

FD-112-580

|  |  |  |                                |                    |
|--|--|--|--------------------------------|--------------------|
| AGENCY FOR INTERNATIONAL DEVELOPMENT<br><b>PROJECT DATA SHEET</b>    |  | 1. TRANSACTION CODE<br><input checked="" type="checkbox"/> A - Add<br><input type="checkbox"/> C - Change<br><input type="checkbox"/> D - Delete | 1A. AMENDMENT NUMBER<br>100165 | DOCUMENT CODE<br>3 |
| 2. COUNTRY/ENTITY<br>Worldwide                                       |  | 3. PROJECT NUMBER<br>931-0453.12   |                                |                    |
| 4. BUREAU/OFFICE<br>Office of Health                                 |  | 5. PROJECT TITLE (maximum 40 characters)<br>Mal Imm & Vacc Res-Biomed Res Inst (BRI)   |                                |                    |
| 6. PROJECT ASSISTANCE COMPLETION DATE (PACD)<br>MM DD YY<br>03/30/91 |  | 7. ESTIMATED DATE OF OBLIGATION<br>(Under "B" below, enter 1, 2, 3, or 4)<br>A. Initial FY 86 B. Quarter 3 C. Final FY 91                        |                                |                    |

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

| A. FUNDING SOURCE      | FIRST FY 86 |        |           | LIFE OF PROJECT |        |           |
|------------------------|-------------|--------|-----------|-----------------|--------|-----------|
|                        | B. FX       | C. L/C | D. Total  | E. FX           | F. L/C | G. Total  |
| AID Appropriated Total | 1,184       |        | 1,184     | 5,093           |        | 5,093     |
| (Grant)                | ( 1,184 )   | ( )    | ( 1,184 ) | ( 5,093 )       | ( )    | ( 5,093 ) |
| (Loan)                 | ( )         | ( )    | ( )       | ( )             | ( )    | ( )       |
| Other U.S.             | 1.          |        |           |                 |        |           |
|                        | 2.          |        |           |                 |        |           |
| Host Country           |             |        |           |                 |        |           |
| Other Donor(s)         |             |        |           |                 |        |           |
| <b>TOTALS</b>          | 1,184       |        | 1,184     | 5,093           |        | 5,093     |

**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) HE           | 540                     | 542                  |         | 4,617                  |         | 476                            |         | 5,093              |         |
| (2)              |                         |                      |         |                        |         |                                |         |                    |         |
| (3)              |                         |                      |         |                        |         |                                |         |                    |         |
| (4)              |                         |                      |         |                        |         |                                |         |                    |         |
| <b>TOTALS</b>    |                         |                      |         | 4,617                  |         | 476                            |         | 5,093              |         |

10. SECONDARY TECHNICAL CODES (maximum 6 codes of 3 positions each)

11. SECONDARY PURPOSE CODES

12. SPECIAL CONCERNS CODES (maximum 7 codes of 4 positions each)

A. Code

B. Amount

13. PROJECT PURPOSE (maximum 400 characters)

The purpose of this project is to develop malaria vaccines against the liver stages of the human malaria parasites, to complete the development of the ISI assay, and to provide infected mosquitoes for malaria vaccine clinical trials.

14. SCHEDULED EVALUATIONS

15. SOURCE/ORIGIN OF GOODS AND SERVICES

Initial MM YY Final MM YY

03/89 04/90

000  941  Local  Other (Specify)

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

This project is amended to increase the life-of-project funding from \$3,735,000 to \$5,092,047, and extend the project activity completion date to March 30, 1991.

17. APPROVED BY

Signature: *Kenneth J. Bart*

Title: Kenneth J. Bart, M.D.  
Agency Director for Health

Date Signed: MM DD YY  
06/21/89

18. DATE DOCUMENT RECEIVED IN AID/W, OR FOR AID/W DOCUMENTS, DATE OF DISTRIBUTION

MM DD YY

## FUNDED EXTENSION - SUMMARY OF PROPOSAL

OBJECTIVE 1. PRODUCTION OF HUMAN AND RODENT INFECTED MOSQUITOES.

- a): Anopheles stephensi mosquitoes infected with P. falciparum, P. berghei and P. yoelii will be produced at current levels.
- b): Production of P. vivax mosquitoes using infected human blood will be studied in collaboration with Martin, USC, or with chimps, Leiden.
- c): Effects of anti-sporozoite antibodies fed to P. falciparum or P. berghei-infected mosquitoes will be investigated with Vaughan, U.MD.

OBJECTIVE 2. IN VITRO ASSAYS CORRELATED WITH PROTECTION.

- a): ISI using HapG2-A16 cells will be used in ongoing P. falciparum/P. vivax CS vaccine trials at U.MD. and WRAIR.
- b): ISI using human hepatocytes will be established.
- c): The use of rRNA stage-specific probes will be further developed.

OBJECTIVE 3. SPOROZOITE-HEPATOCYTE INTERACTIONS.

- a): Vaccines based on the conserved KLKQP sequence will be further studied in the P. berghei mouse challenge system.
- b): Develop anti-KLKQP MAb's.
- c): Localize KLKQP sequence by immuno-electron microscopy in P. berghei and P. falciparum sporozoites and EE stages.
- d): Characterize the putative P. falciparum 16 KD sporozoite ligand that specifically recognizes human hepatocyte membranes.

OBJECTIVE 4. PRE-ERYTHROCYTIC ANTIGENS.

- a): Repeatless CS vaccine; continue epitope (Geyson) mapping with P. falciparum and P. berghei CS plates, identify reactive peptides.
- b): Absorb rabbit anti-repeatless ISI reactive sera with individual peptide sequences.
- c): Immunize mice and rabbits with individual and synthetic DNA constructed fusion proteins and test for ISI reactivity.
- d): Immunize mice with P. berghei and P. yoelii CS non-repeat peptide, measure ISI activity, and test for protection to sporozoite challenge.
- e): Elicit rabbit antisera to sporozoite non-CS antigens, test sera by IFA and ISI and screen P. falciparum libraries with relevant sera.
- f): Use rabbit anti-sporozoite sera that recognize the 42 KD component common to P. falciparum and P. berghei to screen DNA libraries.
- g): Determine whether antibodies, T-cells, or both mediate anti-P. berghei sporozoite protection elicited in mice by P. falciparum.
- h): Purify E. coli expressed P. falciparum LSA antigen, and use to immunize rabbits or mice.
- i): Consider and express LSA in Salmonella with Sadoff (WRAIR).
- j): Clone full length LSA gene.
- k): Investigate the effects of irradiation on sporozoites, particularly for the induction of heat shock proteins, or EE-specific antigens.
- l): Sequence and express C2G1, P. berghei EE/RBC merozoite antigen.
- m): Purify expressed SK47 EE/RBC antigen, make polyclonal sera.
- n): Purify B12 P. falciparum antigen, raise polyclonal sera for gene cloning.

OBJECTIVE 5. P. FALCIPARUM EE PARASITES IN HEPATOCYTES.

- a): Purify 16 KD P. falciparum antigen, raise polyclonal sera, screen P. falciparum DNA libraries.
- b): Localize relevant P. falciparum antigens by immuno-e/m.
- c): Use ISI-human hepatocyte assay in vaccine trials.

BUDGET  
May 1, 1989-March 31, 1990

| PERSONNEL  | Annual Salary | 5.1.89-9.30.89 | 10.1.89-3.31.90* |
|--|---------------|----------------|------------------|
| <b>P.I.</b>  |               |                |                  |
| M. Hollingdale Ph.D.   | 67,015        | 27,923         | 29,598           |
| <b>Investigators</b>   |               |                |                  |
| G. Chen Ph.D.  | 42,400        | 17,667         | 18,727           |
| B. Sina Ph.D.  | 39,000        | 16,250         | 17,225           |
| J. Zhu Ph.D.   | 34,240        | 14,267         | 15,123           |
| <b>Junior Investigator</b>                                       |               |                |                  |
| K. Sakhuja MS  | 27,820        | 11,592         | 12,287           |
| <b>Technicians</b>   |               |                |                  |
| A. Appiah  | 22,540        | 9,392          | 9,955            |
| V. Harrod  | 22,002        | 9,168          | 9,718            |
| D. Hayes   | 29,077        | 12,115         | 12,842           |
| To be filled   | 22,000        | 9,166          | 9,716            |
| M. Plain   | 22,002        | 9,168          | 9,718            |
| L. Graves  | 19,260        | 8,025          | 8,507            |
|  |               | <u>144,733</u> | <u>153,416</u>   |
|  |               |                | <u>298,149</u>   |
| <b>SUPPLIES</b>  |               |                |                  |
| Average for last 6 months = 14,175/month x 10 months, reduce 15% |               |                | <u>120,684</u>   |
| <b>TRAVEL</b>  |               |                |                  |
| 2 P.I. visits to U. Nijmegen                                     |               | 2,000          | 2,000            |
| 1 Trip to Case Western U.  |               | 400            |                  |
| 1 Trip to CDC  |               |                | 400              |
| 1 Trip USC   |               |                | 800              |
| 4 Attendances ASTM Ann. Mtg. L.A.                                |               |                | 5,000            |
|  |               |                | <u>10,600</u>    |
| <b>SUBCONTRACT</b>   |               |                |                  |
| U. Nijmegen, Annual Rate = 35,000 x 10 months                    |               |                | <u>29,167</u>    |
| <b>OVERHEAD</b>  |               |                |                  |
| Calculated at 118.81% personnel direct costs                     |               |                | <u>354,231</u>   |
|  |               | <u>TOTAL</u>   | <u>812,831</u>   |

\*Annual rise = 6%

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PERSONNEL COSTS PER OBJECTIVE

|              | Salary         |           | OBJECTIVE     |               |               |                |
|--------------|----------------|-----------|---------------|---------------|---------------|----------------|
|              |                |           | 1             | 2             | 3             | 4              |
| MRH          | 57,521         | X<br>Cost | 25<br>14,380  | 25<br>14,380  | 25<br>14,380  | 25<br>14,380   |
| Chen         | 36,394         | X<br>Cost |               |               | 25<br>9,098   | 25<br>27,296   |
| Sina         | 33,475         | X<br>Cost |               |               | 25<br>8,368   | 75<br>25,107   |
| Zhu          | 29,390         | X<br>Cost |               | 25<br>7,348   | 25<br>7,348   | 50<br>14,690   |
| Sakhuja      | 23,879         | X<br>Cost |               | 25<br>5,970   |               | 75<br>17,909   |
| Appiah       | 19,347         | X<br>Cost | 25<br>4,837   | 75<br>14,510  |               |                |
| Harrod       | 18,836         | X<br>Cost | 25<br>4,721   | 50<br>9,443   |               | 25<br>4,722    |
| Hayes        | 24,957         | X<br>Cost | 100<br>24,957 |               |               |                |
| Vacant       | 18,882         | X<br>Cost | 50<br>9,441   |               | 25<br>4,721   | 25<br>4,720    |
| Plein        | 18,886         | X<br>Cost | 75<br>14,164  |               |               | 25<br>4,722    |
| Graves       | 16,532         | X<br>Cost | 75<br>12,399  | 25<br>4,133   |               |                |
| <u>TOTAL</u> | <u>298,149</u> |           | <u>84,899</u> | <u>55,785</u> | <u>43,915</u> | <u>113,550</u> |

PIPELINE

Balance as of April 30, 1989 372,831

Outstanding: University of Nijmegen  
Final subcontract payment  
(Reduce 30% from 50,000) 35,000

PIPELINE 337,831

BUDGET 5.1.89 - 3.31.90 812,831

AMOUNT REQUESTED 475,000

JUSTIFICATION AND AUTHORIZATION (J & A )  
FOR OTHER THAN FULL AND  
OPEN COMPETITION

CONTRACTOR:

Biomedical Research Institute

1. AGENCY:

Agency for International Development  
Office of Procurement, A.I.D./W Health and Population  
Projects Division

2. DESCRIPTION OF APPROVAL:

Justification and Approval to procure supplies and services using Other Than Full and Open Competition based on Sole Source Availability.

3. DESCRIPTION OF SERVICES:

The Biomedical Research Institute (BRI) is a Prime Contractor for the Malaria Immunity and Vaccine Research (MIVR) Project. The BRI contract, entitled "The Exoerythrocytic Stage of Human Malaria Parasites" provides unique services to the MIVR Project as a whole, and to the international scientific community. In addition, applied research is conducted at BRI in the development of specific types of malaria vaccines that are not being studied in any other MIVR laboratory.

4. STATUTORY AUTHORITY:

a. 41 U.S.C. 253 (c) (2) as set forth in FAR Subsection 6.302-2.

b. Section 6.302-2 of the Federal Acquisition Regulations cites that this authority applies when "the property or services needed by the executive agency are available from only one responsible source and no other type of property or services will satisfy the needs of the executive agency. Section 6.302-2 further states that this authority applies where it is necessary to award the contract to a particular source in order "to establish or maintain an essential engineering, research, or development capability to be provided by an educational or other non-profit institution or a Federally-funded research and development center".

5. CONTRACTOR'S UNIQUE CAPABILITY AND URGENCY OF EXTENSION:

- a. The BRI contract was awarded June 16, 1986 for a three year period. Under the direction of Dr. Michael Hollingdale, this research contract comprised seven objectives, two of which were to provide supplies and services to the remainder of the A.I.D. Malaria Vaccine "Network" for the successful continuation of research toward a malaria vaccine. These services included (1) the production of malaria-infected mosquitoes which are crucial to studying immunity against the infectious form of the malaria parasite, and (2) the development of an assay, the "Inhibition of Sporozoite Invasion" or ISI assay, for use in clinical trials of prototype vaccines and to assist in immunologic studies in malarious regions worldwide. The success of Dr. Hollingdale's laboratory at performing these services has greatly increased opportunities for research collaboration with the international scientific community in general, thereby strengthening the MIVR Project's capability as a whole to speed the development of one or more vaccines against malaria.

The remaining contractual objectives concern certain prototype malaria vaccines for which the BRI has demonstrated a unique capability to develop and refine. These objectives include (1) studying the invasion process of the malaria parasite into the liver, (2) characterizing and cloning parasite antigens which are unique to the liver stage of its life cycle, (3) continue development of a prototype vaccine that is based on liver-stage antigens. Additional time is needed in order to complete the applied research objectives, which have a great potential for success.

The demand for BRI's services, continued applied research and research collaborations in their prototype vaccines stems not only from the A.I.D.'s concerted effort to develop a malaria vaccine, but from the international scientific community as well. The work being done at BRI bears great relevance to understanding and controlling this devastating disease worldwide.

- b. The current contract ceiling is \$4,947,201 and the contract termination date is June 15, 1989. In order to complete on going work and provide services necessary to the A.I.D. Malaria Vaccine Project, an extension to March 30, 1990 will be needed along with \$475,000 funding for this continuation of support. Obligations to date total \$4,617,047, which leaves \$330,154 remaining obligation authority. The extension will therefore necessitate an increase in the contract ceiling of \$144,846 to \$5,092,047. A detailed budget arranged by research objective and percentage time of each BRI staff member has been submitted to S&T/H to substantiate this need.

c. It would be very difficult for another contractor to assume and complete studies and implementation plans developed by the BRI. All of the activities cited are on-going and any disruption of services would cause serious delays in the vaccine development effort. Cost is also a major factor as the MIVR cannot afford the wasteful start-up costs of establishing a new contractor when successful, productive, dedicated facilities and specially trained staff are already operational at BRI. In addition, indications thus far are that a new contractor with such unique capabilities could not be found.

6. COMMERCE BUSINESS DAILY (CBD) NOTICE:

An announcement will not be published in the CBD in accordance with the exception of FAR Subsection 5.202(2) since the Agency would be seriously injured if it complied with the time period which requires publication at least 15 days before the issuance of a solicitation and a 30 days response time before receipt of proposals. As indicated in the J & A, the time constraints for the work to be accomplished and the fact that some of the work is in process makes it difficult to request additional bidders.

7. COSTS WILL BE FAIR AND REASONABLE:

The anticipated cost will be fair and reasonable based on a detailed budget analysis of supplies, equipment, and personnel costs in connection with each objective or activity. The contractor is a non-profit organization. The total estimated funding requirements are \$475,000, which entails only a \$144,846 increase to the current contract ceiling of \$5,092,047.

8. MARKET SEARCH:

The BRI has submitted an unsolicited proposal for continuation of their current activities under a cooperative agreement, the substance of which is sufficiently unique to justify due consideration and scientific review. An external scientific review of this proposal has recommended continuation of the service components of the laboratory and has judged the research objectives to be meritorious. The Malaria Immunity and Vaccine Research Project will begin solicitations for cooperative agreements for FY 90 funding. Any proposal from BRI will, at that time, be judged in full and open scientific and programmatic competition. Any such awards to be made for this or similar work will be decided by the second quarter of FY 90. Therefore, it is imperative that the current BRI contract be extended and continue to receive support until that time.

9. REQUIRING OFFICE CERTIFICATION:

I hereby certify as to the completeness and accuracy of the information above which form a basis for the foregoing justification.

\_\_\_\_\_  
Kenneth J. Bart, M.D.  
Agency Director for Health

\_\_\_\_\_  
Date

10. CONTRACTING OFFICER CERTIFICATION:

This justification is accurate and complete to the best of the Contracting Officer's knowledge and belief.

\_\_\_\_\_  
Stephen A. Dean  
Contracting Officer  
A.I.D./W Health and Population Branch  
Office of Procurement

\_\_\_\_\_  
date

11. OP DIVISION CHIEF'S CLEARANCE:

\_\_\_\_\_  
James Corley  
Acting Chief,  
A.I.D./W Projects Division  
Office of Procurement

\_\_\_\_\_  
date

12. APPROVAL BY AUTHORIZED OFFICIAL:

Based upon the authority cited in FAR Subpart 6.302-2 and the rationale and justification provided herein, I hereby approve an increase in Contract No. DPE-0453-O-C-00-3051 with the Biomedical Research Institute for an amount not to exceed \$5,092,047 for an extension of nine and half months to March 31, 1990.

\_\_\_\_\_  
Francis J. Moncada  
Acting Director  
Office of Procurement  
Agency for International Development

\_\_\_\_\_  
date

AGENCY FOR INTERNATIONAL DEVELOPMENT

WASHINGTON, D.C. 20623

JUN 1 1989

ACTION MEMORANDUM FOR THE AGENCY DIRECTOR FOR HEALTH

FROM: S&T/H, Ann Van Dusen 

SUBJECT: Increase Life of Project Funding authority and extend the Project Assistance Completion Date for Malaria Immunity and Vaccination Research Project No. 931-0453.12.

Action: Your approval is required to increase life of project funding to \$5,092,447 and extend the Project Assistance Completion Date to 3/30/91 for project 931-0453.12, Malaria Immunity and Vaccination Research, the Biomedical Research Institute (BRI), Rockville, Maryland.

Discussion: This project has been a fundamental component of the Agency's malaria vaccine program, and has conducted seminal work on the exoerythrocytic stages of malaria. This contract originally comprised seven objectives, two of which were to provide unique supplies and services for the A.I.D. Malaria Vaccine "Network" for the successful continuation of research toward a malaria vaccine. This project is of fundamental importance to the A.I.D. malaria program because it provides the only assay correlating with protection against malaria and, as well, provides malaria-infected mosquitoes for vaccine trials and other studies of the infectious stage of the parasite.

For the life of this extension, these much-needed services will be continued as will several on-going research objectives. These research objectives include (1) characterizing and cloning non-circumsporozoitic proteins of the sporozoite surface and antigens unique to the liver stage of the parasite, and (2) development of a prototype vaccine that is based on these antigens, (3) the study of biochemical synthesis of exoerythrocytic antigen that may be involved in the initial invasion of the red blood cells, (4) the interactions between the sporozoite ligand-hepatic receptors, and (5) the immunoelectron microscopic and biochemical characterization of sporozoite invasion of hepatocytes and EE development.

It would be very difficult for another contractor to assume and complete studies and services developed by the BRI. All of the activities cited are on-going and any disruption of services would cause serious delays in the vaccine development effort.

The objectives and a detailed budget arranged by objective is attached for further information.

Justification to the Congress: Project Funding is included in the FY 1989 Congressional Presentation, Annex V Centrally Funded Programs, page 120

Clearances Obtained: This project was originally approved by the A.I.D. external expert review on the basis of scientific methodology, qualifications and experience of the proposed investigator, and the institutional capability in accordance with FPR 1-4.909, FPR 1-4.910 (a) and (c), and FPR 1-4.911. An unsolicited proposal for continuation of BRI's current activities under a cooperative agreement has been reviewed by an expert review panel. Recommendations of this panel support this action memorandum to extend and provide additional funding for continuation of BRI's contractual services until the next round of proposal review and competition for FY 90 agreements.

Recommendation: That you sign the attached authorization.

Attachment:

1. Project Authorization
2. BRI summary of objectives and budget for contract extension
3. Justification and Authorization of O. F. O. C.

Clearances

|                   |                    |      |                |
|-------------------|--------------------|------|----------------|
| S&T/H: JAustin    | <u>[Signature]</u> | Date | <u>3/12/89</u> |
| CDiggs            | <u>[Signature]</u> | Date | <u>3/14/89</u> |
| GPettigrew        | <u>[Signature]</u> | Date | <u>5/31/89</u> |
| AVanDusen         | <u>[Signature]</u> | Date | <u>6/1/89</u>  |
| S&T/POP: DSheldon | <u>[Signature]</u> | Date | <u>6/1/89</u>  |
| GC/CP: STisa      | <u>[Signature]</u> | Date | <u>6-12-89</u> |

Drafter: S&T/H: EP [Signature] Person: ps:x4601:5/25/89:wang#1808s  
revised ASF 5/26/89

PROJECT AUTHORIZATION AMENDMENT NO. 1

Name of Country: Worldwide  
Project Title: Malaria Immunity and Vaccine Research  
Project Number: 931-0453.12, Biomedical Research Institute  
Rockville Md: The Exoerythrocytic stage of  
Human Malaria Parasites

1. Pursuant to Section 104 of the Foreign Assistance Act of 1961, as amended, the centrally-funded project, Malaria Immunity and Vaccine Research was authorized on May 8, 1986. That authorization is hereby amended as follow:

- a) Increase the life-of-project funding from \$3,735,000 to \$5,092,047.
- b) Extend the Project Assistance Completion Date to March 31, 1991.

2. The authorization cited above remains in effect except as modified herein.

Approved BA VanDusen

Disapproved \_\_\_\_\_  
Date June 21 1989

Clearances:

|                  |                   |      |                  |
|------------------|-------------------|------|------------------|
| S&T/H:JAustin    | <u>JH Austin</u>  | Date | <u>31 May 89</u> |
| CDiggs           | <u>CDiggs</u>     | Date | <u>3 May 89</u>  |
| GPettigrew       | <u>GPettigrew</u> | Date | <u>5/21/89</u>   |
| AVandusen        | <u>AVandusen</u>  | Date | <u>6/1/89</u>    |
| S&T/PO :DSheldon | <u>DSheldon</u>   | Date | <u>6/19/89</u>   |
| GC/CP:STisa      | <u>STisa</u>      | Date | <u>6/12/89</u>   |

Drafter: S&T/H: EPeterson ps:x4601:5/25/89:wang#1808s  
revised ASF 5/31/89