

| | | |
|--|---|---------------------------|
| AGENCY FOR INTERNATIONAL DEVELOPMENT PROJECT DATA SHEET | 1. TRANSACTION CODE PD-AAP-830 Amendment Number <input type="checkbox"/> A = Add <input type="checkbox"/> C = Change <input type="checkbox"/> D = Delete | DOCUMENT CODE 3 |
| 2. COUNTRY/ENTITY Worldwide | 3. PROJECT NUMBER 936-5928 | |
| 4. BUREAU/OFFICE S&T/H | 5. PROJECT TITLE (maximum 40 characters) Diarrheal Disease Research Program | |
| 6. PROJECT ASSISTANCE COMPLETION DATE (PACD) MM DD YY 11 23 18 18 | 7. ESTIMATED DATE OF OBLIGATION (Under "B." below, enter 1, 2, 3, or 4) A. Initial FY 84 B. Quarter 4 C. Final FY 88 | |

8. COSTS (\$000 OR EQUIVALENT \$1 =)

| A. FUNDING SOURCE | FIRST FY 84 | | | LIFE OF PROJECT | | |
|------------------------|-------------|--------|------------|-----------------|--------|---------------|
| | B. FX | C. L/C | D. Total | E. FX | F. L/C | G. Total |
| AID Appropriated Total | 975 | | 975 | 14,025 | | 14,025 |
| (Grant) | (975) | () | (975) | (14,025) | () | (14,025) |
| (Loan) | () | () | () | () | () | () |
| Other | | | | | | |
| U.S. | | | | | | |
| Host Country | | | | | | |
| Other Donor(s) | | | | | | |
| TOTALS | 975 | | 975 | 14,025 | | 14,025 |

9. SCHEDULE OF AID FUNDING (\$000)

| A. APPROPRIATION | B. PRIMARY PURPOSE CODE | C. PRIMARY TECH. CODE | | D. OBLIGATIONS TO DATE | | E. AMOUNT APPROVED THIS ACTION | | F. LIFE OF PROJECT | |
|------------------|-------------------------|-----------------------|---------|------------------------|---------|--------------------------------|---------|--------------------|---------|
| | | 1. Grant | 2. Loan | 1. Grant | 2. Loan | 1. Grant | 2. Loan | 1. Grant | 2. Loan |
| (1) U | 511 | 540 | | | | 14,025 | | 14,025 | |
| (2) | | | | | | | | | |
| (3) | | | | | | | | | |
| (4) | | | | | | | | | |
| TOTALS | | | | | | 14,025 | | 14,025 | |

| | |
|---|---------------------------|
| 10. SECONDARY TECHNICAL CODES (maximum 6 codes of 3 positions each) | 11. SECONDARY PURPOSE COD |
| 12. SPECIAL CONCERNS CODES (maximum 7 codes of 4 positions each) | |
| A. Code | |
| B. Amount | |

13. PROJECT PURPOSE (maximum 480 characters)

Develop new interventions for the control and prevention of diarrheal disease.

| | |
|--|--|
| 14. SCHEDULED EVALUATIONS | 15. SOURCE/ORIGIN OF GOODS AND SERVICES |
| Interim MM YY MM YY Final MM YY 09 8 6 03 8 9 | <input type="checkbox"/> 000 <input type="checkbox"/> 941 <input type="checkbox"/> Local <input checked="" type="checkbox"/> Other (Specify) 935 |

16. AMENDMENTS/NATURE OF CHANGE PROPOSED (This is page 1 of a _____ page PP Amendment.)

| | | |
|-----------------|---|---|
| 17. APPROVED BY | Signature | 18. DATE DOCUMENT RECEIVED IN AID/W, OR FOR AID/W DOCUMENTS, DATE OF DISTRIBUTION |
| | Title Senior Assistant Administrator for Science and Technology | Date Signed MM DD YY |

PROJECT AUTHORIZATION

Country: Worldwide

Project Title: Diarrheal
Disease Research

Project No. 936-5928

1. Pursuant to Section 104 of the Foreign Assistance Act of 1961, as amended, I hereby authorize \$14,025,000 in grant funding over the five year period FY 1984 - 1989 for the centrally-funded Diarrheal Disease Research Project. Project funding will be in annual increments and will be subject to the availability of funds, in accordance with normal A.I.D. OYB/allotment procedures.

2. The purpose of the project is to develop better ways to prevent and treat diarrheal diseases by providing support to the International Center for Diarrheal Disease Research, Bangladesh, and to the Diarrheal Disease Control Program of the World Health Organization.

3. The contract or other agreement(s) which may be negotiated and executed by the officer(s) to whom such authority is delegated in accordance with A.I.D. regulations and delegations of authority shall be subject to the following terms and conditions together with such other terms and conditions as A.I.D. may deem appropriate.

4. Source and origin of goods and services

a. Commodities financed by A.I.D. under the project shall have their source and origin in the cooperating country* or the United States, except as A.I.D. may otherwise agree in writing. Except for ocean shipping, the suppliers of commodities or services shall have the cooperating country or the United States as their place of nationality, except as A.I.D. may otherwise agree in writing.

b. Ocean shipping financed by A.I.D. under the project shall, except as A.I.D. may otherwise agree in writing, be financed only on flag vessels of the United States.

7/6/84
Date

N. C. Brady
N. C. Brady
Senior Assistant Administrator, S&T

*Each cooperating country where research, training, technical, or other assistance takes place under the project shall be deemed to be a cooperating country for the purpose of permitting local cost financing.

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Clearances:

S&T/HP, J. Sarn

S&T/PO, G. Eaton

S&T/H, G. Curlin

S&T/H, W. Oglesby

[Handwritten signatures and initials over the typed names]
60 277-1089

JUL 02 1984

**ACTION MEMORANDUM FOR THE SENIOR ASSISTANT ADMINISTRATOR
FOR SCIENCE AND TECHNOLOGY**

FROM: S&T/HP, James Sarn *Heard*
SUBJECT: Approval of a new Project, Diarrheal Disease Research
Project No. 936-5928

Problem: Your approval is required to authorize a new project, Diarrheal Disease Research, to provide grants for the International Center for Diarrheal Disease Research, Bangladesh and the Diarrheal Disease Control Program of the World Health Organization.

Discussion: The proposed new five year project will increase and redirect current A.I.D. support for research on the control of diarrheal diseases. The large number of diarrheal diseases caused by hundreds of agents constitute a continuing threat to the well-being of children throughout the world, causing an estimated 5 million deaths and one billion episodes of disease. Current global efforts can only treat the mortality associated with dehydration from acute diarrheal disease. Recent developments in biotechnology, however, offer an opportunity to prevent diarrheal diseases and treat the actual causes of disease. This would have a marked impact on the growth and development of children in the world, including the United States.

For the past twenty years A.I.D. has provided support for diarrheal disease research through core funding of the International Center for Diarrheal Disease Research, Bangladesh (ICDDR,B). ICDDR,B and its predecessor Agency, The Cholera Research Laboratory, played a major role in the development and testing of oral rehydration therapy, and is currently making important advances in vaccine development. A.I.D. core funding helped establish ICDDR,B as a major international research institution. Although this project will continue core support with a specific support grant to ICDDR,B, an opportunity now exists to direct funds to vaccine development, field trials, and areas of new technology to take advantage of ICDDR,B's unique location and facilities.

The Diarrheal Disease Control Program of the World Health Organization (WHO/CDD) has become, in recent years, a major global research program. The program merits support because of the breadth and quality of research that it supports at major research institutions in the U.S. and elsewhere. This research encompasses biomedical research and operational (health services delivery) research. WHO/CDD is currently the largest and best known integrated diarrheal disease control research and training program in the world. Three Scientific Working Groups review hundreds of proposals annually and help establish research program policy. In 1983 WHO/CDD supported 53 biomedical research projects and 19 operational research projects. Most WHO projects are funded at an annual cost of \$50,000. WHO achieves substantial savings and

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achieves remarkable results because of its multilateral status, much pro bono support from scientists around the world, and its low overhead, since it does not support personnel costs for its researchers.

To summarize, S&T/Health proposes an expanded Diarrheal Disease Research effort to provide better knowledge of diarrheal diseases and better tools for its control. Funding will support the following activities:

1) Field trials of promising new vaccines and increased emphasis on field oriented epidemiological investigation of diarrheal diseases at ICDDR,B;

2) Support for the Research component of the Diarrheal Disease Control Program of the World Health Organization;

Specifically, from the wide range of research opportunities available, S&T/Health has selected the following target areas for research that will be supported by the project.

Biomedical research :

- 1) Epidemiology of diarrheas, particularly cholera and viral diarrheas
- 2) Field tests of a vaccine for rotavirus diarrhea
- 3) Field tests of vaccines for cholera and typhoid.
- 4) Development and dissemination of inexpensive field laboratory kits for the identification of the following diarrheal disease agents which require special therapy

enterotoxigenic Escherichia coli (ETEC)
Campylobacter jejuni
Salmonella species (multiple resistant strains)
Shigella species (multiple resistant strains)
Yersinia enterocolitica
Klebsiella
Entamoeba histolytica
Giardia lamblia

- 5) Better definition of appropriate use for antibiotics in diarrheal disease
- 6) Research into improving the treatment of drinking water and the evaluation of pathogen removal during excreta treatment

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Health Services research:

- 1) Evaluation of ORT programs, including formative or process evaluation, impact and cost-effectiveness of programs at the levels of clinic, community and home
- 2) Studies of alternatives in the preparation and packaging of ORS, including the substitution of citrate for bicarbonate
- 3) investigation of environmental interventions to reduce transmission of diarrhea
- 4) Development and testing of surveillance and sentinel reporting systems
- 5) Studies of the integration of diarrheal disease control methods with other primary health care programs

In addition to the grant support proposed to the two major international institutions involved in diarrheal diseases research, the project will have a third component, support for country-based research. We anticipate that this component will support: 1) critical research into the barriers for use of these improved therapies at the country level, 2) technical assistance for LDC country programs, and 3) coordination and review of diarrheal disease research efforts in all three project components. The welcome growth of A.I.D. and other donor activities in diarrheal disease research and control throughout the world necessitates this third component. Without it, A.I.D. will be unable to respond to requests for research support that arise from, for example, diarrheal disease initiatives generated by PRITECH, ORT-HELP or projects that cannot be funded through PRICOR. The Office of Health will develop a separate PID and PP for this part of the project and will seek your approval for these activities and for amending the project authorization on that basis.

ICDDR,B and WHO/CDD require support this year and continuity of support in subsequent years. Therefore, it was the decision of the Office of Health and the Program Office to request authority for support of ICDDR,B and WHO through this action memorandum.

Recommendation: That you approve \$14.025 million for the support of ICDDR,B and WHO/CDD for five years by signing the attached project authorization.

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Attachments:

1. Tab A--Project Authorization
2. Tab B--The Research Institutions
3. Tab C--Budget

Clearance:
S&T/PO

[Handwritten signature]

Date 6-28-84

S&T/H:CKendall:5/29/84:1316u

THE RESEARCH INSTITUTIONS

ICDDR,B

The International Center for Diarrheal Disease Research, Bangladesh (ICDDR,B) has been the locus of biomedical research into the causes, therapy and preventive approaches to cholera and other diarrheal diseases since December 1960. Initially named the Pakistan SEATO Cholera Research Laboratory (PSCRL), the institution was largely a bilateral U.S. - Pakistan enterprise. Work focused on identifying the causes of diarrhea, understanding the epidemiological patterns of cholera and other diarrheas, testing vaccines for cholera, understanding the pathophysiology of diarrheas, and developing appropriate therapeutic interventions.

Clinical studies at the PSCRL and similar studies in Calcutta, which followed immediately, confirmed earlier observations that glucose would activate an alternative pathway for the absorption of sodium from the small bowel, even when the gut was affected by cholera toxin. (Subsequently it was found to be true of other diarrheal pathogens.) The absorption of water which accompanied the enhanced absorption of sodium would reverse or prevent the lethal dehydration of cholera. This sophisticated observation led to the practical intervention of oral rehydration therapy (ORT) which is the foundation of modern diarrheal disease control programs. It is an excellent example of how investment in biomedical research can pay real dividends to the poor in LDCs.

A.I.D. was associated with the PSCRL since its foundation, although through 1971 the major U.S. agency supporting the laboratory was the Public Health Service. Early in the history of the institution, A.I.D. support was limited to PL480-generated excess local currency and an initial grant. Later A.I.D. contracts were obtained to support additional activities such as demographic studies and family planning service delivery. Following the Pakistan civil war in 1971 and the emergence of Bangladesh as a nation, A.I.D. provided direct dollar support for core activities in addition to project-specific contract support. Direct A.I.D. support was programmed through an Asia Bureau project until the ICDDR,B was established in 1979. Since that date A.I.D. support has been programmed through an ST/H project, ICDDR,B, the direct predecessor of the proposed project. Now that funding has been secured from other donors to cover many of the core budget expenses an opportunity exists to direct A.I.D. funding through this new proposed project more directly toward A.I.D. goals. Although this project will continue core support with a grant to ICDDR,B, an opportunity now exists to direct funds to vaccine development, field trials, and areas of new technology to take advantage of ICDDR,B's unique location and facilities. Currently ICDDR,B reports its expenses in the format found in the attached budget. Beginning in 1985, ICDDR,B has agreed to

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change its accounting practices to show cost by project. A.I.D. will then review, annually, expended and projected expenses. A.I.D. will support those projects outlined in this memo and other such projects as may be deemed significant. In order to assist ICDDR,B in long term planning, however, A.I.D. will agree to maintain support at the current level, \$1.9 million, pending the availability of funds. Maintaining support as core budget support will also allow other A.I.D. offices, such as S&T/POP, to provide additional specific support. This funding support level will represent an increasingly smaller share, however, of ICDDR,B's total budget, as the following table shows:

ICDDR,B PROJECTED BUDGET
and A.I.D. TOTAL* CONTRIBUTION
(in 000's)

| | 1984 | 1985 | 1986 | 1987 | 1988 | TOTAL |
|---------|-------|-------|-------|-------|-------|--------|
| ICDDR,B | 5,750 | 6,500 | 7,000 | 7,500 | 8,000 | 34,750 |
| A.I.D. | 1,900 | 1,900 | 1,900 | 1,900 | 1,900 | 9,500 |

* Including support provided under previous Project #931-1012

Although total U.S. government investment to ICDDR,B through ICA, PHS and A.I.D. is difficult to calculate, it appears that the PSCRL and ICDDR,B have received approximately \$23.5 million dollars from December 1960 to September 1984.

The World Health Organization's Diarrheal Disease Control Program

The WHO Diarrheal Disease Control (CDD) Program was founded in 1978 to meet the mandate of the Thirty-first World Health Assembly in May 1978 to provide a concerted attack on diarrheal disease. The CDD program received in May 1980 the full endorsement of all WHO member states including the United States of America (Resolution WHA 3522). The program has two major components. The Health Services Delivery component provides training and technical assistance to countries to promote four strategies for diarrheal disease control:

- Treatment of cases with ORT
- Health education to promote preventive behaviors, such as breastfeeding
- Improved water and sanitation
- Epidemic surveillance

The organization of the CDD Research component is complex. There are Geneva-based central activities, and WHO Regional Bureau programs in support of national programs. The Central program is oriented toward support of biomedical research, such as vaccine development, therapeutics and pathogenesis. Scientific Working Groups of experts developed by WHO/CDD and

the regional programs have awarded 230 research grants to scientists in 64 countries. Regional activities are oriented toward health services and social science research. Eighty-one projects have been awarded support at the regional level. National programs are devoted to development of diarrheal disease control strategies and implementation of those strategies. In 1983 the program funded 53 biomedical research projects and 19 operational research projects.

The broad biomedical research areas receiving WHO support continue to be: 1) development of more stable and more effective complete oral therapy and home-made solutions and appropriate feeding regimens during diarrhea; 2) etiology and epidemiology of acute diarrhea; 3) development and evaluation of improved diagnostic tests for ETEC, rotavirus, Giardia lamblia, and Entamoeba histolytica; 4) development and testing of oral vaccines against cholera, typhoid, shigellosis, and rotavirus diarrhea; and 5) development and testing of new and existing antidiarrheal drugs and traditional medicines. The majority of health services research projects are concerned with etiology/epidemiology and case management of acute diarrhea, especially the delivery of ORT in local settings. The majority of WHO/CDD research is funded at \$50,000 or less. These economies can be realized because WHO does not fund overhead or principal investigator salaries. Dr. Nate Pierce, a distinguished diarrheal disease researcher, will head WHO/CDD's biomedical research program.

The program has also reviewed new potential control interventions and has identified several priority areas for operational research. These are:

- promotion of breast-feeding
- the relationship of measles immunization and diarrheal disease
- personal and domestic hygiene
- improved weaning practices
- food hygiene

These priorities are in substantial agreement with A.I.D. research priorities.

It is interesting to note that although U.S. university-based investigators already receive a significant portion of the biomedical research funds disbursed by WHO/CDD, the U.S. Government has only contributed a single staff salary to the program. The program is largely funded from non-WHO sources (UNICEF, UNDP, World Bank and many WHO member states). The program is budgeted for 1984 and for 1985 for \$19.6 million. Half of this money is currently pledged to WHO/CDD. The full amount is needed if the program is to deal adequately with the complex problems related to diarrheal disease prevention. Developing interventions to prevent diarrheal disease, such as vaccines and health education programs, requires a longer lead time and involves greater expense than

the development costs of case management with oral rehydration therapy, and their impact may not be felt for many years. A.I.D. funding at this point will be critical to the completion of important ongoing diarrheal disease prevention research projects. Without A.I.D. support these might have to be postponed. A.I.D. investment in this program is an efficient use of A.I.D. research funds, since over 75% of the actual contribution will support direct research costs.

WHO/CDD PROJECTED BUDGET
and A.I.D. CONTRIBUTION
(in 000's)

| | 1984 | 1985 | 1986 | 1987 | 1988 | TOTAL |
|---------|-------|--------|--------|--------|--------|--------|
| WHO/CDD | 8,000 | 11,000 | 15,000 | 20,000 | 20,000 | 74 000 |
| A.I.D. | 500 | 850 | 1,200 | 1,500 | 1,900 | 5,950 |

Proposed Budget
 Diarrheal Disease Research (1984-1988)**
 (In '000's)

| <u>Activity</u> | <u>1984</u> | <u>1985</u> | <u>1986</u> | <u>1987</u> | <u>1988</u> | <u>Total</u> |
|----------------------|-------------|-------------|--------------|--------------|--------------|--------------|
| ICDDR,B TOTAL | 475*** | 1,900 | 1,900 | 1,900 | 1,900 | 8,075 |
| <u>WHO,CDD TOTAL</u> | <u>500</u> | <u>850</u> | <u>1,200</u> | <u>1,500</u> | <u>1,900</u> | <u>5,950</u> |
| PROJECT TOTAL | 975 | 2,750 | 3,100 | 3,400 | 3,800 | 14,025 |

***Support for the global program of WHO is constrained by budgetary concerns in FY 1984. The budget rises annually to match support for ICDDR,B in FY 1988.

***Support for ICDDR,B remains \$1.9 million per year for the life of the project. FY 84 grant reduced to offset funds provided under Project No. 931-1012

ICDDR,B and WHO 1984 Annual Budget for A.I.D. Contributions
(in 000's)

ICDDR,B Specific A.I.D. supported Research Activities
(estimated 1984)

| | |
|--------------|--------------|
| Personnel | 1,650 |
| Travel | 100 |
| Rent, | |
| Utilities | 20 |
| Printing | 20 |
| Contractual | |
| Services | 60 |
| Supplies | 25 |
| Furniture | 25 |
| <u>TOTAL</u> | <u>1,890</u> |

WHO/CDD Research Program Budget (estimated 1984)

| | |
|---------------------------------------|------------|
| Advisory and Management Meetings | 10 |
| Research Funding (75% of total) | 375 |
| <u>Program management and support</u> | <u>115</u> |
| <u>TOTAL</u> | <u>500</u> |

S&T/H:CKendall;6/25/84;1316u