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DOCUMENT THAT IS NOT PURSUANT
TO A HANDBOOK 3 PROJECT AGREEMENT

PD-ABD-97/
76507



AGENCY FOR INTERNATIONAL DEVELOPMENT

UNITED STATES AID MISSION TO PERU

C/O AMERICAN EMBASSY

LIMA, 1 PERU

TELEPHONE: 286200

CABLE: USAID/LIMA

May 21, 1987

Dr. Alberto Cazorla
Rector
Universidad Peruana Cayetano Heredia
Honorio Delgado 932
San Martín de Porres
Lima

Subject: UPCH - Cysticercosis: New Opportunities for Targeting Detection and Treatment Using ELISA Technology. Project No. 936-5542, AID/SCI Proposal No. 7.208. Grant No. 936-5542-G-00-7297-00

Dear Dr. Cazorla:

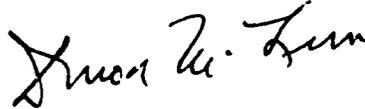
Pursuant to the authority contained in the Foreign Assistance Act of 1961, as amended, the Agency for International Development (hereinafter referred to as "AID" or "Grantor") hereby grants to the Universidad Peruana Cayetano Heredia (hereinafter referred to as "UPCH" or "Grantee") the amount of US\$149,989 (the "Grant") to carry out a research project entitled, "Cysticercosis: New Opportunities for Targeting Detection and Treatment Using ELISA Technology", as described in Attachment 1, the Schedule of this Grant, and Attachment 2, entitled Program Description.

This Grant is effective, and obligation is made, as of the date of this letter and shall apply to commitments made by the Grantee in furtherance of program objectives during the period beginning with the effective date and ending December 31, 1989. All reporting and financial liquidations are to be completed by that date.

This Grant is made to UPCH on condition that the funds will be administered in accordance with the terms and conditions as set forth in Attachment 1, entitled the Schedule, Attachment 2, entitled Program Description, Attachment 3, entitled Mandatory Standard Provisions, and Attachment 4, entitled Optional Standard Provisions.

Please sign all six (6) copies of this Agreement to acknowledge your acceptance of the Grant and the conditions herein established. Five copies should be returned to AID.

Sincerely,

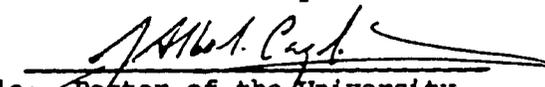


Donor M. Lion
Director

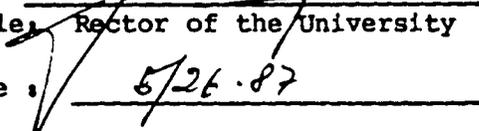
ACKNOWLEDGED:

Universidad Peruana Cayetano Heredia

By:

Title:  Rector of the University

Date:

 5/26.87

ATTACHMENTS:

1. Schedule
2. Program Description
3. Mandatory Standard Provisions AID-1420-53 (1-85)
4. Optional Standard Provisions AID-1420-54 (1-85)

FISCAL DATA:

Appropriation : 72-1171021.6
Budget Allotment Codes: DDSA-87-10600-KG11 (746-36-099-00-19-71)
Project No. : 936-5542
Obligation No. : 7361214
Total Estimated Amount: \$149,989
Total Obligated Amount: \$149,989
Funding Source : AID/Washington

SCHEDULE

A. Purpose of the Grant

The purpose of this Grant is to provide support for a research activity to be carried out by the Universidad Peruana Cayetano Heredia (UPCH). The activity, entitled "Cysticercosis: New Opportunities for Targeting Detection and Treatment Using ELISA Technology", is aimed at developing a simple and rapid assay for the diagnosis of cerebral cysticercosis in developing countries. See Attachment 2, Program Description, for a detailed description.

B. The Grantee

The recipient institution for the Grant is UPCH. The Principal Investigators for project activities are Dr. Robert H. Gilman, Visiting Professor at the Universidad Peruana Cayetano Heredia (UPCH), and Associate Professor of International Health at the Johns Hopkins School of Public Health and Hygiene, and Dra. Elba Miranda, Division of Parasitology, UPCH.

C. Period of the Grant

The effective date of this Grant is the day of its signature. The expiration date of this Grant is December 31, 1989.

D. Approved Project Proposal

The approved Project Proposal consists of the original proposal submitted in August 11, 1986 by Dr. Robert Gilman of UPCH, as revised by AID/SCI's letter of November 26, 1986, approving the proposal, with provisos, and the response thereto, by Dr. Gilman dated January 13, 1987.

E. Amount of Grant and Payment

1. AID hereby obligates the amount of \$149,989 for purposes of this Grant. This represents the maximum total contribution of AID to the project. The Grantee assumes the responsibility to secure any additional resources that might be required to complete project objectives.

2. Payment shall be made to the Grantee in accordance with procedures set forth in Attachment 4, Optional Standard Provision 1, entitled "Payment-Periodic Advance" and in accordance with Section G, Financial Plan. Payment shall be made on a quarterly basis.

F. Required Accounting Records

Grantee hereby agrees to establish a separate banking account and to keep separate accounting records for the funds received under this Grant in accordance with, and as required by, Optional Standard Provision No. 1 of Attachment 4.

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G. Financial Plan

The following is the Grant Budget. It includes local cost financed items, as authorized, as well as some equipment and supplies to be purchased abroad and international travel. Procurement of goods and services shall be implemented in accordance with Optional Standard Provisions 3 through 8 of Attachment No. 4. Revisions to the Grant Budget shall be made in accordance with Mandatory Standard Provision No. 4 (see Attachment 3) entitled "Revision of Grant Budget". Transfers among AID financed categories in the Grant Budget in excess of 15% shall require the written approval of AID.

Grant Budget
(in U.S. Dollars)

| | Year 1 | Year 2 | Total AID | UPCH/GOP Contribution |
|---|----------|----------|------------------|--------------------------|
| 1. <u>Compensation</u> | | | \$96,283 | \$25,600(UPCH) |
| a. Principal Investigator (1) | \$ 3,360 | \$ 4,800 | | |
| b. Chief of Parasitology (1) | 900 | 900 | | |
| c. Study Physicians (3) | 4,800 | 1,800 | | |
| d. Biochemist (1) | 2,600 | 2,600 | | |
| e. ELISA Technician (1) | 2,600 | 2,600 | | |
| f. Tissue Culture Technician (1) | 1,300 | 1,300 | | |
| g. Graduate Students () | 3,671 | 3,340 | | |
| h. Secretary (1) | 1,000 | 1,000 | | |
| i. Fringe Benefit Payments (Peruvian) | 3,643 | 3,450 | | |
| j. Local Consultants (3) | 2,000 | 1,000 | | |
| k. JHU Consultants (4) | 20,804* | 26,815* | | |
| 2. Research Facilities | | | | 16,000(UPCH) |
| 3. Equipment and Supplies (incl. shipping) | | | 27,663 | 20,400(UPCH) |
| a. U.S. Purchase | 15,888* | 7,475* | | |
| b. Local Purchase | 3,100 | 1,200 | | |
| 4. Travel | | | 6,250 | |
| a. International | 2,000* | 2,000* | | |
| b. Local | 250 | 2,000 | | |
| 5. CAT Scan Costs | 1,500 | 500 | 2,000 | 10,000(GOP) |
| 6. Experimental Animals | 250 | 250 | 500 | |
| 7. Communications, Telephone, Stamps | 1,150* | 1,150* | 2,300 | |
| 8. Miscellaneous Administrative Costs | | | 12,729 | |
| a. In Peru | 3,097 | 2,674 | | |
| b. In U.S. | 3,381* | 3,577* | | |
| 9. Contingencies | 1,000 | 1,264 | 2,264 | |
| GRAND TOTALS | | | <u>\$149,989</u> | <u>\$72,000</u> |

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Summary:

| | | |
|----------|---------------|-------------------------|
| AID | Contribution | \$149,989 (67.6%) |
| UPCH/GOP | Contribution | 72,000 (32.4%) |
| | Total Project | <u>\$221,989 (100%)</u> |

Notes:

1. See Approved Project Proposal for more detail on specific names and types of personnel included above, percentages of time they will provide to project, kinds of equipment to be procured, etc.
2. Starred (*) AID figures above represent U.S. Dollar costs totalling \$84,240. All other figures represent expected local cost items totalling \$65,749.
3. Details on the UPCH contribution to the project are in USAID project files.
4. Equipment and supplies to be procured in the U.S. (see Line Item 3-a) will be obtained and shipped with the assistance of Johns Hopkins University in Baltimore.

H. Reporting and Evaluation

1. Interim progress reports are required from the Principal Investigator every six months except for the last six month period, at the end of which, a final report is to be submitted. All reports will be given to the Chief of the Health and Nutrition Division, USAID/Lima, who shall be the AID Project Manager. Submission shall be in accordance with the time schedules indicated below. Five (5) copies of all Interim Progress Reports are to be provided to USAID/Peru, three for AID/Washington to the AID/SCI files, the AID Reference Center and the technical backstop officer, S&T/Health.

The objective of the Interim Progress Reports is to keep the AID Project Manager and AID/SCI informed that the research is proceeding in accordance with this Grant Agreement and to document any changes in the research plan or in key dates or benchmarks. The first Interim Report should report any revisions in key dates based on any revised research schedule and should request administrative changes which may be required in the project. All reports should place emphasis on announcing substantive scientific developments as they occur.

Interim Progress Reports should be submitted no later than 30 days following the periods ending December 31, 1987, June 30, 1988, December 31, 1988 and June 30, 1989. These and the Final Report, may be submitted in the Spanish language if accompanied by an adequate English language summary.

2. The Final Report will be prepared by the Principal Investigator, to be submitted by the Grantee to the USAID/Peru Project Manager for transmittal to AID/SCI. It must be submitted prior to December 31, 1989. Nine (9) copies shall be given to USAID, seven (7) of which shall be transmitted to AID/Washington for AID/SCI, the AID Reference Center and the technical backstop office, S&T/Health. The Final Report shall be sufficiently detailed to substantiate research findings and to permit a scientific evaluation of the research. The Principal Investigator is encouraged to share the draft report with the AID Project Manager for comment prior to final submission.

3. Quarterly financial reports, setting forth amounts of funds received, spent and liquidated in accordance with the Grant Budget and its budget categories, shall be submitted by the Grantee to the AID Project Manager in five (5) copies, three of which shall be forwarded promptly to AID/SCI.

4. Project Evaluation will be based on an analysis of the Final Report and other information deemed appropriate by the AID Project Manager. AID/SCI is prepared to assist in the analysis of the Final Report.

The Evaluation is to be completed by the AID Project Manager within 90 days after the submission by the Grantee of the Final Report and is to be forwarded promptly to AID/SCI. AID/SCI will thereafter prepare the Project Completion Report, drawing upon the Project Evaluation and all other reports submitted by the Principal Investigator and Grantee.

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I. AID/SCI Technical Backstopping

Upon request by USAID/Peru, AID/SCI will arrange for technical backstopping support on technical issues, including assessment of interim and final reports. The AID/SCI Project Monitoring System will keep track of key action dates and remind the Grantee and USAID Project Manager 30 days in advance of when these actions fall due.

J. Special Provisions

1. The following Optional Standard Provisions (AID 1420-54) apply to this Grant: Sections 1, 3, 4, 5, 6, 7, 8, 17 and 20.

2. The Grantee agrees that it will make the results of research supported under this Grant available to AID and that AID is authorized to use and disseminate this information as AID deems appropriate.

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PROGRAM DESCRIPTION

The information presented below under Sections A and B is excerpted from the Approved Project Proposal.

A. Purpose and Nature of the Research

The purpose of this project is to develop a simple and rapid assay for the diagnosis of cerebral cysticercosis in developing countries. The assay can be used for detection and treatment of patients in rural and marginal areas. This simple diagnostic test, which will define which individuals have a high probability of being infected, would permit effective treatment at the lowest possible cost.

Cysticercosis is a common disease in those countries in which pigs are consumed. In Peru the disease is estimated to effect up to 200,000 individuals. Cysticercosis is present throughout much of Latin America, Indonesia, parts of India as well as other Asian countries.

Cysticercosis in man has a very high predilection for localizing in the brain, in contrast to the pig where it is found mainly in muscle tissue. Encystment of the parasite in the brain is accompanied by symptoms similar to those seen with slow growing brain tumors. The brain sits in a non-expandable container, the skull, so that any intracerebral mass compresses the normal brain and, depending on the location, produces a variety of symptoms, among them epilepsy, personality change and cerebral hypertension. These symptoms frequently persist for years and often effect the individual's social and economic functions. Thus, cysticercosis produces damage to its individual host and acts as an economic drain. The victim of the disease not only requires medical care but also needs to be supported by the state because she/he is not competitive on the labor market.

The disease occurs in older children and adults, has a chronic, often debilitating, course, is expensive to diagnose (CAT scan) and is also expensive to treat with the current effective medication, Praziquantel. In third world countries, therapy, which is not targeted to individuals with a high probability of having the disease, is not economically feasible. At the present time, control of the disease through animal inspection in third world countries is generally not achievable due to circumvention of public health measures through either corruption or disregard.

In the last three years, an ELISA assay using crude worm homogenates has been demonstrated to have utility for the detection of neurocysticercosis. This advance is important since previous serological tests were not simple to perform and may not be as sensitive in the detection of neurocysticercosis cases.

In this study, the investigators will further enhance the utility of the ELISA assay through the use of worm secretory antigens to increase the specificity and sensitivity of the assay. In addition, they will adapt the latex - bead modification of the ELISA (CASPIA) for use in the diagnosis of Cysticercosis. This modification will allow them to maintain the sensitivity of the assay, while simplifying the performance of the test, allowing it to be run even in small rural centers. Eventually the test will be usable for seroepidemiological purposes.

B. Specific Research Objectives

a. To isolate and define antigens of Taenia solium using serum free, in vitro cultures of T. solium worms.

b. To use these antigens to prepare diagnostic reagents for the detection of cerebral cysticercosis.

c. To determine, using ELISA assay, the sensitivity and specificity of these reagents for the detection of verified cases of cerebral cysticercosis and compare them with whole worm antigens currently in use.

d. To compare a new latex bead assay, the Centrifugation - Augmented Solid Phase Immunoassay (CASPIA), with the standard ELISA method for the diagnosis of cerebral cysticercosis.

C. Project Implementation and Responsibilities

This is a two and one half year research project which will take place in Peru. It will be administered by UPCH, which will sub-contract with Johns Hopkins University (JHU) for administrative, technical, and logistic assistance. Both JHU and the University of Arizona will be involved in the training of Peruvian project personnel in the techniques of antigen separation, ELISA and CASPIA techniques.

The study will not only serve to establish and validate a new diagnostic test, but will be used as a basis for training graduate students and medical doctors in the principles of protein separation, using affinity chromatography, gel electrophoresis and immunoblotting techniques.

In addition, the sera and cerebral spinal fluid from the patients in the different groups will serve as a valuable resource bank which will not only be useful in Peru but also as a reference bank for other countries including the USA.

The Co-principal Investigators will be Dr. Robert Gilman, a JHU associate professor who is a visiting professor at UPCH, and Dra. Elba Miranda of UPCH's Division of Parasitology. Dra. Miranda will spend about 35% of her professional time on the first year of the project, 50% of the second year.

Dr. Gilman will be involved 20% of his professional time. There will be three part-time physicians in neurology, their functions described in the Approved Project Proposal, as well as a full-time biochemist, full-time ELISA technician, half-time tissue culture specialist, post graduate students and a half-time secretary. Collaborators include; Dr. Charles Sterling of the University of Arizona who will provide expertise in antigen separation, and will train Peruvian students in Tucson; and Dr. Paolo Miotto, a research fellow at the University of Milan, Italy, who will work at UPCH on development of a latex bead technique for the CASPIA disease detection procedure. A consultant in ELISA techniques, Dr. R. Yolken, will also be available on a fixed-fee basis.

UPCH shall enter into a written sub-agreement with Johns Hopkins University (JHU) relating to its participation in this project, including arrangements for administrative, technical and logistics assistance, as described in the Approved Project Proposal. The sub-agreement will be executed in accordance with Optional Standard Provision No. 7 of Attachment No. 4.

The AID Project Manager will be the Chief of the Health and Nutrition Division of USAID/Peru. She will receive and forward reports, make site visits, act in liaison between the research investigators and AID/SCI, prepare and forward the project's Evaluation Report to AID/SCI. AID/SCI will provide, upon request of the AID Project Manager, backstopping support on technical issues, if required, including the assessment of reports, and will prepare the Project Completion Report.

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