peiris, J. S. M., L. P. Perera, C. K. Arunagiri and S. B. Abeykoon. 1987. Arboviruses in Sri Lanka. IV. California encephalitis serogroup viruses. Proc. Sri Lanka Med. Assoc. 100: 49-50.

Peiris, J. S. M., L. P. Perera, C. K. Arunagiri and F. P. Amerasinghe. 1987. A survey of arboviruses in Sri Lanka. Proc. VII Intern. Cong. Virol., Edmonton, Canada. p. 231.

Peiris, J. S. M., C. R. Ratnayake, W. M. S. Kularatne, C. Arunagiri and F. P. Amerasinghe. 1988. Epidemiology of the 1987 Japanese encephalitis outbreak in the Anuradhapura area. I. Correlation of porcine infection with human disease. Proc. Sri Lanka Med. Assoc. 101: 22.

Perera, L. P. 1985. Survey of Mosquito-borne Arboviruses in an Urbanized Environment and an Area Under Agricultural Development. M. Phil. Thesis, University of Peradeniya, Sri Lanka.

Perera, L. P., J. S. M. Peiris and S. Gamage. 1985. A seroepidemiological study of arboviral infections in the Kandy area. Proc. Kandy Soc. Med. 8: 31-32.

Perera, L. P. and J. S. M. Peiris. 1986. Arboviruses in Sri Lanka. II. Bunyaviruses of the Simbu serogroup. Proc. Sri Lanka Assoc. Advancement Sci. 42(1): 21.

Perera, L. P., J. S. M. Peiris, F. P. Amerasinghe and N. B. Munasingha.

1986. Arboviruses in Sri Lanka. I. Batai virus. Proc. Sri Lanka Assoc. Advancement Sci. 42(1): 20.

Perera, L. P., J. S. M. Peiris, D. J. Weilgama and C. K. Arunagiri. 1986. Arboviruses in Sri Lanka. III. Tick-borne arboviruses. Proc. Sri Lanka Assoc. Advancement Sci. 42: 21-22.

Prasittisuk, C., M. Prasittisuk, S. Ketrangsee, A. Lucchini, S. Phatipongse, B. Aumaung and S. Malikul. 1989. *Anopheles dirus* species A, a major malaria vector in Eastern Thailand. Third Conf. Malar. Res., Thailand. WHO(SEARO). Chiang Mai, Thailand. p. 172.

Prasittisuk, C., M. Prasittisuk, S. Phatipongse, S. Ketrangsee, S. Krachaiklin, B. Aumaung, P. Chaiprasitthigul, A. Lucchini and S. Ngarmathom. 1989. Epidemiological aspects of malaria transmission in eastern Thailand. Third Conf. Malar. Res., Thailand. WHO(SEARO). Chiang Mai, Thailand. pp. 22-23.

Prasittisuk, M., C. Prasittisuk, T. Chareonviriyaphap, P. Chaiprasitthikul, B. Aumaung, S. Ngarmpathom and R. A. Wirtz. 1989. Malaria sporozoite density from natural population of *Anopheles dirus*. Third Conf. Malar. Res., Thailand. WHO(SEARO). Chiang Mai, Thailand. p. 211.

Prasittisuk, M., C. Prasittisuk, S. Phatipongse, J. Gingrich, P. Mongklangkul and S. Ruangthai. 1989. Day-biting anopheline mosquitoes: possible daytime malaria transmission. Third Conf. Malar. Res., Thailand. WHO(SEARO). Chiang Mai, Thailand. p. 213.

Quinones, M. L. and M. F. Suarez. 1989. Irritability to DDT of natural populations of the primary malaria vectors in Colombia. J. Am. Mosq. Control Assoc. 5(1): 56-59.

Rajkulchai, P., S. Tungpradubkul and S. Panyim. 1986. Molecular cloning of repetitive DNA from *Anopheles dirus A*. Proc. 12th Conf. Sci. Technol. Thailand. p. 410.

Ratanatham, E., S. Upatham, C. Prasittisuk, W. Rojanasunan, N. Theerasilp, A. Tremongkol and V. Viyanant. 1988. Bionomics of *Anopheles minimus* and its role in malaria transmission in Thailand. Southeast Asian J. Trop. Med. Public Health 19(2): 283-289.

Sallum, M. A. M., K. Uramoto and O. P. Forattini. 1988. Redescription and resurrection from synonymy of *Aedes (Ochlerotatus) rhyacophilus* Costa Lima, 1933. Mem. Inst. Oswaldo Cruz 83: 67-77.

Suarez, M. F., S. K. Narang and J. A. Seawright. 1987. Variaciones en los patrones de pigmentacion y de color de larvas de poblaciones naturales de *Anopheles albimanus* de Colombia. Biomedica 6(3): 489-494.

Upatham, S., C. Prasittisuk, S. Ratanatham, C. A. Green, W. Rojanasunan, P. Setakana, N. Theerasilp, A. Tremongkol, V. Viyanant, S. Pantuwatana and R. G. Andre. 1988. Bionomics of *Anopheles maclatus* complex and their role in malaria transmission in Thailand. Southeast Asian J. Trop. Med. Public Health 19(2): 259-269.

Wijesundera, M. de S., D. Athureliya and C. S. Ariyaratne. 1985. Studies on transmission of filariasis in Kandy. Proc. Kandy Soc. Med. 8(1): 28-29.

Wijesundera, M. de S., J. Seneviratne and C. S. Ariyaratne. 1987. Chloroquine resistant falciparum malaria: is amodiaquine of value? Abst. 47th Ann. Sess. Galle Clinical Soc. pp. 25-26.

Wijesundera, M. de, J. S. M. Peiris, J. Seneviratne and C. S. Ariyaratne. 1987. An outbreak of falciparum malaria in the vicinity of Kandy: I. Epidemiological characteristics. Proc. Kandy Soc. Med. 10: 7-8.

Wijesundera, M. de S., J. Seneviratne and C. S. Ariyaratne. 1987. An outbreak of falciparum malaria in the vicinity of Kandy: II. Clinical profile. Proc. Kandy Soc. Med. 10: 8-9.

Wijesundera, M. de S. 1988. Malaria outbreaks in new foci in Sri Lanka. Parasitol. Today 4(5): 147-150.

Wijesundera, M. de S., J. S. M. Peiris, C. S. Ariyaratne and S. Kularatne. 1989. A study of malaria in Mahaweli System C: Morbidity patterns. Proc. Sri Lanka Med. Assoc. 102: 46-47.

Wijesundera, M. de S., J. S. M. Peiris, Y. G. Ariyarathne, A.S. Verdini, A. Pessi and G. del Guidice. 1989. The sporozoite antibody response in an outbreak of falciparum malaria in a non-endemic area in Sri Lanka. Proc. Sri Lanka Med. Assoc. 102: 47-48.

Wijesundera, M. de S., J. S. M. Peiris, Y. G. Ariyarathne, A. S. Verdini, A. Pessi and G. del Guidice. 1990. Antibodies to *Plasmodium falciparum* sporozoites following a malaria outbreak in a non-endemic area in Sri Lanka. Trans. R. Soc. Trop. Med. Hyg. 84: 35-39.

Yasothornsrikul, S., N. Tirawanchai, P. Rajkulchai, S. Tungpradabkul and S. Panyim. 1985. A simple method for extraction of high molecular weight DNA, with quality suitable for recombinant DNA experiments from whole mosquitoes. Proc. 11th Conf. Sci. Technol., Thailand. p. 300.

Yasothornsrikul, S., S. Tungpradabkul, S. Kertbundit, P. Rajkulchai, A. Kashemsanta and S. Panyim. 1986. DNA probe for anopheline mosquito sibling species identification. Proc. 2nd Conf. Malaria Res., Thailand. p. 166.

Yasothornsrikul, S., S. Tungpradabkul and S. Panyim. 1986. Species specific DNA probe for identification of *Anopheles dirus* sibling species D. ICSU Short Rep. 6: 142-143.

Yasothornsrikul, S., S. Tungpradabkul, S. Panyim and R. Rosenberg. 1988. Diagnostic restriction fragment patterns of DNA from the four isomorphic species of *Anopheles dirus*. Southeast Asian J. Trop. Med. Public Health 19(4): 703-707.

RAPID EPIDEMIOLOGIC ASSESSMENT

Albala, C., M. L. Alvarez, M. Aguayo, M. Araya, D. Ballester, O. Brunser, I. Contreras, J. Espinoza, G. Figueroa, V. Gattás, N. González, S. Jarpa, F. Mardones-Restat et al. 1988. Prevención de la desnutrición durante los primeros años de vida. pp. 139-171. *in* Monckeberg, F. (ed.). Desnutrición infantil: fisiopatología clinica, tratamiento y prevención. Nuestra experiencia chilena. Santiago, Chile. Impresora Creces Ltda.

Baltazar, J., J. Briscoe and B. Young. 1988. Case-control studies of the effect of environmental sanitation on diarrhoea morbidity: methodological implications of field studies in Africa and Asia. Int. J. Epidemiol. 17(2): 441-447.

Baltazar, J., J. Briscoe, V. Mesola, C. Moe, F. Solon, J. Vanderslice and B. Young. 1988. Can the case-control method be used to assess the impact of water supply and sanitation on diarrhoea? A study in the Philippines. Bull. WHO 66(5): 627-635.

Baltazar, J. C. and F. S. Solon. 1989. Disposal of faeces of children under two years old and diarrhoea incidence: a case-control study. Int. J. Epidemiol. 18, No. 4 (Suppl. 2): S16-S19.

Barreto-Lins, M. H., F. A. Campos, M. C. Azevedo and H. Flores. 1988. A re-examination of the stability of retinol in blood and serum, and effects of a standardized meal. Clin. Chem. 34(11): 2308-2310.

Bicego, G., A. Augustin, S. Musgrave, J. Allman and P. Kelly. 1989. Evaluation of a simplified method for estimation of early childhood mortality in small populations. Int. J. Epidemiol. 18 (Suppl 2): S20-S32.

Campos, F. A. C. S., H. Flores and B. A. Underwood. 1987. Effect of an infection on vitamin A status of children as measured by the relative dose response (RDR). Am. J. Clin. Nutr. 46(1): 91-94.

Chew, F., J. Villar, N. W. Solomons and R. Figueroa. 1988. *In vitro* hydrolysis with a beta-galactosidase for treatment of intolerance to human milk in very low birthweight infants. Acta Paediatr. Scand. 77(4): 601-602.

Coreil, J., A. Augustin, E. Holt and N. A. Halsey. 1989. Use of ethnographic research for instrument development in a case-control study of immunization use in Haiti. Int. J. Epidemiol. 18, No. 4 (Suppl. 2): S33-S37.

Domingo, E. O., A. L. Lingao, M. A. Lansang, J. Y. Lao and S. K. West. 1985. Epidemiology and prevention of persistent HBV infection; country report from the Philippines. pp. 97-105, *in* Hepatocellular Carcinoma in Asia. Japan International Center for Medical Research.

Durkin, M., L. Davidson, M. Hasan, N. Khan, M. Thorburn and S. Zaman. 1990. Screening for childhood disabilities in community settings. pp. 179-199, *in* Thorburn, M. J., K. Morfo and others (eds.). Practical Approaches to Childhood Disability in Developing Countries: Insights from Experience and Research. Project SEREDEC, Memorial University of Newfoundland, St. John's, Canada.

Flores H., F. Campos, M. Azevedo and B. A. Underwood. 1987. A novel delivery device of massive doses of vitamin A. Xerophthalmia Bull. 36: 1-2.

Flores H., F. Campos and B. A. Underwood. 1987. Effect of an infection on vitamin A status of children as measured by the relative dose response (RDR)[1-3]. Am. J. Clin. Nutr. 46: 91-94.

Flores, H., R. A. Ramalho and A. R. Ribeiro. 1988. Intrahepatic distribution of vitamin A in humans and rats. Int. J. Vitam. Nutr. Res. 58(3): 276-280.

Flores, H. 1989. Vitamin A and Mortality in Caruaru, NE Brazil. Xerophthalmia Bull. 42: 1-2.

Freire, W. B. 1989. Hemoglobin as a predictor of response to iron therapy and its use in screening and prevalence estimates. Am. J. Clin. Nutr. 50(6): 1442-1449.

Kestler, E., J. Dorgan, R. Sibrian, O. Aquino and J. Villar. 1987. Epidemiologic identification of infants with low birth weight in urban areas of Latin America: I. Organization, population, and methodology of the Guatemalan perinatal study. Bull. Pan Am. Health Organ. 21(4): 369-376.

Lanata, C. F., G. Stroh, Jr. and R. E. Black. 1988. Lot quality assurance sampling in health monitoring. Letters to the Editor. Lancet 1(8577): 122-123.

Lanata, C. F., G. Stroh, Jr., R. E. Black, and H. Gonzales. 1990. An evaluation of lot quality assurance sampling to monitor and improve immunization coverage. Int. J. Epidemiol. 19(4): 1086-1090.

Lansang, M. A., E. O. Domingo, A. L. Lingao, S. K. West and E. Alisago. 1987. Sensitivity and specificity of capillary blood HBsAg as a surrogate marker for HBeAg in pregnant women. J. Gastroentero. Hepatol. 2: 159-165.

Lansang, M. A., E. Domingo, A. Lingao, S. West. 1989. A cost-effectiveness analysis of a simple micromethod for hepatitis B screening in hepatitis B virus control programmes. Int. J. Epidemiol. 18, No. 4 (Suppl 2): S38-S43.

Lingao, A. L., E. O. Domingo, S. West, C. M. Reyes, S. Gasmen, G. Viterbo, E. Tiu and M. A. Lansang. 1986. Seroepidemiology of hepatitis B virus in the Philippines. Am. J. Epidemiol. 123: 473-480.

Lingao, A. L., N. T. Torres, N. Munoz, M. A. Lansang, S. K. West, F. X. Bosch and E. O. Domingo. 1989. Mother to child transmission of hepatitis B virus in the Philippines. Infection 17(5): 275-279.

Mardones-Restat, F. 1984. Beneficios de la seguridad social en el cuidado de la nutrición y salud de la madre y el niño en Chile. Rev. Chil. Nutr. 12: 23-27.

Mardones-Restat, F. 1984. Algunos indicadores materno-perinatales en América

Latina. pp. 1-3, *in* Perez, A. (ed.) Perinatologia. Santiago: Public. Técnicas Mediterráneo.

Mardones-Restat, F. 1985. Fecundidad en la adolescencia: un factor de riesgo en la mortalidad infantil? Rev. Creces 6: 27-30.

Mardones-Restat, F. 1985. Cobertura del PNAC y tasas de desnutrición infantil (1982-1983). Carta al Editor. Rev. Chil. Nutr. 13(1): 54-55.

Mardones-Restat, F. 1985. Defunciones de menores de un año, según peso al nacer. Chile 1978-84. Carta al Editor. Rev. Chil. Pediatr. 56(4): 282.

Mardones-Restat, F. and G. Jones. 1985. Predicción de fallas en el crecimiento infantil. Rev. Chil. Nutr. 13(3): 156-169.

Mardones-Restat, F. and G. Jones. 1986. Fecundidad en la adolescencia: un factor de riesgo en la mortalidad infantil? pp. 235-249, *in* Muzzo S. and R. Burrows, (eds.). Adolescencía. Santiago: Editorial Universitaria.

Mardones-Restat, F. 1986. Una tabla con la distribucion de los pesos de nacimientos. Carta al Editor Rev. Chil. Pediatr. 57(1): 97.

Mardones-Restat, F. 1986. In Condiciones de Eficiencia de los Servicios de Atención Materno Infantil. N. Baranchuk, ed. Buenos Aires: Editorial Científica Interamericana.

Mardones-Restat, F. 1987. La divulgación cientifica puede contribuír a mejorar la alimentación. Rev. de Alimentación y Salud 15: 22-23.

Mardones-Restat, F. 1987. Mortalidad infantil tardia y contribucion de la desnutricion. Causas basicas y asociadas. Chile 1978-1985. Rev. Chil. de Nutr. 15(2): 128.

Mardones-Restat, F. 1987. Hambre en EE.UU. Rev. Creces 9(11): 31-32.

Mardones-Restat, F. 1987. Mortalidad infantil tardia. Contribucion de 3 causas. Asociacion negative entre tasas de mortalidad infantil por accidentes y muertr subita, en un grupo de paises. Carta al Editor. Rev. Chil. de Pediatria. 58(5): 419.

Mardones-Restat, F. 1987. Prediction of poor infant growth. Bull. Pan Am. Health Organ. 21(4): 341-357.

Mardones-Restat, F., R. Chateauneuf, A. Hott and A. Campery. 1987. Tendencia del consumo de pan en Chile. Rev. Chil. Nutr. 15(1): 46-48.

Mardones-Restat, F. and G. Jones. 1987. Prediccion de fallas en el crecimiento en niños menores de un año. Bull. Pan Am. Health Organ. 103(5): 450-462.

Mardones-Restat, F. 1988. Capítulo: Predicción de fallas en el crecimiento en menores de un año. pp. 53-67, *in* Cusminsky, M., E. Moreno and N. Surez-Ojeda (eds.). Crecimiento y desarrollo: hechos y tendencias. Publicación Cientifica 510/OPS. Washington, D.C.

Mardones-Restat, F. 1988. Ruralidad un Factor de Riesgo en la Salud Infantil? Grupo de Investigaciones Agrias. pp. 136-146.

Mardones-Restat, F. 1989. Lactancia materna y crecimiento infantil, compracion

en las muestras de Santiago y Muble (periferia de Chillan). Carta al Editor. Rev. Chil. Nutr. 17(1): 68.

Mardones-Restat, F. 1989. La salud del joven. Carta al Editor. Rev. Chil. Pediatr. 60(5).

Mardones-Restat, F. 1989. De la Pediatria Social al Enfoque de Riesgo. Rev. Enfoques en Antencion Primaria pp. 3-13.

Mardones-Restat, F. 1989. Programa Integrado de Educación Rural (PIER). Informe a la I. Municipalidad de Lautaro. IX Región y Depto. de Lenguas, Facultad de Educación de la Universidad de la Fientera de Temurn.

Mardones-Restat, F., G. Jones, F. Mardones S., N. Dachs, J. P. Habicht and M. Diaz. 1989. Growth failure prediction in Chile. Int. J. Epidemiol. 18, No. 4 (Suppl. 2): S44-S49.

Mardones-Santander, F., N. Gonzalez, F. Mardones-Restat, J. Salinas and C. Albala. 1986. Programa nacional de alimentación complementaria en Chile en el período 1937-1982. Carta al Editor. Rev. Chil. de Nutr. 14: 173-182.

Mardones-Santander, F. and F. Mardones-Restat. 1987. Mortalidad infantil neonatal y tardia del pequeno para la edad gestacional. Rev. Chil. Pediatr. 58(1): 100-101.

Mardones-Santander, F., F. Mardones-Restat, P. Rosso, M. Díaz and G. Icaza. 1987. Infant mortality for the gestation age in Chile. Rev. Latinoam. Perinat. 7(1): 33-41.

Monckeberg, F., F. Mardones-Restat and S. Valiente. 1985. Evolución de la desnutrición y mortalidad infantil en Chile. Cuadernos de la Universidad de Chile 4: 165-204.

Monckeberg, F., F. Mardones-Restat and S. Valiente. 1986. Evolution of malnutrition and mortality in infants and young children over the past 20 years in Chile. pp. 295-321, *in* Hansluwka, H., A. D. Lopez, Y. Porapakkham and P. Prasartkul (eds.). New development in the analysis of mortality and cases of death. Bangkok: Mahidol University Faculty of Public Health, Institute of Population and Social Research.

Monckeberg, F., S. Valiente and F. Mardones-Restat. 1987. Infant and preschool nutrition: economical development versus intervention strategies: the case of Chile. Nutr. Res. 7: 327-342.

Murray-Martinez, R. T. 1987. Validacion de un instrumento predictor de riesgo de fallas en el crecimiento ponderal infantil en niños atendidos en el consultorio No. 1 del Hospital San Martin de Quillota. Thesis, M.S., Universidad de Antofagasta, Santiago, Chile.

Muzzo, S., R. Burrows, M. L. Alvarez, F. Mardones-Restat and J. Rosselot. 1986. Bases para la promoción intersectorial de la salud y bienestar en la adolescencia y en la juventud. *in* Muzzo, S. and R. Burrows, (eds.). Adolescencía. Santiago: Editorial Universitaria.

Ngelangel, C. A. 1989. Hospital visitor-companions as a source of controls

for case-control studies in the Philippines. Int. J. Epidemiol. 18, No. 4 (Suppl. 2): S50-S53.

Ritenbaugh, C. K., A. K. Said, O. M. Galal and G. G. Harrison. 1989. Development and evaluation of a colour-coded scale for birthweight surveillance in rural Egypt. Int. J. Epidemiol. 18, No. 4 (Suppl. 2): S54-S59.

Rosero-Bixby, L., C. Grimaldo and C. Raabe. 1990. Monitoring a primary health care programme with lot quality assurance sampling: Costa Rica, 1987. Health Policy and Planning 5(1): 30-39.

Rosselot, J. and F. Mardones-Restat. 1988. Antecedentes históricos y perspectivas de la seguridad alimentaria infantil y familiar en Chile. Rev. Pediatría 31: 115-131.

Rosselot, J. and F. Mardones-Restat. 1989. Salud de la familia y paternidad responsable. Rev. Creces 10(9-10): 6-9 and 50-54.

Schantz, P. M. and E. Sarti-Gutierrez. 1989. Diagnostic methods and epidemiologic surveillance of *Taenia solium* infection. Acta Leidensia 57(2): 153-163.

Thorburn, M.J., K. Marfo and others. 1990. Practical approaches to childhood disability in developing countries: insights from experience and research. Project SEREDEC, Memorial University of Newfoundland, St. John's, Canada.

Valverde, V., H. Delgado, R. Flores, R. Sibrian and M. Palmieri. 1985. The school as a data source for food and nutrition surveillance systems in Central America and Panama. Food Nutr. Bull. 7(4): 32-37.

Valverde, V., H. Delgado, R. Flores, R. Sibrian and M. Palmieri. 1986. Uses and constraints of school children's height data for planning purposes: national experiences in Central America. Food Nutr. Bull. 8(3): 42-48.

Venkataswamy, G., J. M. Lepkowski, T. Ravilla, G. E. Brilliant, C. A. K. Shanmugham, K. Vaidyanathan, R. L. Tilden and the Aravind Rapid Epidemiologic Assessment Staff. 1989. Rapid epidemiologic assessment of cataract blindness. Int. J. Epidemiol. 18, No. 4 (Suppl. 2): S60-S67.

Villar, J., E. Kestler, P. Castillo et al. 1987. Improved lactose digestion during human pregnancy in primary lactose maldigestion. Am. J. Clin. Nutr. 46: 528.

Villar, J., E. Kestler, P. Castillo, A. Juarez, R. Menendez and N. W. Solomons. 1988. Improved lactose digestion during pregnancy: a case of physiological adaptation? Obstet. Gynecol. 71(5): 697-700.

Villar, J., J. Dorgan, R. Menendez, L. Bolanos, G. Pareja and E. Kestler. 1988. Perinatal data reliability in a large teaching obstetric unit. Br. J. Obstet. Gynaecol. 95(9): 841-848.

Villar, J., E. Kestler and G. Pareja. 1989. Measurement error in clinical perinatal data. Am. J. Obstet. Gynecol. 160(2): 380-382.

Zaman, S., N. Khan, S. Islam, S. Barns, S. Dixit, P. Shrout and M. Durkin.

1990. Validity of the ten questions for screening serious childhood disability: results from urban Bangladesh. Int. J. Epidemiol. 19(3): 613-620.

ACUTE RESPIRATORY INFECTIONS

Ajello, G. W., G. A. Bolan, P. S. Hayes, D. Lehmann, J. Montgomery, J. C. Feeley, C. A. Perlino and C. V. Broome. 1987. Commercial latex agglutination tests for detection of *Haemophilus influenzae* type b and *Streptococcus pneumoniae* antigens in patients with bacteremic pneumonia. J. Clin. Microbiol. 25(8): 1388-1391.

Avila, M. M., G. Carballal, H. Rovaletti, B. Ebekian, M. Cusminsky and M. Weissenbacher. 1989. Viral etiology in acute lower respiratory infections in children from a closed community. Am. Rev. Respir. Dis. 140(3): 634-637.

Avila, M., G. Carballal, H. Salomon, M. C. Cerqueiro, M. Catalano, O. Messad, P. Murtagh, J. Harisiadi, N. Ferrero and M. Weissenbacher. 1990. Etiologia de las infecciones agudas del tracto respiratorio inferior en ninos menores de 5 anos en la ciudad de Buenos Aires. Infectologia y Microbiologia Clinica 2(2): 39-47.

Avila, M., H. Salomon, G. Carballal, B. Ebekian, N. Woyskovsky, C. Cerqueiro and M. Weissenbacher. 1990. Isolation and identification of viral agents in Argentinian children with acute lower respiratory tract infection. Rev. Infect. Dis. 12 (Suppl. 8): S974-S981.

Barker, J., M. Gratten, I. Riley, D. Lehmann, J. Montgomery, M. Kajoi, H. Gratten, D. Smith, T. F. Marshall, M. P. Alpers. 1989. Pneumonia in children in the Eastern Highlands of Papua New Guinea: a bacteriologic study of patients selected by standard clinical criteria. J. Infect. Dis. 159(2): 348-352.

Borrero, I., L. Fajardo, A. Bedoya, A. Zea, F. Carmona and M. F. de Borrero. 1990. Acute respiratory tract infections among a birth cohort of children from Cali, Colombia, who were studied through 17 months of age. Rev. Infect. Dis. 12 (Suppl. 8): S950-S956.

Cano, F., J. R. M. Chavez and J. R. Cruz. 1989. Antibiotic susceptibility of *Streptococcus pneumoniae* associated with acute respiratory disease in Guatemala. Apua Newsletter. 7(3): 1-8.

Carballal, G., M. Siminovich, P. Murtagh, C. Cerqueiro, M. Avila, H. Salomon, M. Catalano and M. Weissenbacher. 1990. Etiologic, clinical and pathologic analysis of 31 fatal cases of acute respiratory tract infection in Argentinian children under 5 years of age. Rev. Infect. Dis. 12 (Suppl. 8): S1074-S1080.

Catalano, M., M. A. Almiron, A. M. Romeo, E. Caruso, P. Murtagh and J. Harisiadi. 1990. Comparison between parental report and results of microbiological agar assay for presence of antibiotic in urine of Argentinian children with acute lower respiratory tract infection. Rev. Infect. Dis. 12 (Suppl. 8): S998-S1000.

Cerqueiro, M. C., P. Murtagh, A. Halac, M. Avila and M. Weissenbacher. 1990. Epidemiologic risk factors for children with acute lower respiratory tract infection in Buenos Aires, Argentina: a matched case-control study. Rev. Infect. Dis. 12 (Suppl. 8): S1021-S1028.

Chiparelli, H., J. C. Russi, E. Martorell, J. R. Arbiza, E. Canepa and M. Hortal. 1988. Comparacion entre la inmunofluorescencia y el ensayo inmunoenzimatico para el diagnostico rapido del virus respiratorio sincicial en secreciones nasofaringeas. Rev. Argent. Microbiol. 20: 201-204.

Cruz, J. R., G. Pareja, A. de Fernandez, F. Peralta, P. Caceres and F. Cano. 1990. Epidemiology of acute respiratory tract infections among Guatemalan ambulatory pre-school children. Rev. Infect. Dis. 12 (Suppl. 8): S1029-S1034.

Cruz, J. R., E. Quinonez, F. Peralta and A. de Fernandez. 1987. Isolation of viruses from nasopharyngeal secretions: Comparison of aspiration and swabbing as means of sample collection. J. Infect. Dis. 156(2): 415-416.

Ghafoor, A., N. K. Nomani, Z. Ishaq, S. Z. Zaidi, F. Anwar, M. I. Burney, A. W. Qureshi and S. A. Ahmad. 1990. Diagnoses of acute lower respiratory tract infections in children in Rawalpindi and Islamabad, Pakistan. Rev. Infect. Dis. 12 (Suppl. 8): S907-S914.

Gonzaga, N. C., E. E. Navarro, M. G. Lucero, S. C. Queipo, I. Schroeder and T. E. Tupasi. 1990. Etiology of infection and morphologic changes in the lungs of Filipino children who die of pneumonia. Rev. Infect. Dis. 12 (Suppl. 8): S1055-S1064.

Hortal, M., A. Benitez, M. Contera, P. Etorena, A. Montano and M. Meny. A community-based study of acute respiratory tract infections in children in Uruguay. 1990. Rev. Infect. Dis. 12 (Suppl. 8): S966-S973.

Hortal, M., C. Mogdasy, C. Russi, C. Deleon and A. Suarez. Microbial agents associated with pneumonia in children from Uruguay. 1990. Rev. Infect. Dis. 12 (Suppl. 8): S915-S922.

Hortal, M., A. Montano and M. Meny. 1989. Simple clinical signs for diagnosis of acute respiratory infections. Lancet. 2/8674: 1275.

Hortal, M., J. C. Russi, J. R. Arbiza, E. Canepa, H. Chiparelli and A. Illarramendi. 1990. Identification of viruses in a study of acute respiratory tract infection in children from Uruguay. Rev. Infect. Dis. 12 (Suppl. 8): S995-S997.

Hortal, M., J. C. Russi, J. R. Arbiza, A. Martorell, H. Chiparelli, E. Canepa, A. Illarramendi, G. Algorta, G. Pirez, C. Mogdasy, M. Repetto, A. Rodriguez, N. Nunez and H. J. Munoz. 1986. Infecciones respiratorias agudas en ninos menores de 5 anos hospitalizados: estudio etiologico prospective. Rev. Med. Uruguay. 3: 213-226.

Huq, F., M. Rahman, N. Nahar, A. Alam, M. Haque, D. A. Sack, T. Butler and R. Haider. 1990. Acute lower respiratory tract infection due to virus among hospitalized children in Dhaka, Bangladesh. Rev. Infect. Dis. 12 (Suppl. 8): S982-S987.

Iqbal, J., F. Azmi, Z. Ishaque, M. A. Khan, A. Ghafoor and M. I. Burney. 1987. Viral diagnosis in acute respiratory infections using the indirect immunofluorescence technique. J. Pak. Med. Assoc. 37(11): 280-284.

Jayanetra, P., M. Vorachit, A. Rittaporn, A. Nawaniruttisai, S. Suwanjutha, K. Vathanophas and C. Wasi. 1990. *Haemophilus influenzae* and *Streptococcus pneumoniae* in children with acute respiratory infection. Southeast Asian J. Trop. Med. Public Health. 21(2): 195-202.

Kajon, A. E., P. Murtagh, S. Garcia Franco, M. C. Freire, M. C. Weissenbacher and J. Zorzopulos. 1990. A new genome type of adenovirus 3 associated with severe lower acute respiratory infection in children. J. Med. Virol. 30(1): 73-76.

Lehmann, D., P. Howard and P. Heywood. 1988. Nutrition and morbidity: acute lower respiratory tract infections, diarrhoea and malaria. Papua New Guinea Med. J. 31(2): 109-116.

Lucero, M. G., T. E. Tupasi, M. L. O. Gomez, G. L. Beltran, A. U. Crisostomo, V. V. Romano and L. M. Rivera. 1990. Respiratory rate greater than 50 per minute as a clinical indicator of pneumonia in Filipino children with cough. Rev. Infect. Dis. 12 (Suppl. 8): S1081-S1083.

Mastro, T. D., A. Ghafoor, N. K. Nomani, Z. Ishaq, F. Anwar, D. M. Granoff, J. S. Spika, C. Thornsberry and R. R. Facklam. 1991. Antimicrobial resistance of pneumococci in children with acute lower respiratory tract infection in Pakistan. The Lancet 337: 156-159.

Mogdasy, C., J. C. Russi, C. Deleon, A. Suarez, H. Chiparelli, E. Canepa, T. Camou and M. Hortal. 1988. Agentes asociados a la neumonia del nino. Arch. Pediatr. Uruguay 60: 105-111.

Montgomery, J. M., D. Lehmann, T. Smith, A. Michael, B. Joseph, T. Lupiwa, C. Coakley, V. Spooner, B. Best, I. D. Riley and M. P. Alpers. 1990. Bacterial colonization of the upper respiratory tract and its association with acute lower respiratory tract infections in Highland children of Papua New Guinea. Rev. Infect. Dis. 12 (Suppl. 8): S1006-S1016.

Navarro, E., N. C. Gonzaga, M. G. Lucero, S. C. Queipo, I. Schroeder, M. L. O. Gomez and T. E. Tupasi. 1990. Clinicopathologic studies of children who die of acute lower respiratory tract infections: mechanisms of death. Rev. Infect. Dis. 12 (Suppl. 8): S1065-S1073.

Osinusi, K. and C. O. Oyejide. Child care practices with respect to acute respiratory tract infection in a poor, urban community in Nigeria. 1990. Rev. Infect. Dis. 12 (Suppl. 8): S1039-S1041.

Oyejide, C. O. and K. Osinusi. 1990. Acute respiratory tract infection in children in Idikan community, Ibadan, Nigeria: severity, risk factors, and frequency of occurrence. Rev. Infect. Dis. 12 (Suppl. 8): S1042-S1046.

Puthavathana, P., C. Wasi, U. Kositanont, S. Suwanjutha, T. Chantarojanasiri, W. Kantakamalakul, P. Kantawateera and P. Thongcharoen. 1990. A hospital-based study of acute viral infections of the respiratory tract in Thai

children, with emphasis on laboratory diagnosis. Rev. Infect. Dis. 12 (Suppl. 8): S988-S994.

Rahman, M., F. Huq, D. A. Sack, T. Butler, A. K. Azad, A. Alam, N. Nahar and M. Islam. 1990. Acute lower respiratory tract infections in hospitalized patients with diarrhea in Dhaka, Bangladesh. Rev. Infect. Dis. 12 (Suppl. 8): S899-S906.

Russi, J. C., H. Chiparelli, A. Montano, P. Etorena and M. Hortal. 1989. Respiratory syncytial virus subgroups and pneumonia in children. Lancet. 2/8670: 1039-1040.

Russi, J. C., A. Delfraro, J. R. Arbiza, H. Chiparelli, C. Orvell, M. Grandien and M. Hortal. 1989. Antigenic characterization of respiratory syncytial virus associated with acute respiratory infections in Uruguayan children from 1985 to 1987. J. Clin. Microbiol. 27(7): 1464-1466.

Salomon, H. E., J. C. Russi, M. Grandien, C. Orvell, M. M. Avila, M. Hortal and M. Weissenbacher. 1988. Variantes antigenicas del virus respiratorio sincicial en Argentina y Uruguay. [Antigenic variants of the respiratory syncytial virus in Argentina and Uruguay.] Rev. Argent. Microbiol. 20(3): 147-150.

Salomon, H., A. Kajon, M. Avila, M. C. Cerqueiro, B. Ebekian, N. Woyskovsky, G. Carballal and M. Weissenbacher. 1989. Applicabilidad de tecnicas rapidas de diagnostico para la identificacion de virus sincicial respiratorio y adenovirus. Infectologia y Microbiologia Clinica 1(4): 99-106.

Salomon, H., M. Grandien, M. Avila, C. A. Pettersson and M. C. Weissenbacher. 1989. Comparison of three techniques for detection of respiratory viruses in nasopharyngeal aspirates from children with lower acute respiratory infections. J. Med. Virol. 28(3): 159-162.

Salomon, H. "Aislamiento e identificacion de agentes virales en ninos con infeccion respiratoria aguda." Ph.D. Thesis, University of Buenos Aires. 1989.

Smith, T., D. Lehmann, C. Coakley, V. Spooner and M. P. Alpers. 1990. Relationships between growth and acute lower respiratory infections among children aged <5 years in a highland population of Papua New Guinea. Am. J. Clin. Nutr. 53, In press.

Spika, J. S., M. H. Munshi, B. Wojtyniak, D. A. Sack, A. Hossain, M. Rahman and S. K. Saha. 1989. Acute lower respiratory infections: a major cause of death in children in Bangladesh. Ann. Trop. Paediatr. 9(1): 33-39.

Spooner, V., J. Barker, S. Tulloch, D. Lehmann, T. F. Marshall, M. Kajoi and M. P. Alpers. 1989. Clinical signs and risk factors associated with pneumonia in children admitted to Goroka Hospital. Papua New Guinea. J. Trop. Pediatr. 35(6): 295-300.

Suwanjutha, S., T. Chantarojanasiri, C. Wasi, P. Puthavathana, S. Sirinavin, S. Hotrakitya, S. Ruangkanchanasetr, S. Watthana-kasetr, N. Wongpaitoon,

S. Oaunpoklang and S. Santati. 1988. Epidemiology of acute respiratory infection in Thai children under 5 years: A hospital-based study. pp. 283-87, *in* Tongcharoen P. and E. Kurstak (eds.). Virus Diseases in Asia. Aksornsmai Publishing Co., Bangkok, Thailand.

Suwanjutha, S. and T. Chantarojanasiri. 1989. Lower respiratory tract infection: an update. pp. 99-106, *in* Watana, T. and S. Lolekha, (eds). Recent Advances in Clinical Pediatrics. H. N. Publishing Co., Bangkok, Thailand, 99-106.

Suwanjutha, S., T. Chantarojanasiri, S. Watthana-kasetr, S. Sirinavin, S. Ruangkanchanasetr, S. Hotrakitya, C. Wasi and P. Puthavathana. 1990. A study of nonbacterial agents in acute lower respiratory tract infection in Thai children. Rev. Infect. Dis. 12 (Suppl. 8): S923-S928.

Tupasi, T. E., C. A. Miguel, V. L. Tallo, T. M. Bagasao, J. N. Natividad, L. B. Valencia, M. E. De Jesus, S. Lupisan and F. Medalla. 1989. Child care practices of mothers: implications for intervention in acute respiratory infections. Ann. Trop. Paediatr. 9(2): 82-88.

Tupasi, T. E., L. E. de Leon, S. Lupisan, C. U. Torres, Z. A. Leonor, M. E. S. Sunico, N. Mangubat, C. A. Miguel, F. Medalla, S. T. Tan and M. Dayrit. 1990. Patterns of acute respiratory tract infection in children: a longitudinal study in a depressed community in Metro Manila. Rev. Infect. Dis. 12 (Suppl. 8): S940-S949.

Tupasi, T. E., M. G. Lucero, D. M. Magdangal, N. V. Mangubat, M. E. S. Sunico, C. U. Torres, L. E. de Leon, J. F. Paladin, L. Baes and M. C. Javato. 1990. Etiology of acute lower respiratory tract infection in children from Alabang, Metro Manila. Rev. Infect. Dis. 12 (Suppl. 8): S929-S939.

Tupasi, T. E., N. V. Mangubat, M. E. S. Sunico, D. M. Magdangal, E. E. Navarro, Z. Leonor, S. Lupisan, F. Medalla and M. G. Lucero. 1990. Malnutrition and acute respiratory tract infections in Filipino children. Rev. Infect. Dis. 12 (Suppl. 8): S1047-S1054.

Vathanophas, K., R. Sangchai, S. Raktham, A. Pariyanonda, J. Thangsuvan, P. Bunyuaratabhandu, S. Athipanyakom, S. Suwanjutha, P. Jayanetra, C. Wasi, M. Vorachit and P. Puthavathana. 1990. A community-based study of acute respiratory tract infection in Thai children. Rev. Infect. Dis. 12 (Suppl. 8): S957-S965.

Wafula, E. M., P. M. Tukei, T. M. Bell, H. Nzanze, A. Pamba, J. O. Ndinya-Achola, D. T. Hazlett and G. R. Ademba. 1984. How should primary health workers diagnose and treat acute respiratory infections (ARI)? East Afr. Med. J. 61(10): 736-744.

Wafula, E. M., P. M. Tukei, T. M. Bell, H. Nzanze, J. O. Ndinya-Achola, D. T. Hazlett, G. R. Ademba and A. Pamba. 1985. Aetiology of acute respiratory infections in children aged below 5 years in Kenyatta National Hospital. East Afr. Med. J. 62(11): 757-767.

Wafula, E. M., P. M. Tukei, T. M. Bell, H. Nzanze, J. O. Ndinya-Achola, D. T. Hazlett, G. R. Ademba and A. Pamba. 1987. Diagnosis of acute respiratory infections (ARI) among under fives in the paediatric observation ward (POW), Kenyatta National Hospital, Nairobi. East Afr. Med. J. 64(4): 263-269.

Wafula, E. M., D. B. Tindyebwa and F. E. Onyango. 1989. The diagnostic value of various features for acute lower respiratory infection among under fives. East Afr. Med. J. 66(10): 678-684.

Wafula, E. M., F. E. Onyango, W. M. Mirza, W. M. Macharia, I. Wamola, J. O. Ndinya-Achola, R. Agwanda, R. N. Waigwa and J. Musia. 1990. Epidemiology of acute respiratory tract infections among young children in Kenya. Rev. Infect. Dis. 12 (Suppl. 8): S1035-S1038.

Wasi, C. and P. Puthavathana. 1988. Laboratory diagnosis of respiratory viruses. J. Infect. Dis., Antimicrob agents. 5: 129-136. (In Thai).

Weinberg, G. A., A. Ghafoor, Z. Ishaq, N. K. Nomani, M. Kabeer, F. Anwar, M. I. Burney, A. W. Qureshi, J. M. Musser, R. K. Selander and D. M. Granoff. 1989. Clonal analysis of *Hemophilus influenzae* isolated from children from Pakistan with lower respiratory tract infections. J. Infect. Dis. 160(4): 634-643.

Weinberg, G. A., D. Lehmann, T. E. Tupasi and D. M. Granoff. 1990. Diversity of outer membrane protein profiles of nontypable *Haemophilus influenzae* isolated from children from Papua New Guinea and the Philippines. Rev. Infect. Dis. 12 (Suppl. 8): S1017-S1020.

Weinberg, G. A., E. D. Spitzer, P. R. Murray, A. Ghafoor, J. Montgomery, T. E. Tupasi, D. M. Granoff and BOSTID *Haemophilus* Susceptibility Study Group. 1990. Antimicrobial susceptibility patterns of *Haemophilus* isolates from children in eleven developing nations. Bull. WHO 68(2): 179-184.

Weissenbacher, M., G. Carballal, M. Avila, H. Salomon, J. Harisiadi, M. Catalano, C. Cerqueiro and P. Murtagh. 1990. Etiologic and clinical evaluation of acute lower respiratory tract infections in young Argentinian children: an overview. Rev. Infect. Dis. 12 (Suppl. 8): S889-S898.

Witt, C. S., J. M. Montgomery, W. Pomat, D. Lehmann and M. P. Alpers. 1990. Detection of *Steptococcus pneumoniae* and *Haemophilus influenzae* type b antigens in the serum and urine of patients with pneumonia in Papua New Guinea: Comparison of latex agglutination and counterimmuno–electrophoresis. Rev. Infect. Dis. 12 (Suppl. 8): S1001-S1005.

Witt, C. S., W. Pomat and M. P. Alpers. 1989. Pneumococcal antibody concentrations in young Papua New Guinean Highland children with pneumonia. Pediatr. Infect. Dis. J. 8(8): 533-534.

NATIONAL ACADEMY PRESS
The National Academy Press was created by the National Academy of Sciences to publish the reports issued by the Academy and by the National Academy of Engineering, the Institute of Medicine, and the National Research Council, all operating under the charter granted to the National Academy of Sciences by the Congress of the United States.

Digitized by Google