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DOCUMENT THAT IS NOT PURSUANT
TO A HANDBOOK 3 PROJECT AGREEMENT

PD-ABD-973
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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: Studies in the Transmission of Cryptosporidium, A Pathogen
Associated with both Malnutrition and Infant Mortality,
Project No. 936-5542, Proposal No. 7.234.
Grant No. 936-5542-G-00-7298-00

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\$150,000 (the "Grant") to carry out a research project entitled, "Studies in the Transmission of Cryptosporidium, A Pathogen Associated with both Malnutrition and Infant Mortality", as described in Attachment 1, the Schedule of this Grant, and Attachment 2, entitled Program Description.

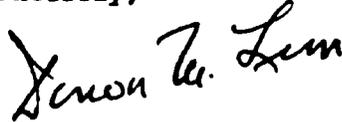
This Grant is effective, and obligation is made, as of the date of this letter and shall apply to commitments made by the Grantee in furtherance of program objectives during the period beginning with the effective date of the project and ending December 31, 1989. All reporting and financial liquidations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

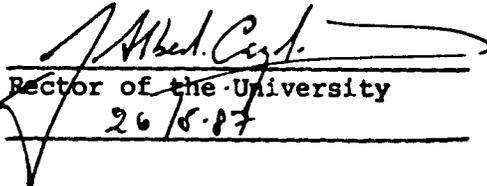
Sincerely,



Donor M. Lion,
Director

ACKNOWLEDGED:

Universidad Peruana Cayetano Heredia:

By : 
Title: Rector of the University
Date: 26/8-87

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. : 7361256
Total Estimated Amount: \$150,000
Total Obligated Amount: \$150,000
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 "Studies in Transmission of Cryptosporidium, A Pathogen Associated with both Malnutrition and Infant Mortality", will focus on determining the main ways in which this parasital disease - which attacks infants - is transmitted in a shanty town in Lima, Peru. See Attachment 2, Program Description, for a detailed description.

B. The Grantee

The recipient institution for the Grant is UPCH. The Principal Investigator for project activities is Dr. Jorge Naranjo, Department of Microbiology, Universidad Peruana Cayetano Heredia (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 1986 by Dr. Jorge Naranjo of UPCH, as revised by AID/SCI's letters of November 26, 1986 and March 2, 1987, approving the proposal, with provisos, and the responses thereto, letters to AID/SCI from Dr. Naranjo, dated January 30, 1987 and March 28, 1987.

E. Amount of Grant and Payment

1. AID hereby obligates the amount of \$150,000 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.

G. Financial Plan

The following constitutes 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.

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Grant Budget
(in U.S. Dollars)

	<u>Year 1</u>	<u>Year 2</u>	<u>Total AID</u>	<u>UPCH Contribution</u>
1. <u>Compensation (incl. Benefits)</u>			\$104,624	\$9,800
a. Principal Investigator (1)	\$ 2,214	\$ 2,214		
b. Professional Assistant (1)	1,230	1,230		
c. Field Workers (4)	11,808	8,856		
d. Parasitologist (2)	5,904	4,428		
e. Immunologist (1)	3,444	3,444		
f. Graduate Students (2)	2,400	2,400		
g. Data Entry (1)		3,444		
h. Driver (1)	2,952	2,214		
i. U.S. Consultants (3)	23,590*	22,852*		
2. Research Facilities				16,000
3. Equipment and Supplies (incl. shipping)			24,237	25,450
a. U.S. Purchase	13,057*	6,380*		
b. Local Purchase	2,400	2,400		
4. Travel			5,500	
a. International	2,000*	2,000*		
b. Local	750	750		
5. Purchase/Feeding of Animals	500	500	1,000	
6. Miscellaneous Adm. Costs.			13,139	
a. In Peru	3,435	3,263		
b. In U.S.	3,319*	3,122*		
7. Contingency	750	750	1,500	
GRAND TOTALS.	\$79,753	\$70,247	\$150,000	\$51,250

Summary

AID Contribution	\$150,000 (74.6%)
UPCH Contribution	<u>51,250</u> (25.4%)
Total Project	\$201,250 (100%)

Notes:

1. See Approved Project Proposal for more detail on specific types of personnel included above, percentages of time they will provide to the project, commodities to be ordered, etc.
2. Starred (*) AID figures above represent U.S. Dollar costs, totalling \$76,320. All other figures represent expected local cost items, totalling \$73,680.
3. Details on the UPCH contribution 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.

5

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 of which will be transmitted to AID/Washington for AID/SCI, the AID Reference Center and the technical backstop office, 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/SCI for AID/Washington distribution. 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.

6

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

A. Purpose and Nature of the Research

The research will focus on determining the main ways in which the parasitid disease, *Cryptosporidium* (hereafter denoted by CS), is transmitted in a shanty town in Lima, Peru. This information can lead to more effective preventive and treatment strategies. The study will concentrate on children below the age of two because they are the humans most commonly infected and most seriously affected. Preliminary studies in Peru have shown that when CS infected infants go through a diarrheal episode, they suffer significantly higher malnutrition and death rates than children whose diarrhea derives from other sources.

It is known, with certainty, that the sources of CS infection in children are human to human, animal to human and water-borne. It is possible that the CS infection is also food-borne, most likely in raw milk or soup. The researchers will carefully study the actual transmission facts in Lima shanty town households, and will arrive at conclusions on what the most effective intervention strategies will be for the protection and treatment of human infants.

At present, no effective therapy exists for CS in human infants or domestic animals which are also affected. It is expected that the transmission patterns for CS discovered here could be applicable to other third world countries and have considerable relevance for public health and animal husbandry programs throughout the world. This project will further develop techniques for the detection of antigens and antibodies, determine the differences in CS strains and of course, lead towards the development of a future vaccine strain and its route of delivery.

B. Specific Research Objectives

1. To examine 120 children from 0 - 2 years of age in a Lima shanty town once a week over a 16 months period to detect the presence of CS infection. Household environments of children found to be infected will be examined and compared to non-infected control households. Parents, other children, household animals, all water sources, soup, bottled or canned milk fed to the child will be evaluated in determining the relative importance of different possible sources of infection;

2. To examine diarrhea rates, decreased velocity of growth, presence of stool fat in infected children, to examine the factors causing some children to have severe diarrhea when infected with CS; and whether symptomatic children differ in regard to serum antibody response and or delayed hypersensitivity reaction at the time of infection;

3. To determine whether vaccination, using three different preparations of CS antigen derived from purified oocysts (lysed by sonification), will protect animals challenged with *Cryptosporidium*.

Preliminary studies suggest that about 25% of the 120 children in the study will become infected with CS during the 16 month period. This being the case, researchers should be able to detect differences between the "cases" and controls" at a 95% confidence level.

C. Project Implementation and Responsibilities

This is a two and one half year research project to be carried out in households and the UPCH laboratories. It does not involve any experimentation on human subjects. As indicated above, field studies will last about 16 months. Data processing, analysis and the vaccine protection studies with animals will start at the end of the second year.

The Principal Investigator is Dr. Jorge Naranjo, Professor of Microbiology at UPCH. An experienced investigator in parasitology and immunology, he will devote about 5% of his time to supervising this project, assisted by 10% of the time of his colleague in the Division of Parasitology, Dra. E. Miranda, and 100% of the time of four field workers, two parasitologists, one immunologist, two students and a driver. Assisting UPCH in the supervision of field studies will be Grace Marquis, a local nutritionist. U.S. collaborators include Dr. Charles R. Sterling, head of the Department of Veterinary Science at the University of Arizona, who will provide monoclonal reagents and expertise in protein separation techniques and improved detection methodologies. Dr. Sterling is also training Peruvian participants in this research in Tucson. Dr. Beth Unger of the National Institute of Health in Bethesda, Md. will provide advice on ELISA technology and will help with the epidemiological design and field study aspects. Dr. Robert Gilman, Associate Professor of International Health at Johns Hopkins School of Public Health and Hygiene, will coordinate field and laboratory studies, assist in experimental and epidemiological design and will train students and technicians involved in the project.

UPCH shall enter into written sub-agreement(s) with Johns Hopkins University (JHU) relating to its participation in this project, including arrangements for administrative, technical and logistic assistance as described in the approved project proposal. Such Sub-Agreement(s) will be executed in accordance with Optional Standard Provision No. 7 of Attachment No. 4.

The investigations to be carried out are complex and detailed and will not be described further herein. They are found in the Approved Project Proposal.

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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