



UNITED STATES AGENCY for INTERNATIONAL DEVELOPMENT

NEW DELHI, INDIA

August 31, 1987

Mr. Cyrus S. Poonawalla
President
Serum Institute of India Research Foundation
212/2 Hadapsar
Pune 411028
India

Subject: A.I.D. Grant No. 398-0282-G-00-7235-00

Dear Mr. Poonawalla:

Pursuant to the authority contained in the Foreign Assistance Act of 1961, as amended, the United States Government, represented by the Agency for International Development (hereinafter referred to as "A.I.D." or "Grantor"), hereby grants to the Serum Institute of India Research Foundation (hereinafter referred to as the "Foundation" or "Grantee") the sum of \$400,000 to provide partial assistance and support to strengthen the research and technology development capabilities of the Foundation, as more fully described in Attachment 1 of the Grant entitled "Schedule" and Attachment 2 entitled "Program Description."

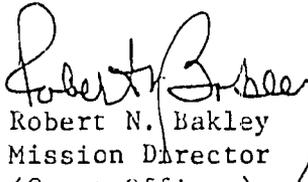
This grant is effective as of September 1, 1987 and obligation is made as of the date of this letter and shall apply to commitments made by the Grantee in furtherance of program objectives during the period beginning with the effective date and ending September 30, 1990.

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

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Please sign the original and three copies of this letter to acknowledge your acceptance of this Grant and return the original and two copies to the Grant Officer.

Sincerely yours,


Robert N. Bakley
Mission Director
(Grant Officer)

Attachments: 1. Schedule
2. Program Description
3. Standard Provisions

ACKNOWLEDGED:

THE SERUM INSTITUTE OF INDIA RESEARCH FOUNDATION

By: 
Typed Name: F.J. Dastoor
Title: Controller of Finance
Date: August 31, 1987

FISCAL DATA

Appropriation Symbol:	72-1171021
Budget Plan Code:	QDHA-87-27386-KG-12 (\$280,000) Res.#. P-70021 QDSA-87-27386-KG-12 (\$ 50,000) Rs. # P-70022
PIO/T No.:	398-0282-70001
Project No. & Title:	396-0282, Technical Collaboration
Total Estimated Grant Amount:	\$400,000
Total A.I.D. Grant Amount Obligated:	\$330,000

SCHEDULE

A. PURPOSE OF GRANT

1. The purpose of this Grant is to support the Foundation's program to improve the production and quality control testing of biologicals, in general, and measles and rabies vaccines, in particular, and to strengthen the research and technology development capabilities of the Foundation, as more fully described in Attachment 2 of this Grant entitled "Program Description."

B. PERIOD OF GRANT

1. The effective date of this Grant is September 1, 1987 and the completion date is September 30, 1990.

2. Funds obligated hereunder are available for program expenditures for the estimated period September 1, 1987 through September 30, 1989 as shown in the Grant Budget below.

C. AMOUNT OF GRANT AND PAYMENT

1. The total estimated amount of this Grant for the period shown in B.1 above is \$400,000.

2. A.I.D. hereby obligates the amount of \$330,000 for program expenditures under this Grant during the period set forth in B.2 above and as shown in the Grant Budget below.

3. Additional funds up to the total amount of the Grant shown in C.1 above may be obligated by A.I.D. subject to the availability of funds, and to the requirements of the Standard Provision of this Grant entitled "Revision of Grant Budget".

4. Payment shall be made to the Grantee in accordance with procedures set forth in Attachment 3, Standard Provision of this Grant entitled "Payment - Cost Reimbursement".

5. The Payment Office, to which the payment documentation required by the aforesaid Standard Provisions should be sent, is: Office of the Controller, U.S. Agency for International Development, American Embassy, Chanakyapuri, New Delhi - 110 021, India.

D. GRANT BUDGET

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

GRANT BUDGET
(All figures in U.S. Dollars)

<u>Cost Component</u>	<u>Obligated</u>	<u>Estimated</u>	<u>TOTAL</u>
	<u>Amount</u>	<u>Additional</u>	
	<u>From 9/01/87</u>	<u>10/01/89</u>	<u>9/01/87</u>
	<u>9/30/89</u>	<u>9/30/90</u>	<u>9/30/90</u>
Equipment	255,000	20,000	275,000
Post Doctoral Training - 2 Candidates @ \$25,000 p.a. for 2 years	50,000	50,000	100,000
Study Tours & Participation at International Conferences	5,000	-	5,000
U.S. Technical Consultations	20,000	-	20,000
Total:	<u>330,000</u>	<u>70,000</u>	<u>400,000</u>

ESTIMATED CONSOLIDATED BUDGET
(All figures in U.S. Dollars)

<u>Cost Component</u>	<u>Contribu-</u> <u>tions by the</u> <u>Foundation</u>	<u>Contribu-</u>		<u>TOTAL</u>
		<u>tions by A.I.D.</u> <u>1st</u> <u>Increment</u>	<u>2nd</u> <u>Increment</u>	
Equipment	175,000	255,000*	20,000*	450,000
Duty on Equipment	280,000	-	-	280,000
Land & Building	230,000	-	-	230,000
Salaries	30,000	-	-	30,000
Utilities	52,000	-	-	52,000
Post Doctoral Training - 2 Candidates @ \$25,000 p.a. for 2 years	-	50,000	50,000	100,000
Study Tours & Participation at International Conferences	10,000	5,000	-	15,000
U.S. Technical Consultations	-	20,000	-	20,000
Total	<u>777,000</u>	<u>330,000</u>	<u>70,000</u>	<u>1,177,000</u>

* An illustrative equipment list and estimated costs for equipment can be found at Annex 1 to Attachment 2, Program Description.

2. A.I.D. shall not be liable for reimbursing the Grantee for allowable costs in excess of the obligated amount. Except as specified in the Standard Provision of this Grant entitled "Revision of Grant Budget", as shown in Attachment 3, the Grantee may adjust line item amounts within the total Grant Amount as may be reasonably necessary for the attainment of program objectives.

3. Notwithstanding the effective date of this Grant, and subject to the Standard Provisions entitled "Allowable Costs", only those costs which are incurred on or after September 1, 1987, shall be eligible for reimbursement hereunder. Such costs are included in the grant budget shown above.

E. TITLE TO PROPERTY

Title to property acquired hereunder shall vest in the Grantee. The Standard Provision of this Grant entitled "Title To and Use of Property (Grantee Title)" applies.

F. REPORTING AND EVALUATION

REPORTING

1. Technical Reporting

The Foundation shall submit to A.I.D. semi-annually a performance report (technical report) that briefly presents the following information for each program, function, or activity involved:

- a. A comparison of actual accomplishments with the goals established for the period, the findings of the investigator, or both. If the output of programs can be readily quantified, such quantitative data should be related to cost data for computation of unit costs.
- b. Reasons why established goals were not met.
- c. Other pertinent information including, when appropriate, analysis and explanation of cost overruns or high unit costs.

2. Financial Reporting

Financial reports will be submitted by the Foundation to the USAID/India Office of Technology Development and Enterprise on a semi-annual basis. The report will identify proposal-related expenditures made by the Foundation during the reporting period, as well as cumulatively, using the categories provided in the Estimated Budget in Section D of this Attachment 1.

(1) They are limited only if acquired by the producer in the form in which they were imported; and

(2) The total cost to the producer of such components (delivered at the point of production) may not exceed 50% (unless another percentage is specified herein) of the lowest price (excluding the cost of ocean transportation and marine insurance) at which the supplier makes the commodity available for export sale (whether or not financed by A.I.D.).

(d) Any component from a country not included in A.I.D. Geographic Code 935 makes the commodity ineligible for A.I.D. financing hereunder.

5. Nationality of Supplier. Except as specified in the Standard Provisions of this Grant entitled "Air Travel and Transportation", "Ocean Shipment of Goods", and "AID Eligibility Rules for Goods and Services", in order to be eligible for A.I.D. financing hereunder, any supplier of goods or services hereunder must fit one of the following categories:

(a) A privately-owned commercial (i.e., for profit) corporation or partnership supplying services must be incorporated or legally organized under the laws of a country or area included in the authorized geographic code set forth in paragraph G.1. above; must have its principal place of business in a country or area included in the authorized Geographic Code; and must meet the criteria set forth in subparagraph (1) or (2) below:

(1) The corporation or partnership is more than 50% beneficially owned by individuals who are citizens of a country or area included in the authorized Geographic Code. In the case of corporations, "more than 50% beneficially owned" means that more than 50% of each class of stock is owned by such individuals; in the case of partnerships, "more than 50% beneficially owned" means that more than 50% of each category of partnership interest (e.g., general, limited) is owned by such individuals. With respect to stock or interest held by companies, funds, or institutions, the ultimate beneficial ownership of individuals is controlling; or

(2) The corporation or partnership:

(i) has been incorporated or legally organized in the United States for more than 3 years prior to the issuance date of this solicitation;

(ii) has performed within the United States similar administrative and technical, professional, or construction services under a contract or contracts for services, and derived revenue therefrom in each of the 3 years prior to the issuance date of this solicitation;

(iii) employs United States citizens in more than half its permanent full-time positions in the United States; and

(iv) has the existing capability in the United States to perform the contract.

(b) A nonprofit organization (e.g., educational institutions, foundations, and associations) supplying services must meet all the criteria in subparagraphs (1), (2), and (3) below. NOTE: International Agricultural Research Centers and such other international research centers as may be, from time to time, formally listed as such by the Senior Assistant Administrator of the A.I.D. Bureau of Science and Technology, are considered to be of U.S. nationality.

(1) The nonprofit organization must be organized under the laws of a country or area included in the authorized Geographic Code; and

(2) The nonprofit organization must be controlled and managed by a governing body, a majority of whose members are citizens of countries or areas included in the authorized Geographic Code; and

(3) The nonprofit organization must have its principal facilities and offices in a country or area included in the authorized Geographic Code.

(c) An individual supplying services must be a citizen of, and have his or her principal place of business in, a country or area included in the authorized geographic code; or, must be a non-U.S. citizen lawfully admitted for permanent residence in the United States and have his or her principal place of business in the United States. The foregoing nationality provision for an individual supplying services does not apply to the employees of the Grantee or contractors and subcontractors, but all Grantee, contractor and subcontractor employees engaged in providing services under this contract must be citizens of countries included in Geographic Code 935, or non-U.S. citizens lawfully admitted for permanent residence in the United States.

(d) A joint venture or unincorporated association supplying services must consist entirely of individuals, corporations, partnerships, or nonprofit organizations which are eligible under paragraphs (a), (b), or (c) above.

(e) A supplier of goods must meet any one of the criteria in subparagraphs (1), (2), (3), or (4) below.

(1) The supplier must be an individual who is a citizen or legal resident of a country or area included in the authorized Geographic Code; or

(2) The supplier must be a corporation or partnership organized under the laws of a country or area included in the authorized Geographic Code; or

(3) The supplier must be a controlled foreign corporation of which more than 50% of the total combined voting power of all classes of stock is owned by United States shareholders within the meaning of Section 957 et seq. of the Internal Revenue Code (26 USC 957); or

(4) The supplier must be a joint venture or unincorporated association consisting entirely of individuals, corporations, or partnerships which are eligible under any of the foregoing criteria.

(f) A government owned organization, i.e. a firm operated as a commercial company or other organizations (including nonprofit organizations other than public educational institutions) which are wholly or partially owned by governments or agencies thereof, are not eligible for A.I.D. financing hereunder.

(g) A local supplier of construction services, when the Cooperating Country is an authorized source for services and the estimated cost of the construction services is \$5 million or less, a corporation or partnership which is determined by A.I.D. to be an integral part of the local economy is eligible (such A.I.D. determination is contingent on first ascertaining that no U.S. construction company with the required capability is currently operating in the Cooperating Country, or, if there is such a company, that it is not interested in bidding for the proposed construction contract). A corporation or partnership is an integral part of the local economy provided:

(1) it has done business in the Cooperating Country on a continuing basis for not less than three years prior to the issuance date for the solicitation (i.e., invitation for bids, request for proposals);

(2) it has demonstrated capability to undertake the proposed activity;

(3) all, or substantially all, of its directors of local operations, senior staff, and operating personnel are resident in the Cooperating Country; and

(4) most of its operating equipment and physical plant are in the Cooperating Country.

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(n) Notwithstanding the foregoing, an A.I.D. Geographic Code 941 supplier of construction or engineering services must be approved in advance by the Grant Officer.

6. Eligibility of Commodities Determined by Ineligibility of Carrier and Marine Insurance

(a) Commodities shipped by a transportation medium owned, operated, or under the control of any country not included in A.I.D. Geographic Code 935 are ineligible for A.I.D. financing hereunder, regardless of whether such transportation costs are financed hereunder.

(b) Commodities are ineligible for A.I.D. financing hereunder if shipped on a vessel which A.I.D. has designated as ineligible, regardless of whether such transportation costs are financed hereunder.

(c) With respect to paragraph (c) of the clause of the Standard Provision of this Grant entitled "AID Eligibility Rules for Goods and Services", if the Cooperating Country discriminates against any marine insurance company authorized to do business in any state of the United States, failure to insure all AID-financed commodities with U.S. insurance companies shall render the commodities ineligible for A.I.D. financing hereunder.

(d) Commodities are ineligible for A.I.D. financing hereunder if shipped under an ocean or air charter that has not received prior approval of AID/Washington, regardless of whether such transportation costs are financed hereunder.

7. A.I.D. Geographic Codes

A.I.D. Geographic Codes are defined in Appendix D of A.I.D. Handbook 18, which, as from time to time amended, is incorporated herein as a part of this Grant by reference.

8. Approvals

In accordance with paragraph 13 of Attachment B of OMB Circular A-122, which requires prior A.I.D. approval of certain equipment and other capital expenditures, the Grant Officer does hereby provide approval for such expenditures; PROVIDED, however, that such purchases must be within the terms and conditions of this Grant, and shall serve to promote the purposes and objectives of this Grant.

H. PAYMENT REIMBURSEMENT

Standard Provision attached hereto is amended to read as follows:

USAID will reimburse the Grantee for actual expenditures incurred under the Grant on submission of U.S. Government voucher forms SF-1034 and 1034(a) duly supported by an itemized statement of expenditures in accordance with the detailed grant budget. The SF-1034 for reimbursement shall contain the following certification duly signed by an authorized official of Grantee:

a

"Certified that the invoice is just and correct and that payment thereof has not been received."

Grantee shall retain and make available to USAID or its designated representative for inspection all supporting documents for the reimbursement received from USAID for three years from the date of final payment by USAID.

I. MAILING ADDRESS

1. For Financial Reports
& Disbursement: U.S.A.I.D.
Office of the Controller
American Embassy
Chanakyapuri
New Delhi - 110 021, India

2. For Technical Reports
Other Grant related
matters: U.S.A.I.D.
Office of Technology Development
& Enterprise (TDE)
American Embassy
Chanakyapuri
New Delhi - 110 021, India

1. THE GRANTEE

- 1.1. The Serum Institute of India Research Foundation (The Foundation) was established in 1977 to conduct medical research in the fields of biologicals, pharmaceuticals and chemicals.
- 1.2. It is a non-profit organization registered under the Bombay Public Trust Act and is recognized as a Scientific Research Association by both the Indian Council of Medical Research and the Department of Science & Technology, Government of India.
- 1.3. The Foundation laboratory is located in Pune, Maharashtra, where it shares certain facilities with its associated manufacturing unit, the Serum Institute of India (Private) Limited.
- 1.4. The Foundation is registered with the Ministry of Home Affairs under Foreign Contribution (Regulation) Act, 1976.

2. GRANT PROPOSAL

- 2.1. Measles is one of the most ubiquitous of human viruses and can cause disease in any climate or environment. Since patients are most infectious during the prodromal period, quarantine measures after the emergence of clinical symptoms seem of little purpose. Prophylaxis and ultimate control, therefore, is dependent on the proper use of safe and effective vaccines.
- 2.2. Measles vaccination is part of the World Health Organization's Expanded Program of Immunization (EPI). Vaccines against diphtheria, pertussis, tetanus, poliomyelitis, and other infections can be administered simultaneously with the measles vaccine. The annual requirement of measles vaccine in India is about 20 million doses for 80 percent coverage. Presently the vaccine is not produced in the country. A dependable and standardized vaccine, produced with modern techniques, is necessary to meet the country's needs.
- 2.3. The World Health Organization Expert Committee on Rabies made the following recommendation in September, 1983. "The Committee supports the trend to limit or abandon completely--where economically and technically possible--the production of such encephalitogenic brain tissue vaccines and strongly advocates the production and use of inactivated cell culture rabies vaccines in both developed and developing countries."
- 2.4. In the last two decades, rabies vaccines have been developed with hamster kidney cells, human diploid cell lines, and similar suitable cell lines. These vaccines have proved to have acceptable potency and safety.

- 2.5. Vaccines for diphtheria, tetanus, pertussis, poliomyelitis, rabies, measles, other infectious diseases, and more modern vaccines for rabies and pertussis have been developed in other parts of the world. The Foundation therefore proposes that the technology for these vaccines be transferred to India for ultimate production. Initial efforts will be concerned with, but not necessarily limited to, the development of measles and rabies vaccines. A prerequisite to achieving this production capability for measles and rabies vaccine at the Serum Institute of India (Private) Limited would be a related research and development effort at the Foundation to adapt current technology to the conditions and facilities existing at the laboratories.
- 2.6. The proposal has two components. The majority of the effort will be spent on research and development to improve the production and quality control testing of biologicals in general and measles and rabies vaccines in particular. In addition, there will be a post-doctoral research training program in the basic sciences to strengthen the research and technology development capabilities of the Foundation.
- 2.7. Consultations with and project review by appropriate scientific experts are provided in the proposal.
- 2.8. Under the proposal, the Foundation, intends to -
 - 2.8.1. Study available virus production strains in suitable cell culture systems and standardize growth parameters.
 - 2.8.2. Evaluate and modify, where appropriate, available production methods.
 - 2.8.3. Undertake physical, chemical and antigenic characterization of vaccine production strains and evaluate their suitability for the manufacture of uniform vaccine lots.
 - 2.8.4. Develop and validate the technology and methods required for large scale production of measles and rabies vaccine.
 - 2.8.5. Study and evaluate stabilizers used in the lyophilisation of vaccine with particular reference to ease of lyophilisation, ability to resuspend/resolubilise, retention of physical characteristics and thermal lability of the vaccine.
 - 2.8.6. Produce pilot lots of measles and rabies vaccines for laboratory evaluation.

- 2.8.7. Produce pilot lots of measles and rabies vaccines in compliance with accepted good manufacturing practices for use in clinical trials.
 - 2.8.8. Develop or install laboratory control tests necessary to evaluate the vaccines.
 - 2.8.9. Develop or install laboratory control tests necessary to evaluate the antibody responses of the Indian population.
 - 2.8.10. Initiate clinical trials to demonstrate safety for measles and rabies vaccines.
 - 2.8.11. Initiate clinical trials to demonstrate potency/efficacy for measles and rabies vaccines.
- 2.9. There is and there will continue to be a need for short-term training of senior technical personnel, and this will be arranged on an individual basis. In addition to training at this level, capable scientists who have recently completed their doctoral education and who have indicated a desire to enter and remain in vaccine-related research will be recruited. In order to initiate the process of recruiting employees with recent doctoral education in the basic sciences and intensive post doctoral training in vaccine related research and development, the Foundation proposes the following:

Two post-doctoral fellowships to be awarded for study in a U.S. laboratory (or laboratories) engaged in basic research on subject-related vaccine research and development. The selection of candidates will be competitive and made on merit and with the concurrence of the participating U.S. laboratory scientist. The period of each fellowship will be two years. With the agreement of all parties and additional financial support, the fellowships could be extended on an annual basis.

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As needed, U.S. consultants can be used to advise on the resolution of issues which include but are not limited to the following:

- Laboratory problems
- Scaling up from laboratory to production facility
- Production/manufacturing problems
- Quality control problems
- Design, execution and analysis of clinical trials

3.

IMPLEMENTATION SCHEDULE

3.1. The implementation schedule is according to the following chart :

TECHNICAL PROGRAM SCHEDULE

	<u>START</u>	<u>COMPLETE</u>
1. Procure cell culture seed & virus production strains	SEP 87	JAN 88
2. Study virus production strains in suitable cell culture systems & standardise growth parameters	JAN 88	JUL 88
3. Evaluation of production method and modification of the same whenever necessary	MAY 88	OCT 88
4. Physical, chemical & antigenic characterization of vaccine production strains	JUL 88	NOV 88
5. Develop methodology for large scale production	NOV 88	APR 89
6. Studies related to lyophilization and stabilizer	FEB 89	MAY 89
7. Pilot scale production	MAY 89	SEP 89
8. Quality control tests for evaluation of vaccine	SEP 89	DEC 89
9. Clinical trials for safety of vaccine	DEC 89	FEB 90
10. Clinical trials for potency/ efficacy of vaccine	FEB 90	MAY 90
11. Evaluation of antibody responses of vaccinees	MAY 90	SEP 90

4. PROPOSAL ELEMENTS

4.1. Land and Building

A modern laboratory designed for microbiological work is being constructed for the Foundation at 212/2, Hadapsar, Pune - 411028. An area of about 10,000 square feet will be made available for the purpose of this grant proposal.

4.2. Equipment, Supplies and Machinery

The laboratory will be furnished with modern equipment necessary for microbiological work. Some of the facilities available to the Foundation include:

- water filtration, softening and demineralization plant and water distillation unit;
- limited cold storage facilities including ultra-low temperature cabinets;
- glassware washing and sterilization facility;
- supply of small laboratory animals.

An illustrative list of equipment to be financed under this Grant is found in Annex I to this Attachment 2.

4.3. Utilities

Utility services such as electricity, different grades of water, steam and compressed air will be financed by the Foundation.

4.4. Manpower

The Foundation employs a multidisciplinary team of highly qualified scientists including microbiologists, biochemists and chemical engineers. For the purpose of this grant proposal the Foundation will make available the following:

Project Manager	1
Research Officer	1
Laboratory Technicians	2
Laboratory Attendants	3

4.5. U.S. Training

The Foundation will recruit two individuals to participate in a two-year post doctoral program in the United States. The Grant will also make funds available for short-term study tours and the Foundation's participation in relevant international conferences and workshops.

4.6. U.S. Technical Consultations

This Grant will finance the travel, per diem and, when necessary, the salaries of U.S. scientists requested by the Foundation for technical consultations.

LIST OF PROPOSED IMPORTED EQUIPMENT

All Figures U.S. Dollars

Equipment	Qty.	Estimated C.I.F. Value
Roller Bottle Equipment with Roller Bottles/Cell- virus Cultivation Equipment	8	75,000
CO2 Incubators	3	16,000
High Performance Ultra Filtration (Pellicon) System	1	17,000
Microplate Reader and Related Equipment	1	25,000
Electrophoresis Equipment	1	6,000
Ultrafiltration Systems	2	17,000
Peristaltic Pumps	2	4,000
Gel Chromatography	-	10,000
Misc. Items	-	20,000
TOTAL		\$ 190,000

NOTE: The above is an illustrative list and may be altered by the Grantee according to technical requirements.

Annex 1 to Attachment 2
(Contd.)

LIST OF INDIGENOUS EQUIPMENT

All Figures U.S. Dollars

Item	Qty.	Estimated Cost in U.S. Dollars
Air Condition & Handling System	-	42,000
Laminar Air Flow Systems	6	16,000
Sterilizer	1	12,000
Deep Freezers	4	8,000
Misc. Equipment	-	7,000
TOTAL		<u>\$85,000</u>

Note: A.I.D. Funds for Imported Equipment \$ 190,000
A.I.D. Funds for Indigenous Equipment \$ 85,000
Total A.I.D. Funds for Equipment \$ 275,000