

AGENCY FOR INTERNATIONAL DEVELOPMENT  
WASHINGTON, D.C. 20523

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PDCBK 199

September 28, 1989

Dr. Polly Harrison, Director  
Institute of Medicine  
National Academy of Sciences  
2101 Constitution Avenue  
Washington, D.C. 20418

*Handwritten:* Journal  
348-158

Subject: Grant No. ANE-0158-G-SS-9035-00

Dear Dr. Harrison:

Pursuant to the authority contained in the Foreign Assistance Act of 1961, as amended, the Agency for International Development (hereinafter referred to as "A.I.D." or "Grantor") hereby provides to the National Academy of Sciences (hereinafter referred to as "NAS" or "Grantee") the sum of \$405,000 for the Mid-East Regional Health Research and Development Program For the Control of Infectious Diseases, more fully described in Article II of the Schedule entitled "Purpose". Additional funds totalling \$3,887,968 may be added to the Grant in the future, subject to the availability of funds.

This Grant and its initial obligation of \$405,000 is made effective as of the date of this letter, and shall apply to commitments made by the Grantee in furtherance of program objectives from September 1, 1989 to August 31, 1994.

This Grant is made to NAS on condition that the funds shall be administered in accordance with the terms and conditions as set forth in: Attachment 1, Schedule, Attachment 2, Program Description, and Attachment 3, Standard Provisions, which have been agreed to by your organization.

Please sign the original and seven (7) copies of this letter to acknowledge receipt of this Grant, and return all but one copy to the undersigned.

Sincerely,



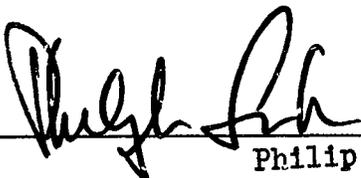
Judith D. Johnson  
Grant Officer  
Overseas Division - ANE  
Office of Procurement

Attachments

- 1. Schedule
- 2. Program Description
- 3. Standard Provisions (Mandatory & Optional)

Acknowledged

National Academy of Sciences - IOM

By  \_\_\_\_\_  
 Name/Title Philip M. Smith  
Executive Officer  
 Date OCT 27 1989

FISCAL DATA

PIO/T No.	 -9636610
Approp. No.	72-119/01037
BPC	QES9-89-37398-KG12
DUNS	041964057
Total Est. Amount	\$4,292,968
Total Obligation	\$ 405,000
Tech. Office	ANE/TR/HPN

FUNDS AVAILABLE

  
 SEP 30 1989  
 4190

Program Acctg Fin Division  
Office of Financial Management

## Attachment 1 - Schedule

### Article I - Purpose of Grant

The purpose of this Grant is to provide support for the Mid-East Regional Health Research and Development Program for the Control of Infectious Diseases, as more specifically described in Attachment 2 to this Grant, entitled "Program Description".

### Article II - Period of Grant

The period of this Grant is September 1, 1989 to August 31, 1994.

### Article III - Amount of Grant and Payment

- A. The total estimated amount of this Grant for the period shown in Article II is \$4,292,968.
- B. A.I.D. hereby obligates \$405,000 for program expenditures during the above period, in accordance with the Financial Plan set forth below. It is estimated that this amount will cover expenditures through May 31, 1990.
- C. Payment shall be made to the Grantee in accordance with the Standard Provision entitled "Payment - Letter of Credit".
- D. Additional funds up to the total amount of the grant shown in III.A. above may be obligated by A.I.D. subject to availability of funds and to the requirements of the Grant Standard provision entitled "Revision of Grant Budget."

### Article IV - Financial Plan

The following is the Grant Budget, including local cost financing items, if authorized. Revisions shall be made in accordance with the Standard Provision to this Grant entitled "Revision of Grant Budget".

LIFE-OF-PROJECT BUDGET (ESTIMATE)

	Administration U.S.	Scientific Cooperation U.S.	SUB-GRANTS		TOTAL
			Research Grants	Collaboration & Support Israel Collaboration & Support Egypt	
Salaries & Wages Professional Secretarial	\$ 256,444 47,432		0 0	0 0	\$ 256,444 47,432
Fringe Benefits @ 23% of Salaries & Wages	69,891		0	0	69,891
Overhead @ 66.5% of Salaries & Wages & Fringe Benefits	246,555		0	0	
Other Personnel Services		139,700	0	0	139,700
Travel Expenses		135,510	0	0	135,510
Other direct Costs	183,170		0	0	183,170
Grants			2,450,196	165,500	2,836,696
Subtotal	805,493	275,210	2,450,196	165,000	3,919,399
General & Admin. @8% of Grants above \$200,000 @12% of all other items			31,563 167,772	690 24,000	32,253 341,316
	\$ 902,152	\$ 308,235	\$2,649,531	\$165,500	\$4,292,968

## Article V - Reporting

### A: Financial

1. Financial reporting requirements shall be in accordance with the Standard Provision entitled "Payment - Letter of Credit".
2. Two concurrent copies of the financial reports (SF-269 & SF-272) shall also be submitted to the cognizant Project Officer.
3. The frequency of the financial reports shall be as indicated in the above cited Standard Provision, and each report shall indicate the actual reporting period of the report.
4. The SF-269s shall be prepared so that the heading for each project activity, as well as its respective budgeted amount (as shown in the Life-of-Project Budget) appear across the top of the verticle columns "(a) - (f)".
5. One of the quarterly SF-269 reports shall be submitted with each annual report required under the Program Description, Article IV. This report should also include projections of funds required during the following six-month period. The submission of these reports should be timed so that the periods covered are the same.

### B. Performance (Technical)

Technical performance reporting requirements are set forth in the Program Description at Article IV.

## Article VI - Indirect Cost Rate

It is understood that the Office of Naval Research (ONR) is the U.S. Government activity having cognizance for establishing a negotiated indirect cost rate agreement with NAS. Since a current indirect cost rate agreement is still pending, the following rates are hereby established as provisional rates, in accordance with the Standard Provision entitled "Negotiated Indirect Cost Rates - Provisional". When final rates are negotiated with ONR this grant will be amended to establish such rates on whatever basis the parties have agreed, and the appropriate Standard Provision will be made applicable.

### Provisional Rates

<u>Account</u>	<u>Rate</u>	<u>Base</u>
Fringe	23%	Direct Salaries/Wages
Overhead	66.5%	Direct Sals./Wages + Fringe
G&A (Regular)	12%	Total Cost, excluding subcontracts greater than \$200,000
G&A (Subs)	3%	Total subcontracts greater than \$200,000.

## Article VII - Procurement

- A. Procurement of goods and services under the Grant shall be in accordance with the Standard Provisions entitled "Procurement of Goods and Services" and "AID Eligibility Rules for Goods and Services". Under the latter provision, the rules which shall apply are for the total procurement element exceeding \$250,000. The authorized Geographic codes are "000" (United States), "263" (Host Country - Egypt), and "271" (Host Country - Israel).
- B. Local cost financing is authorized, and shall be in accordance with the Standard Provision entitled "Local Cost Financing".

## Article VIII - Title to Property

In accordance with the Standard Provision entitled "Title To And Use of Property (Grantee Title)", the Grantee shall have title to property procured under this Grant. Where Grant funds are used for procurements under subgrants, however, title to said property shall vest in the subgrantee(s), and the reference Standard Provision shall be made applicable in the Subgrant(s).

## Article IX - Subagreements

Subagreements under this Grant shall be in accordance with the Standard Provision entitled "Subagreements". The Grantee will undertake subagreements in accordance with its own policy and procedures and the requirements set forth in Attachment 2, Section II entitled "Grant Administration and Implementation Arrangements." The Grantee shall submit copies of subagreements negotiated with subgrantees over \$200,000. Applicable flow-down provisions described in the Standard Provisions will be included in all subgrants to which they are applicable.

## Article X - Special Provisions

### A. Human Subjects & Biosafety

1. The Grantee shall comply with the applicable provisions of the Code of Federal Regulations 45 CFR 46, "Protection of Human Subjects". Prior to any experimentation involving human subjects, thorough protocols which ensure the wellbeing of human subjects shall be prepared. Copies of the patient informed consent forms shall be reviewed for adequacy, and the approval of the relevant Israeli and/or Egyptian institutional ethical review committee shall be obtained, as well as that of the N.R.C. Committee to Review Human Studies. The Grantee's procedures with respect to the protection of human subjects are considered adequate to fulfill the approval requirements set forth in Standard Provision No. 17.
2. Prior to any handling of human pathogens under the Grant, the Grantee shall ensure that all relevant biosafety precautions are observed, and that all relevant U.S., Egyptian, and/or Israeli regulations are met. Certification that applicable containment standards have been met shall be provided to the cognizant Project Officer prior to the commencement of any work.

### B. Salary Supplements

The Grantee shall comply with A.I.D.'s "Policy Guidance on Criteria for Payment of Salary Supplements For Host Government Employees", as found in A.I.D. Handbook #1, Part VII.7.

### C. Care of Laboratory Animals

No animals will be used in the research to be performed under this grant.

PROGRAM DESCRIPTION

I.

A. PURPOSE:

This grant will promote the mutual exchange of technology and knowledge to support cooperation between Israelis and Egyptians. Specifically, the purpose of the grant is to strengthen the information base needed to prevent and control infectious diseases, specifically hepatitis B (HB) and chronic diarrhea (CD), in Egypt and Israel, through a collaborative program which focuses on institution building and research.

The research, to be conducted between Egyptian and Israeli institutions will be conducted over a five-year period following initial obligation of funds. Both areas of research were selected because of their importance to the health status of Egypt and Israel.

B. OBJECTIVES:

1.) Blood-borne Viral Diseases Component. Work carried out under this component will serve to inform national policy and enhance capability for diagnosis, prevention, control, and management of blood-borne viral infections and morbidity in Israel and Egypt. The subproject will attempt to:

- a.) strengthen capabilities to use diagnostic tools for blood screening;
- b.) evaluate prognostic value of various serological markers of Hepatitis B virus HBV in disease progression;
- c.) perform cost-effectiveness analyses of these methods;
- d.) assist in identifying the populations at risk for hepatitis, analyzing the dynamics of evaluation and transmission of the disease in hepatitis carriers and their families, and in estimating prevalence.

2.) Chronic Diarrhea Component. Research conducted under this component will attempt to:

- a.) identify etiologic factors responsible for the chronic diarrhea syndrome; and
- b.) develop and test diagnostics for identifying those factors, thereby leading to better understanding of that syndrome and interventions for its prevention.

## II. Grant Administration and Implementation Arrangements.

As a part of the A.I.D. Regional Cooperation Program, this subproject will be coordinated and administered by the National Academy of Sciences' Institute of Medicine. A grant is appropriate given NAS/IOM's capability to implement this effort without substantial involvement of A.I.D. The IOM will be the primary intermediary between A.I.D. and the overall program, and will assume responsibility for all the U.S.-based activity and overall program coordination. It will facilitate the research, and foster and expedite scientific exchanges between Egyptian and Israeli researchers. The IOM will review the scientific merit of the proposed research protocols prior to award of subagreements via an external peer review group and will monitor the scientific quality of the research via a Scientific Advisory Committee (SAC). The SAC will recommend revisions to scientific protocols on the basis of reviewers comments, and will monitor progress in meeting scientific and regional cooperation objectives for the life of the project.

Program management at the national level in Israel will be coordinated by Ben-Gurion University of the Negev. In Egypt overall program management will be done by Ain Shams University.

A.I.D. funding will cover NAS core costs (U.S. experts costs, certain supplies and publication costs, and administration and overhead) plus research grants, consultant services, evaluations and audits, technical exchange, and equipment and materials' costs in Egypt and Israel. Egypt and Israel will be making substantial contributions in cash and in kind towards carrying out the grant activities.

Egypt and Israel have requested the NAS/IOM to serve as the primary grantee with A.I.D. for assisting in carrying out the subproject. NAS/IOM will:

- a. arrange with Egyptian and Israeli Grantee Institutions for execution of the scope of work;
- b. coordinate all peer and SAC reviews of scientific research proposals and all planning sessions, workshops and project review meetings;
- c. secure specialized consultant services from U.S. institutions;
- d. procure all non-locally purchased equipment and supplies from the U.S., and monitor all such local procurements under the subgrants;

- e. provide for periodic audits and at least two evaluations of the subproject;
- f. ensure that the appropriate host country institutions responsible for control and intervention activities receive copies of reports and recommendations, and that representatives are invited to evaluations and technical reviews;
- g. submit to A.I.D. periodic fiscal and progress reports;
- h. assure compliance with applicable requirements relative to insuring the well-being of human subjects and biosafety in the handling of human pathogens;
- i. monitor compliance with A.I.D.'s policy with regard to payments of salary supplements to host government employees; and
- j. perform other functions as agreed between NAS/IOM and A.I.D.

### III. Statement of Work

The NAS/IOM, in implementing the project through the sub-grant recipients, will ensure that the research methodologies proposed by investigators to attain subproject objectives (Section I, above) are scientifically meritorious and feasible. The NAS/IOM will provide technical oversight and coordination of research activities and pre-approve any modification of protocols, as required in the course of the project. As estimated funds become available, the following summarizes, briefly, the proposed activities in each of two main areas of research in Israel and Egypt.

#### A.) Epidemiology and Prevention of Blood-borne Viral Diseases:

##### 1.) Egypt

- a.) Prevalence of Hepatitis B (HBsAg) Among Blood Donors in Egypt (Establish the infrastructure to determine the magnitude of HBsAg due to lack of blood screening in Egypt.)
  - 1.)-Identify specific markers useful for detecting hepatitis-infected blood.
  - 2.)-Estimate the prevalence rate of blood donors who are positive for HB markers (HBsAg and anti-HBc) and for HV antibodies.
  - 3.)-Identify high-risk groups (for HBV transmission) within the blood-donor population.

- 4.)-Estimate the proportion of HBsAg carriers who are also infected by the delta agent.
- 5.)-Assess the cost-effectiveness of screening blood using the available antigen and antibody detection kits for HB.
- 6.)-Develop laboratory capability to modify and/or develop diagnostic tools suitable for use in local conditions and populations

**b.) Maternal-Infant Transmission of HBV Infections in Egypt** (to determine magnitude of vertical and horizontal intra-family transmission of HBsAg)

- 1.)-The prevalence of HBsAg carrier rate among pregnant women in Egypt, and among members of their families.
- 2.)-The prevalence of high-risk mothers, by testing for HBsAg among the HBsAg-positives.
- 3.)-The perinatal, maternal-infant infection rate.
- 4.)-The proportion of newborns thus infected who become chronic HBsAg carriers.

cont. (Blood-borne Viral Diseases Research)

**A. (2) Israel**

**a.) Infrastructure for Research**

Establish diagnostic capability at Ben Gurion University to support the necessary clinical and screening services for HBsAg.

**b.) Identification of Diagnostic Markers**

Test the infrastructure through a cross sectional pilot study to identify simple, yet sensitive diagnostic markers for early treatment and control of acute and chronic morbidity due to viral hepatitis B and non-A-non B (NANB).

**c.) Diagnostic Value of HBV Markers**

Analyze the correlation between diagnostic markers of HBV and the clinical and biochemical manifestations of the disease; estimate the risk of progression to chronic liver disease among "healthy" HBsAg carriers; and introduce a protocol for management and follow-up of those carriers.

**d.) Natural History of the Chronic HBsAg Carriers--Family**

**Studies:** Estimate the magnitude and the importance of horizontal and vertical transmission of HB infection within families.

## B. Epidemiology and Pathogenesis of Chronic Diarrhea

### 1.) Egypt

#### a.) Host Factors contributing to chronic diarrhea-in hospitalized pediatric populations.

Carry out the classification and analysis of isolated enteric pathogens; identify strains of differential virulence and compare with strains identified from two basic control groups of hospitalized children -- those with acute diarrhea and those without.

#### b.) Longitudinal Study of Non - host risk factors in rural communities, including the domestic environment, care seeking behavior, and feeding and food consumption patterns.

c.) Identify policy and program implication of findings from non-host risk studies to design improved case management protocols, delivery strategies, and health education approaches.

### 2.) ISRAEL

a.) Identification, through hospital-based research (in-patient and out-patient) of the role of environmental factors, infectious agents, and non-infectious conditions in the development of chronic diarrhea in childhood, and determination of the interrelationships between those factors and the nutritional and immunologic status of the host. Data from compatible studies in Egypt will be compared during years 2-3, and further relevant studies will be designed and implemented.

b.) Study of the prevalence, at the community level, of enteric pathogens, to: determine the prevalence of symptomatic vis-a-vis asymptomatic infections; correlate the clinical symptoms with children's growth parameters, food consumption patterns, and nutritional and immune status; and prospectively evaluate which of these factors might predispose to progression from acute to chronic diarrhea. The efficiency of simple screening tests as a method for diagnoses will be assessed.

### C.) Cooperative Activities

The project will establish both formal and informal means of cooperation between Egyptian and Israeli scientists. The mechanisms for cooperative activities include: the meetings of

the Scientific Advisory Committee (SAC, including its functions to review/approve project designs and plans: and to conduct annual meetings with project Principal Investigators and Program Coordinators from Israel and Egypt), consultations among researchers, shared use of facilities, working site visits, exchange of specimen samples, or data for analysis/typing/isolation, etc. Additional occasions for collaboration will be constituted by joint publications of scientific reports; joint presentations at scientific meetings, and periodic workshops for planning and review of research findings and implication for disease control policy and management.

The NAS/IOM shall ensure that the above-described mechanisms are utilized to the fullest extent possible and that project activities are conducted in a fully collaborative manner to maximize cooperative contact between the Israeli and Egyptian collaborating institutions and individuals. Specifically, the IOM will:

- 1.) Program and arrange periodic meetings of the Scientific Advisory Committee to review/approve project design, and to convene the Program Coordinators and Principal Investigators from Israel and Egypt.
- 2.) Program and arrange international meetings and exchange visits, particularly in Egypt and Israel relative to project planning, implementation, and evaluation as needed. Specifically, the collaborative exchanges will include, but not be limited to:
  - a) Collaboration on development of laboratory tests (e.g., simple, rapid, sensitive, and inexpensive techniques for screening and diagnosis of viral hepatitis, and assays for detection of enteric pathogens and noninfectious conditions contributing to chronic diarrhea).
  - b) Mutual visits of investigators, for observation and scientific collaboration (e.g., observation and collaboration in respective laboratories on various nutritional and gastrointestinal function assessment techniques and microbiological methods).
  - c) Development of comparable protocols and analytic plans for studies with similar objectives and methodologies (e.g., post-transfusion hepatitis, community-based chronic diarrhea).

- d) Exchange of clinical material (e.g., cross-testing of blood samples, to check validity and reliability of methodologies used; trading of isolates of enteropathogens, to better characterize virulent strains existing in one country but not in another; sharing of intestinal biopsy material for immunopathological studies).
- e) Annual workshop for Egyptian, Israeli, and U.S. investigators, to exchange experience with methods, data and, eventually, results.
- 3.) Arrange for the publication and distribution of project reports, including research results. To the degree feasible, scientific reports and publications should be jointly-prepared by participating Egyptian and Israeli Scientists, respectively, in accordance with a common reporting format.
- 4.) Monitor and report regularly (as specified in the section on Reporting, below), including the extent to which project objectives are being met;
- 5.) Arrange for U.S. technical, logistical (including commodity procurement), and administrative support, as dictated by approved project implementation plans, and as requested by the Egyptian and Israeli collaborating institutions, and endorsed by the Scientific Advisory Committee.

#### IV. Evaluation and Reporting Requirements

The NAS/IOM will furnish A.I.D. with the following reports in English:

- 1.) Year One Implementation Plan. An implementation plan, outlining the research objectives and proposed activities for the first year of the Project, should be submitted within three months of execution of the grant subagreement. Thereafter, research objectives and activities proposed for implementation within subsequent twelve-month increments will be included in the Annual Report.
- 2.) An Annual Report prepared by NAS/IOM which summarizes scientific developments, documents the status of regional cooperation, and relates research activities and accomplishments to project objectives. The Annual Report will also provide a brief assessment of the attainment of research objectives and activities outlined in the previous year's implementation plan, along with a discussion of

unplanned effects, and a brief description of objectives and activities planned for the coming year.

Annual technical progress reports will be required from each collaborating institution on research findings, and financial status. Those reports received from collaborating institutions will be submitted as annexes to the NAS/IOM annual report. A list of all international travelers along with their positions, purposes, destinations, and dates of travel will be included.

One of the quarterly Financial Reports, as required by Schedule Article V should also be included in each annual report. The annual report and the financial report should be timed so that the periods covered are the same.

3.) A Final Report to be prepared within 90 days of the end of the Grant project, summarizing the achievements and failures of the project with an overall analysis of the project's effect in achieving stated objectives. The format should be similar to that used in the Annual Reports. The final reports should also provide a final financial report, using the same format used for reporting during the life-of-the-project.

4.) Any scientific publications resulting from research work (3 copies each).

#### 5.) Evaluation

Midterm and final external evaluations will be arranged by NAS/IOM with A.I.D. participation in the preparation of scopes of work for team members and as a possible member of those teams. Evaluations will specifically cover:

- Progress towards attaining scientific, cooperation, and control objectives;
- unanticipated effects;
- overall project administration;

- determination and recommendations concerning the progressive financial independence of the institutions;
- likelihood of self-sustainable institutional and institutionalized cooperation between researchers or the relevant Israeli and Egyptian research institutions. Five copies each of Research/Cooperation, Financial Reports, and Evaluation Reports will be submitted to the ANE/TR/HPN project officer for distribution.

In addition, five information copies of the NAS/IOM subgrant agreements with the collaborating Egyptian and Israeli institutions will be submitted to the A.I.D. project officer.