

Agency for International Development  
Washington, D.C. 20523

598-0657  
Health & Nutrition  
Technical Services  
PDKAX536

Dr. Carlyle Guerra de Macedo  
Director, Pan American Health Organization  
525 23rd St., N.W.  
Washington, D.C. 20037

Subject: Studies on Hemorrhagic Fever Vaccine  
Project No. 598-0657,  
Grant No. LAC 0657-G-00-1054-00

Dear Dr. Guerra de Macedo:

1. I have the honor to refer to your letter request of August 30, 1991 relating to a proposal entitled, Studies on Argentine Hemorrhagic Fever Vaccine.
2. I am pleased to inform you that, pursuant to the authority contained in the Foreign Assistance Act of 1961, as amended, the Government of the United States of America, acting through the Agency for International Development (hereinafter "A.I.D.") hereby grants to the Pan American Health Organization (hereinafter "PAHO" or "Grantee"), the sum of three hundred and fifty thousand, four hundred and thirty-eight United States Dollars (U.S. \$350,438) (the "Grant") to be used for the purchase of hemorrhagic fever vaccine, shipment of same, and monitoring and evaluating the research protocols of the Government of Argentina (GOA). The project purpose is to assist the GOA in controlling the spread of Argentine Hemorrhagic Fever (AHF) through the purchase of experimental vaccine produced in the United States, and assisting the GOA with expanding research field trials of the subject vaccine.
3. A.I.D.'s total contribution to this project will not exceed three hundred fifty thousand four hundred thirty eight United States dollars (U.S. \$350,438), to be provided for activities occurring during the period September 25, 1991 through September 25, 1993. The Government of Argentina ("GOA") has already provided U.S.\$ 141,422 for an initial emergency shipment of the vaccine and proposes to contribute an additional U.S. \$108,578 for vaccine procurement during the grant period for a total contribution of U.S.\$ 250,000. The GOA will also incur additional expenses including an educational campaign, personnel time, transport, equipment and supplies. PAHO will contribute up to U.S. \$92,209.
4. It is understood that PAHO will make every effort to seek to transport vaccines from the U.S. to Argentina via U.S. Department of Defense air transport services at no cost to the project. In this event, the U.S. \$6,792 budgeted for international air freight shipment and allocated as a cost to A.I.D. will not be used.

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5. This Grant is effective and obligation is made as of the date of this letter and shall apply to expenditures made by the Grantee in furtherance of project objectives during a period starting on the date of signature of this letter and ending two years after the date of signature. Funds disbursed by A.I.D. but uncommitted by the Grantee at the expiration of this period shall be refunded to A.I.D.

6. This Grant is made to the Grantee on condition that the funds will be administered in accordance with the terms and conditions as set forth in Attachment 1 (the Schedule); Attachment 2 (the PAHO Proposal - the Project Description; and Attachment 3 (the Standard Provisions); all of which have been agreed to by your organization.

7. It is understood that financial records, including documentation to support entries on accounting records and to substantiate charges to this Grant shall be maintained in accordance with the Grantee's usual accounting procedures, which shall follow generally accepted accounting practices. All such financial records shall be maintained for at least (3) years after final disbursement of funds under this Grant.

8. It is understood that the funds granted hereunder shall be disbursed as set forth in Standard Provision 12., "Payment (Letter of Credit)".

9. The Parties agree that this Grant and the activities financed therewith shall be managed by the Grantee in accordance with its established policies and procedures. The proposed budget for this Grant is provided in paragraph D of the Schedule.

10. The Grantee shall prepare and submit to A.I.D. the required financial and technical reports in accordance with page (14) of the PAHO proposal.

11. This Agreement may be terminated in accord with Standard Provision 4., "Termination Procedures."

12. Please indicate your acceptance of this Grant by signing the original and eight (8) copies of this letter in the space provided below and returning the original and six (6) copies to the Grant Officer. Two copies may be retained for your files.

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13. The A.I.D. Technical Office responsible for monitoring this Grant is the Health, Population, and Nutrition Division, Office of Development Resources, Bureau for Latin America and the Caribbean (AID/LAC/DR/HPN), Room 2247A-NS, Washington, D.C. 20523-0010.

Agency for International Development

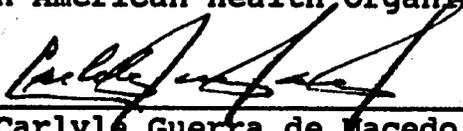
BY:   
Aaron Williams

TITLE: Acting Assistant Administrator  
Bureau for Latin America  
and the Caribbean

DATE: 9/27/91

ACCEPTED:

Pan American Health Organization

BY:   
Carlyle Guerra de Macedo

TITLE: Director

DATE: 9/27/91

Attachments:

1. Schedule
2. PAHO Proposal (program description)
3. Standard Provisions

Appropriation Nos. 72-1111021.8 and 72-1111021.7  
Allotment No. 148-65-598-00-69-11  
Obligation Nos. 1653010 and 1653412

**FISCAL DATA**

**LAC REGIONAL**

**Project: 598-0657, Health and Nutrition Technical Services  
Support (Studies on Argentina Hemorrhagic Fever  
Vaccine)**

**Total Amount: \$350,438**

**BPC: LDHA91-35598-KG12  
Obligation No: 1653010  
Appropriation: 72-1111021.8 (148-65-598-00-69-11)  
Amount: \$251,000**

**BPC: LDCA91-35598-KG12  
Obligation No: 1653412  
Appropriation: 72-1111021.7 (147-65-598-00-69-11)  
Amount: \$99,438**

**FUNDS RESERVED BY:**

Initials: ew

Date Posted: 9/26/91

PFM/PM/A/PNP

**OFFICE OF FINANCIAL MANAGEMENT**

**SCHEDULE**

**A. Purpose of Grant**

The purpose of this Grant is to assist the GOA in controlling the spread of Argentine Hemorrhagic Fever (AHF) through the purchase of experimental vaccine produced in the United States, and assisting the GOA with expanding research field trials of the subject vaccine.

**B. Period of Grant**

1. The effective date of this Grant is September 25, 1991. The estimated expiration date of this Grant is September 25, 1993.

2. Funds obligated hereunder are available for project expenditures for the period from September 25, 1991 to approximately September 25, 1993.

**C. Amount of Grant**

1. The total amount of this Grant for the period shown in B.1. above is U.S. \$350,438.

2. A.I.D. hereby obligates the amount \$350,438 for project expenditures during the period set forth in B.2. above and as shown in the Grant Budget below.

3. Payment shall be made to the Grantee in accordance with procedures set forth in Attachment 3 (the Standard Provisions).

**D. Grant Budget**

The following is the Grant Budget. Revisions to this Budget shall be made in accordance with the Standard Provision of the Grant entitled "Revision of Grant Budget."

ITEM	SOURCE OF FUNDING				AID BUDGET BY YEAR	
	AID	PAHO	GOA	TOTAL	FY 92	FY 93
<b>I. VACCINE:</b>						
A) Vaccine	\$310,246		\$108,578	\$418,824	\$310,246	
B) U.S. Transport	\$5,400			\$5,400	\$5,400	
C) Interntnl Trspt	\$6,792			\$6,792	\$6,792	
<b>II. PERSONNEL</b>						
A) Virologist		\$33,696		\$33,696		
B) Secretary		\$11,210		\$11,210		
C) Procurement Off		\$1,740		\$1,740		
<b>III. TRAVEL</b>						
A) AIR FARE						
8 round trips	\$16,000			\$16,000	\$8,000	\$8,000
B) Per Diem						
60 days	\$8,000			\$8,000	\$4,000	\$4,000
<b>IV. MISCELLANEOUS</b>	\$4,000			\$4,000	\$2,000	\$2,000
<b>V. OVERHEAD</b>		\$45,563		\$45,563		
<b>TOTAL</b>	<b>\$350,438</b>	<b>\$92,209</b>	<b>\$108,578</b>	<b>\$551,225</b>	<b>\$336,438</b>	<b>\$14,000</b>

**E. Reporting**

The PAHO Project Manager will submit to the Project Officer at AID/LAC/DR/HPN, room 2247A New State, Washington, D.C. 20523-0010, a bi-annual progress report covering implementation progress and projected activities for the next bi-annual period. The format of this report should be consistent with all LAC Bureau reports and will be provided by the AID/LAC Project Officer. A final report will be submitted to A.I.D. within ninety (90) days of the completion of this Grant.

**F. Procurement**

PAHO may apply its own procurement procedures and policies, except that no motor vehicles may be financed under this grant, unless otherwise agreed by A.I.D..



**PAN AMERICAN HEALTH ORGANIZATION**  
*Pan American Sanitary Bureau, Regional Office of the*  
**WORLD HEALTH ORGANIZATION**

525 TWENTY-THIRD STREET, N.W., WASHINGTON, D.C. 20037, U.S.A.

CABLE ADDRESS: OFSANPAN

TELEPHONE 861-3200

IN REPLY REFER TO: HPT/VIR/H6/28/2

August 30, 1991

Dear Ambassador Michel:

Thank you for your letter of August 20, 1991, informing me that the Agency for International Development (AID) has agreed in principle to provide \$311,200 for the purchase of the vaccine against Argentinean Haemorrhagic Fever. We understand that these funds can be available only in the context of a research project in which the safety, immunogenicity and efficacy of the vaccine will be investigated further.

In response to the three specific points raised in your letter, please note the following:

- a) The Pan American Health Organization (PAHO) is willing to receive a grant from AID to complement the funds provided by the Government of Argentina (GOA) in order to purchase and package the vaccine. Taking into account the figures provided by the Department of Defense (DOD) on the costs of these two items and PAHO's calculations on the cost of transportation of the vaccine, travel of personnel for monitoring the project, and miscellaneous commodities, a total estimate of \$350,483 was determined for the grant (please see attached budget). If DOD absorbs the costs of transportation of the vaccine as it did for its first shipment, then the estimation would be reduced to \$343,691.
- b) PAHO will assist the GOA to develop and review the research protocols and to monitor and evaluate the studies. In addition, PAHO will provide progress reports and a final report to AID.

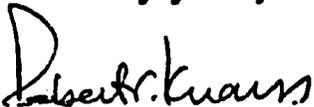
The Honorable James H. Michel  
Assistant Administrator  
for Latin America and the Caribbean  
Agency for International Development  
Washington D.C. 20523-0092

- c) PAHO will waive the overhead charges on this grant and will absorb the cost of salaries of its staff involved in the purchase of the vaccine and in all technical phases related to the research project.

Finally, we are pleased to enclose an outline of the project proposal entitled "Studies on Argentinean Haemorrhagic Fever Vaccine". We trust that the document contains all necessary information required by your Agency for the preparation of the Grant Agreement.

Looking forward to hearing from you, I remain,

Sincerely yours,

  
✓ Carlyle Guerra de Macedo  
Director

**Project Title:** Studies on Argentine Haemorrhagic Fever Vaccine

**Project Location:** Argentina (Provinces of Santa Fé, Buenos Aires and Cordoba)

**Project Duration:** Two years (US Fiscal Years 1992 and 1993).

**Implementing Entity:** PAHO and the Government of Argentina

**Contact Person:** Dr. Francisco Pinheiro (202) 861-3271  
Dr. Gabriel Schmunis (202) 861-3272

**Date of submission to AID:** 30 August 1991

**A. PROJECT PURPOSE AND DESCRIPTION**

**A.1 Problem Statement**

A live attenuated vaccine (Candid-1) has been developed against Argentine Haemorrhagic Fever (AHF). Studies involving some 6,700 human volunteers have shown that Candid-1 is safe, immunogenic and efficacious against AHF. It is essential, however, to confirm such findings in a larger number of Argentine volunteers before implementing a well planned routine vaccination program against AHF. Such program will lead to a drastic reduction in the incidence of this major public health problem in Argentina.

**A.2 Project Purpose**

The objectives of the project are to validate the immunogenicity and efficacy of Candid-1 and to observe for the occurrence of rare clinical adverse reactions in a large group of volunteers. The main beneficiaries of the study will be the rural population living and/or working in the AHF endemic area.

**A.3 General Description of Project and Reason for its Importance**

The target population (persons 15 to 65 years old) will be vaccinated and monitored for the occurrence of adverse reactions

following a standard clinical form. The immune response to the vaccine and persistence of immunity will be evaluated in selected subsets of volunteers. Vaccine efficacy will be determined taking into account historical data provided by a Phase III double blind randomized placebo controlled study conducted among Argentine volunteers during 1988-90. The reduction in annual incidence of AHF following widespread vaccination in comparison to incidence over the preceding four years (1988-1991) in a given area to be covered by immunization with Candid-1 will also serve to estimate vaccine protection. Such information will be of great significance since vaccination is the only effective intervention of practical use for the prevention of AHF. The project will be coordinated and managed by the Instituto Nacional de Estudios sobre Virosis Hemorrágicas (INEVH), Pergamino, in close collaboration with health departments of the Argentine provinces where AHF occurs, and under the supervision of the Argentine Ministry of Health.

#### A.4 End of Project Status

The data from this study will provide useful information for planning and implementation of a sustainable wide-scale immunization program against AHF. At the end of the project Argentine investigators will be well informed with respect to the safety and efficacy of the vaccine and will be in a position to make a judgement on the wider routine clinical application of the vaccine in the high risk area.

#### B. PROJECT BACKGROUND

Background: AHF is a severe viral infection that occurs predominantly in the rich farmland of north-central Argentina known as

humid pampa. In most years, 200-400 cases of AHF are seen in this region. However, periodic large epidemics occur involving up to 1,000 individuals. As a consequence, the disease has had a considerable impact on the welfare and economy of Argentina. AHF ranges from a mild flu-like illness to severe disease and death. Typically, fever to 104°F or more, headache, loss of appetite, back pain, muscle aches, dizziness, constipation or diarrhea, a skin rash and bleeding gums are seen, and last for 7-10 days. Improvement will begin in most patients during the second week, while those with more severe disease will develop extensive bleeding from the nose, mouth, intestines and/or urinary tract, or a progressive neurological disease with tremors, delirium, ataxia, convulsions and coma. In some patients, a mixture of these severe disease types and shock may occur. The mortality, in untreated cases, is 20-30%. Successful therapy has been developed for AHF through administration of plasma obtained from persons who have had AHF and recovered. Specific antibodies present in the plasma seem to be capable of neutralizing the virus causing AHF. If this immune plasma is administered in therapeutic doses within 8 days after the onset of symptoms, the mortality drops to less than 1%. Unfortunately, this approach is complicated by potential hazards associated with giving blood products, that is, viral hepatitis or other transfusion-borne diseases. Moreover, a curious late neurologic syndrome (generally benign) has been seen 2-6 weeks after plasma administration in 8-10% of patients.

Candid-1 is a live-attenuated vaccine derived from the prototype XJ strain of Junin virus developed at the United States Army Medical Research Institute of Infectious Diseases (U.S.A.M.R.I.I.D.) between

1979 and 1985 under a collaborative project of the Government of Argentina, PAHO and U.N.D.P. The vaccine virus is believed to be attenuated based upon the absence of disease in experimental animals (guinea pigs and Rhesus monkeys), and upon certain laboratory characteristics. A previous AHF vaccine, developed by Argentine scientists in the 1960s, was derived from the same lineage as the present vaccine strain. This earlier vaccine, XJ clone 3, was administered to 636 human volunteers in Argentina nearly 20 years ago but was moderately reactogenic. The current vaccine, Candid-1, has been compared to XJ clone 3 in experimental animal models, and has produced fewer adverse reactions. It is highly immunogenic as very small doses (16 PFU) were required to confer immunity against a lethal virus challenge in Rhesus monkeys.

Studies conducted in more than 6,700 human volunteers between 1985-91 have shown that Candid-1 vaccine is safe and highly immunogenic for humans.

To study the protective efficacy of this vaccine, a total of 6,500 human volunteers from 41 localities of the endemic area of AHF of the Province of Sante Fé were inoculated in a double blind, randomized, prospective trial. Inoculation was conducted over a two-year period.

First cohort:	Inoculation began:	3 October 1988
	Inoculation completed:	14 January 1989
	Total inoculated:	5,927
Second cohort:	Inoculation began:	8 November 1989
	Inoculation completed:	16 December 1989
	Total inoculated:	573
TOTAL INOCULATED:		6,500

These volunteers were followed during two epidemic seasons (1989-1990), and enrollment of cases for purposes of analysis was terminated 31 July 1990. A consensus reached with regard to a case definition of AHF (definite or probable) which included: fever or history of fever coupled with indisputable laboratory evidence of recent Jumin virus infection (positive virus isolation and/or unequivocal seroconversion), a total white cell count of less than 2,500 and platelet count of less than 100,000.

On 19 November 1990 a meeting was held at U.S.A.M.R.I.I.D. in order to break the study code. Two primary analyses were conducted to determine vaccine efficacy: one analysis ("A" in the Table below) to determine the efficacy of the vaccine in preventing AHF according to the case definition, and the other ("B" below) in preventing any febrile illness (not necessarily meeting all clinical criteria for AHF) associated with laboratory evidence of recent Jumin virus infection.

Results:

Season Inoculated	Inoculated	Total	Cases	
			AHF(A)	Febrile (B)
1988	Vaccine	2968	1	4
	Placebo	2959	20	23
1990	Vaccine	287	0	0
	Placebo	286	2	2
TOTAL	Vaccine	3255	1	4
	Placebo	3245	22	25

p=0.000028      p=0.000057

VACCINE EFFICACY

95.5%

84%

Placebo cases-vaccine cases x 100

Placebo cases

PAHO has been involved in projects related to AHF vaccine since 1979 and has given technical and administrative support to the Argentine Government and to U.S.A.M.R.I.I.D. (the US Department of Defense sponsor for the vaccine).

C. PROJECT ANALYSIS

The present project will expand upon data obtained from previous studies with an investigational vaccine against AHF. Therefore, it will provide necessary information to establish a well oriented immunization program against AHF. In turn, this program should reduce considerably the incidence of the disease, thereby bringing considerable social, health, and economic benefits to Argentina. In addition, experimental studies with non-human primates have shown that Candid-1 vaccine protects against the agent of Bolivian Hemorrhagic Fever (BHF); consequently Candid-1 should be considered for use in Bolivia for the prevention of BHF.

The INEVH has extensive experience in different aspects of AHF including immunization trials. Therefore the INEVH will play a major role in coordinating and conducting the project in conjunction with Argentine Provincial and Federal health agencies.

D. PROJECT DESCRIPTION

D.1 Research

- a) This research will be carried out in Argentina under the exclusive responsibility of Argentinean investigators. It is anticipated that the following staff of the INEVH will play the principal role in the project:

Julio Maiztegui (Director), M.D., M.P.H.  
Delia A. Enria, M.D., M.P.H.  
Ana M. Briggiler, M.D.  
María R. Feuillade, Ph.D.  
Silvana Levis, Ph.D.

- b) The research protocols will be reviewed by an existing PAHO Internal Advisory Committee on Health Research. This committee has long been established by PAHO in order to review investigation protocols to be undertaken in the American Region. In case it is needed, external consultation will be sought in order to review the present project.
- c) Protocols will be submitted for review and approval by the existing PAHO/WHO Ethical Review Committee (PAHOERC). The PAHOERC function is to provide a mechanism for the assessment of ethical implications of research projects involving human subjects. The PAHOERC follows the principles established by the: 1) Helsinki II Declaration of the World Medical Association; 2) the Standards of Conduct for Research carried out by or under the auspices of the World Health Organization;

3) the Council for International Organizations of Medical Sciences (CIOMS) general guidelines and principles, with some exceptions to reflect actual local conditions in the Hemisphere.

The PAHOERC is composed by six PAHO staff members (physicians, lawyer) and one researcher from NIH/Bethesda.

#### D.2 Implementation Plan

At the national level all activities of this project will be implemented by the Government of Argentina. Specifically this includes: a) approval of the protocols by a recognized ethical committee; b) recruitment of volunteers; c) obtaining informed consent from all vaccine recipients; d) administration of the vaccine; e) monitoring of clinical adverse reactions and health care for any volunteer suspected of suffering from a vaccine reaction; f) evaluation of vaccine immunogenicity and protection; g) analysis of data and preparation of reports.

PAHO's role will comprise both technical issues (review of protocols, monitoring and evaluation) and administrative actions (e.g. administration of USAID grant, purchase and shipment of the vaccine). The vaccine will be supplied by the Department of Defense (DOD) on a cost reimbursable basis. Due to the extensive and essential past assistance provided by DOD to the development and testing of the AHF vaccine, it is anticipated that DOD will also provide expertise in several phases of the preparation, implementation and evaluation of the project.

In due time, PAHO will procure the vaccine from DOD and will make the shipments in accordance with its administrative procedures. There will be three <sup>to four</sup> shipments of vaccine, each one consisting of 50,400 one milliliter doses of Candid-1 vaccine. In principle the shipments will be made every four months, starting in late November 1991; alternatively the last two 50,400 doses may be combined in a single shipment to be done in July/August 1992.

PAHO's staff will make site visits approximately every six months from the beginning of the project, in order to assess the project's progress.

The following activities will be performed by the GOA.

- a) Preparation of detailed protocols for the study and its approval by a recognized ethical committee.
- b) Implementation of Plan:
  - b.1 Recruitment of volunteers: up to 151,200 men and women, 15 to 65 years of age, residents and/or workers of selected rural localities of the endemic area of AHF of the Province of Buenos Aires, Córdoba and Santa Fé.
  - b.2 Informed consent: Every individual receiving the vaccine will be informed of the objectives of the investigational nature of the project, the objectives of the study, and an informed consent will be signed before the inoculation with Candid-1 vaccine.

**b.3 Entry Evaluation and Criteria:**

**b.3.1 Criteria for inclusion:**

- a) Generally healthy men and women, 15 to 65 years of age.
- b) No clinical history of AHF.
- c) No prior history of allergies to the components of Candid-1 vaccine.
- d) Rural residents and/or workers of selected areas.
- e) Sign informed consent.
- f) All women must have a negative serum pregnancy test performed within 48 hours prior to inoculation with Candid-1 vaccine or provide documentation of infertility (e.g. surgical hysterectomy).
- g) No history of chronic diseases.

**b.4 Preparation and Administration of Candid-1 Vaccine:**

The vials of Candid-1 vaccine will be transported to Argentina on dry ice, and will be stored at  $-40^{\circ}\text{C}$  or below at the INEVH. Once the vaccine has been delivered to the INEVH, that institution will be responsible for insuring its appropriate storage and handling. Then it will be transported to the field inoculation sites on dry ice, and kept at these sites at  $-20^{\circ}\text{C}$  for a period of up to 10 days. At the inoculation sites the lyophilized material will be rehydrated on the day of inoculation and kept at  $+4^{\circ}\text{C}$ . Every participant will be inoculated with a  $10^4$  PFU of Candid-1 virus, by intramuscular injection.

### D.3. Monitoring and Evaluation

The following two steps will be essential for the evaluation of infrequent adverse reactions, both of which will be undertaken by the Argentine investigators.

- a) **Clinical Evaluation:** A passive case detection system will be in place throughout the study period. Any of the participants feeling ill will be requested to go to his local (designated) clinic. Local physicians will have listings of all participants in the study. All participants requiring admission will be sent to the INEVH. All cases with a presumptive diagnosis of AHF will be treated with immune plasma.
  
- b) **Laboratory Evaluation:** In addition to all routine clinical laboratory examinations, blood samples taken during the acute period from patients admitted at INEVH will be kept at -70<sup>o</sup> C for viral isolation attempts. Acute and convalescent (30, 60 and 90 days) serum samples will be obtained in all cases, and analysed in ELISA and/or neutralization tests with Jumin virus.

The determination of vaccine protection will be done by comparing the annual incidence of AHF in selected areas after the immunization with the incidence in the same areas over the preceding four years (1988-1991).

During PAHO's visits to Argentina at approximately six months intervals, discussions will be held mainly with the staff of INEVIH in order to analyze and evaluate the clinical, laboratory and epidemiological information collected by the investigators. Other national health authorities will be also contacted and if necessary interviews will be held with local physicians attending the volunteers.

**E. FINANCIAL PLAN AND BUDGET**

The following table shows the breakdown of costs by category and by agency)

**ESTIMATED COSTS, BY AGENCY**

	Source of funds	Total cost (US\$)	USA Fiscal year	
			1992	1993
<b>VACCINE</b>				
a) 151,200 doses (\$2.77/dose)	GOA	108,578	108,578	-
Total cost \$ 418,824	AID	310,248	310,248	-
b) Packing and local transport.	AID	5,400	5,400	-
c) Air freight shipment (Three shipments, Philadelphia/B. Aires)	AID a)	6,792	6,792	-
<b>PERSONNEL</b>				
a) Virologist, 3 1/2 months	PAHO	33,896	16,848	16,848
Secretary, 3 1/2 months	PAHO	11,210	5,605	5,605
Proc. Officer, 1/2 month	PAHO	1,740	1,740	-
b) GOA Personnel	GOA b)	(b)	-	-
<b>TRAVEL</b>				
a) PAHO staff (2 trips/year)				
Air fare (2 round trips/year)	AID	8,000	4,000	4,000
Per diem (15/days/year)	AID	4,000	2,000	2,000
b) STC (2 trips/year)				
Air fare (2 round trips/year)	AID	8,000	4,000	4,000
Per diem (15 days/year)	AID	4,000	2,000	2,000
MISCELLANEOUS (expenditures)	AID	4,000	2,000	2,000
OVERHEAD (waived)	PAHO	45,563	45,563	-
<b>Total</b>	GOA b)	108,578	108,578	-
	AID	350,438	336,438	14,000
	PAHO	92,209	69,756	22,453
=====				
<b>TOTAL</b>		551,225	514,772	36,453

- a) There is a possibility that vaccine shipment will be made through USA military aircraft, at no charge to the Project.
- b) Other expenses to be incurred by the GOA such as educational campaign, materials (syringes, dry ice) gasoline, etc., are not included in this budget. Also, cost of GOA personnel is not included.

b) Method of Financing and Reporting

Payment under this Grant shall be by means of a Letter of Credit (LOC) in accordance with the terms and conditions of the LOC and any instructions issued by AID's Office of Financial Management. A Financial Status Report will be submitted quarterly no later than 30 days after the end of the period, in an original and two copies to AID and the final report will be submitted within 90 days after the conclusion of the Grant.

F. REPORTING

All reports will be prepared by Argentine investigators, if necessary with the assistance of PAHO staff and PAHO consultants. There will be bi-annual progress reports and a final report which will be submitted by PAHO to USAID.

G. CONDITIONS

The Government of Argentina has already indicated its strong commitment to undertake an immunization program with Candid-1 vaccine (see enclosure). If required by USAID a formal and specific approval from the Government of Argentina will be sought by PAHO.

PAHO will be committed to provide technical, administrative and financial resources (salary of staff, waiver of overhead costs, etc.). Similarly, the Government of Argentina will commit personnel (investigators, health workers, administrators) and funding (sharing of vaccine purchase, local costs).

**STANDARD PROVISIONS FOR  
GRANTS TO PUBLIC INTERNATIONAL ORGANIZATIONS**

- |                                  |  |
|----------------------------------|--|
| 1. Allowable Costs               | 10. Publications   |
| 2. Refunds                       | 11. Audit and Records (Select and include only the applicable version as specified in the applicability statement of the provision.) |
| 3. Revision of Grant Budget      | 12. Payment (Select and include only the applicable version as specified in the applicability statement of the provision.)           |
| 4. Termination Procedures        |  |
| 5. Disputes                      |  |
| 6. U.S. Officials Not to Benefit |  |
| 7. Nonliability                  |  |
| 8. Amendment                     |  |
| 9. Notices                       |  |

**1. ALLOWABLE COSTS (JULY 1988)**

(a) The grantee shall be reimbursed for costs incurred in carrying out the purposes of this grant which are reasonable, allocable, and allowable.

(1) Reasonable shall mean those costs that do not exceed those which would be incurred by an ordinarily prudent person in the conduct of normal business.

(2) Allocable shall mean those costs which are necessary to the grant.

(3) Allowable shall mean those costs which are reasonable and allocable, and which conform to any limitations set forth in this grant.

(b) Prior to incurring a questionable or unique cost, the grantee is encouraged to obtain the grant officer's written determination as to whether the cost will be allowable.

**2. REFUNDS (JULY 1988)**

(a) The grantee is encouraged to utilize interest bearing accounts where feasible and shall remit to A.I.D. all interest earned on funds provided by A.I.D.

(b) Funds obligated by A.I.D. but not disbursed to the grantee at the time the grant expires or is terminated shall revert to A.I.D., except for such funds encumbered by the grantee by a legally binding transaction applicable to this grant. Any funds advanced to but not expended by the grantee at the time of expiration or termination of the grant shall be refunded to A.I.D. except for such funds encumbered by the grantee by a legally binding transaction applicable to this grant.

(c) If, at any time during the life of the grant, or as a result of final audit, it is determined that A.I.D. funds provided under this grant have been expended for purposes not in accordance with the terms of this grant, the grantee shall refund such amount to A.I.D.

**3. REVISION OF GRANT BUDGET (JULY 1988)**

(a) The approved grant budget is the financial expression of the grantee's program as approved during the grant award process.

(b) The grantee shall immediately request approval from the grant officer when there is reason to believe that within the next 30 calendar days a revision of the approved grant budget will be necessary for any of the following reasons:

(1) To change the scope or the objectives of the project and/or revise the funding allocated among project objectives.

(2) Additional funding is needed.

(3) The grantee expects the amount of A.I.D. authorized funds to exceed its needs by more than \$5,000 or five percent of the A.I.D. award, whichever is greater.

(c) Except as required by other provisions of this grant specifically stated to be an exception from this provision, the Government shall not be obligated to reimburse the grantee for costs incurred in excess of the total amount obligated under the grant. The grantee shall not be obligated to continue performance under the grant (including actions under the "Termination Procedures" provision) or otherwise to incur costs in excess of the amount obligated under the grant, unless and until the grant officer has notified the grantee in writing that such obligated amount has been increased and has specified the new grant total amount.

**4. TERMINATION PROCEDURES (JULY 1988)**

This agreement may be terminated, in whole or in part, by either party at any time upon 30 days written notice of termination. Upon receipt of and in accordance with a termination notice from the grant officer, the grantee shall take immediate action to cease all expenditures financed by this grant and to cancel all unliquidated obligations if possible. Further, upon receipt of notice of termination, the grantee shall not enter into any further obligations under this grant. Except as provided below, no further reimbursement shall be made after the effective date of termination. The grantee shall within 30 days of the effective date of termination repay to the Government all unexpended A.I.D. funds which are not otherwise obligated by a legally binding transaction applicable to this grant. Should the funds paid by the Government to the grantee prior to the effective date of termination be insufficient to cover the grantee's obligations in a legally binding transaction, the grantee may submit to the Government within 90 days after the effective date of termination a written claim for such amount. The grant officer shall determine the amount(s) to be paid by the Government to the grantee under such claim in accordance with the "Allowable Costs" provision of this grant.

5. DISPUTES (JULY 1988)

(a) Any dispute under this grant shall be decided by the A.I.D. grant officer. The grant officer shall furnish the grantee a written copy of the decision.

(b) Decisions of the A.I.D. grant officer shall be final unless, within 30 days of receipt of the decision of the grant officer, the grantee appeals the decision to the Administrator of A.I.D. Any appeal made under this provision shall be in writing and addressed to the Administrator, Agency for International Development, Washington, D.C. 20523. A copy of the appeal shall be concurrently furnished to the grant officer.

(c) In connection with any appeal proceeding under this provision, the grantee shall be given an opportunity to be heard and to offer evidence in support of its appeal.

(d) A decision under this provision by the Administrator or an authorized representative shall be the final decision of A.I.D.

6. U.S OFFICIALS NOT TO BENEFIT (JULY 1988)

No member of or delegate to the U.S. Congress or resident U.S. Commissioner shall be admitted to any share or part of this grant or to any benefit that may arise therefrom.

7. NONLIABILITY (JULY 1988)

A.I.D. does not assume liability for any third party claims for damages arising out of this grant.

8. AMENDMENT (JULY 1988)

The grant may be amended upon mutual consent of the parties by formal modifications to the basic grant document or by means of an exchange of letters between the grant officer and an appropriate official of the grantee.

9. NOTICES (JULY 1988)

Any notice given by A.I.D. or the grantee shall be sufficient only if in writing and delivered in person, mailed, or cabled as follows:

To the A.I.D. grant officer, at the address specified in the grant.

To grantee, at grantee's address shown in the grant or to such other address designated within the grant.

Notices shall be effective when delivered in accordance with this provision, or on the effective date of the notice, whichever is later.

10. PUBLICATIONS (JULY 1988)

(This provision is applicable when publications are financed under the grant.)

(a) If it is the grantee's intention to identify A.I.D.'s contribution to any publication resulting from this grant, the grantee shall consult with A.I.D. on the nature of the acknowledgement prior to publication.

(b) The grantee shall provide the A.I.D. project officer with one copy of all published works developed under this grant and with lists of other written work produced under the grant.

(c) Except as otherwise provided in the terms and conditions of the grant, the author or the recipient is free to copyright any books, publications, or other copyrightable materials developed in the course of or under this grant, but A.I.D. reserves a royalty-free nonexclusive and irrevocable right to reproduce, publish, or otherwise use, and to authorize others to use the work for U.S. Government purposes.

11. AUDIT AND RECORDS (STANDARD) (JULY 1988)

(This provision is applicable when A.I.D. is not the sole contributor to the grant program.)

The grantee shall maintain books, records, documents, and other evidence in accordance with the grantee's usual accounting procedures to sufficiently substantiate charges to the grant. The Grantee confirms that this program will be subject to an independent audit in accordance with the Grantee's usual auditing procedure, and agree to furnish copies of these audit reports to A.I.D. along with such other related information as may be requested by A.I.D. with respect to questions arising from the audit report.

**12. PAYMENT (LETTER OF CREDIT) (JULY 1988)**

(This provision is applicable when a Letter of Credit is requested by the grantee and approved by A.I.D.'s Office of Financial Management.)

(a) Payment under this grant shall be by means of a Letter of Credit (LOC) in accordance with the terms and conditions of the LOC and any instructions issued by the A.I.D. Office of Financial Management, Program Accounting and Finance Division (M/FM/PAFD).

(b) As long as the LOC is in effect, the terms and conditions of the LOC and any instructions issued by M/FM/PAFD constitute the payment conditions of this grant superseding and taking precedence over any other clause of this grant concerning payment.

(c) If the LOC is revoked, payment may be made on a cost-reimbursement basis, in accordance with paragraph (e) of this clause.

(d) Revocation of the LOC is at the discretion of M/FM/PAFD after consultation with the grant officer. Notification to the recipient of revocation must be in writing and must specify the reasons for such action. The recipient may appeal any such revocation to the grant officer, in accordance with the Disputes clause of this grant. Pending final decision, payments under the contract will be in accordance with paragraph (e) of this clause

(e) If the LOC is revoked, the grantee shall submit to the A.I.D. Controller an original and 3 copies of SF 1034, "Public Voucher for Purchases and Services Other Than Personal" and SF 1034A, Continuation of SF 1034, normally once a month, but in any event no less than quarterly. Each voucher shall be identified by the grant number and shall state the total costs for which reimbursement is being requested.